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 001-34620

IRONWOOD PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation or organization)	**04-3404176** (I.R.S. Employer Identification Number)
100 Summer Street, Suite 2300 **Boston, Massachusetts** (Address of Principal Executive Offices)	**02110** (Zip Code)

(617) 621-7722
(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
Class A Common Stock, $0.001 par value	IRWD	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 15(d) of the Exchange Act. Yes ☐ No ☒

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

Indicate by check mark whether the Registrant has submitted electronically 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 and post 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 Exchange Act). Yes ☐ No ☒

Aggregate market value of voting stock held by non-affiliates of the Registrant as of June 30, 2022: $1,555,346,291

As of January 31, 2023, there were 154,158,046 shares of Class A Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the definitive proxy statement for our 2023 Annual Meeting of Stockholders are incorporated by reference into Part III of this report.

NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, including the sections titled "Business," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations", contains forward-looking statements. All statements contained in this Annual Report on Form 10-K other than statements of historical fact are forward-looking statements. Forward-looking statements include statements regarding our future financial position, business strategy, budgets, projected costs, plans and objectives of management for future operations. The words "may," "continue," "estimate," "intend," "plan," "will," "believe," "project," "expect," "seek," "anticipate," "could," "should," "target," "goal," "potential" and similar expressions may identify forward-looking statements, but the absence of these words does not necessarily mean that a statement is not forward-looking. These forward-looking statements include, among other things, statements about:

- the demand and market potential for our products in the countries where they are approved for marketing, as well as the revenues therefrom;
- the timing, investment and associated activities involved in commercializing LINZESS® by us and AbbVie Inc. in the U.S.;
- the commercialization of CONSTELLA® in Europe and LINZESS in Japan and China, as well as our expectations regarding revenue generated from our partners;
- the timing, investment and associated activities involved in developing, obtaining regulatory approval for, launching, and commercializing our products and product candidates by us and our partners worldwide;
- our ability and the ability of our partners to secure and maintain adequate reimbursement for our products;
- our ability and the ability of our partners and third parties to manufacture and distribute sufficient amounts of linaclotide active pharmaceutical ingredient, finished drug product and finished goods, as applicable, on a commercial scale;
- our expectations regarding U.S. and foreign regulatory requirements for our products and our product candidates, including our post-approval development and regulatory requirements;
- the ability of our product candidates to meet existing or future regulatory standards;
- the safety profile and related adverse events of our products and our product candidates;
- the therapeutic benefits and effectiveness of our products and our product candidates and the potential indications and market opportunities therefor;
- our ability and the ability of our partners to obtain and maintain intellectual property protection for our products and our product candidates and the strength thereof, as well as Abbreviated New Drug Applications filed by generic drug manufacturers and potential U.S. Food and Drug Administration approval thereof, and associated patent infringement suits that we have filed or may file, or other action that we may take against such companies, and the timing and resolution thereof;
- our ability and the ability of our partners to perform our respective obligations under our collaboration, license and other agreements, and our ability to achieve milestone and other payments under such agreements;
- our plans with respect to the development, manufacture or sale of our product candidates and the associated timing thereof, including the design and results of pre-clinical and clinical studies;
- the in-licensing or acquisition of externally discovered businesses, products or technologies, or other strategic transactions, including our option to acquire an exclusive license from COUR Pharmaceutical Development Company, Inc., or COUR, to research, develop, manufacture and commercialize in the U.S.,

products containing CNP-104 for the treatment of primary biliary cholangitis, as well as partnering arrangements, including the timing of potential clinical development and regulatory milestones and expectations relating to the completion of, or the realization of the expected benefits from, such transactions;

- our expectations as to future financial performance, revenues, expense levels, payments, cash flows, profitability, tax obligations, capital raising and liquidity sources, and real estate needs, as well as the timing and drivers thereof, and internal control over financial reporting;

- our ability to repay our outstanding indebtedness when due, or redeem or repurchase all or a portion of such debt, as well as the potential benefits of the note hedge transactions and capped call transactions described herein;

- asset impairments, and the drivers thereof, and purchase commitments;

- our ability to compete with other companies that are or may be developing or selling products that are competitive with our products and product candidates;

- the status of government regulation in the life sciences industry, particularly with respect to healthcare reform;

- trends and challenges in our potential markets;

- our ability to attract, motivate and retain key personnel;

- the financial and operational impacts of the COVID-19 pandemic on our business and results of operations, including impacts on our day-to-day operations, collaborative arrangements revenue and marketing efforts, manufacturing and supply chain and clinical development of our pipeline; and

- other factors discussed elsewhere in this Annual Report on Form 10-K.

Any or all of our forward-looking statements in this Annual Report on Form 10-K may turn out to be inaccurate. These forward-looking statements may be affected by inaccurate assumptions or by known or unknown risks and uncertainties, including the risks, uncertainties and assumptions identified under the heading “Risk Factors” in this Annual Report on Form 10-K. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this Annual Report on Form 10-K may not occur as contemplated, and actual results could differ materially from those anticipated or implied by the forward-looking statements.

You should not unduly rely on these forward-looking statements, which speak only as of the date of this Annual Report on Form 10-K. Unless required by law, we undertake no obligation to publicly update or revise any forward-looking statements to reflect new information or future events or otherwise. You should, however, review the factors and risks we describe in the reports we will file from time to time with the U.S. Securities and Exchange Commission, or the SEC, after the date of this Annual Report on Form 10-K.

Summary of Risks Associated with our Business

Our business is subject to a number of risks, which are discussed more fully under the heading “Risk Factors” in this Annual Report on Form 10-K. These risks include the following:

- We are highly dependent on the commercial success of LINZESS® (linaclotide) in the United States, or the U.S., for the foreseeable future.
- Our products may cause undesirable side effects or have other properties that could limit their commercial potential.

- We are subject to uncertainty relating to pricing and reimbursement policies in the U.S. which, if not favorable for our products, could hinder or prevent our products’ commercial success.

- We must work effectively and collaboratively with AbbVie Inc. (together with its affiliates) to market and sell LINZESS in the U.S., and must adapt our commercial model and market strategy to the evolving landscape for LINZESS to achieve its maximum commercial potential.
- We face competition and new products may emerge that provide different or better alternatives for treatment of the conditions that our products are approved to treat.
- Even though LINZESS is approved by the U.S. Food and Drug Administration for use in adult patients, post-approval development and regulatory requirements still remain, which present additional challenges.
- If we are unable to execute on our strategy to in-license or acquire externally developed products or product candidates, or engage in other transactions with value creation potential, our business and prospects would be materially adversely affected.
- Our failure to successfully develop and commercialize additional product candidates or approved products would impair our ability to grow and/or adversely affect our business.
- Because we work with partners to develop, manufacture and commercialize linaclotide, we and our partners are dependent upon third parties, and our and our partners' relationships with those third parties, in our and our partners' efforts to obtain regulatory approval for, and to commercialize, linaclotide, as well as to comply with regulatory and other obligations with respect to linaclotide.
- Limitations on our ability to obtain patent protection and/or the patent rights relating to our products and our product candidates may limit our ability to prevent third parties from competing against us.
- Our indebtedness could adversely affect our financial condition or restrict our future operations.
- Public health emergencies, epidemics, or pandemics, such as the COVID-19 pandemic, impact our business.

NOTE REGARDING TRADEMARKS

LINZESS® and CONSTELLA® are trademarks of Ironwood Pharmaceuticals, Inc. Any other trademarks referred to in this Annual Report on Form 10-K are the property of their respective owners. All rights reserved.

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PART I

Item 1. *Business*

Our Company

We are a gastrointestinal, or GI, healthcare company dedicated to advancing the treatment of GI diseases and redefining the standard of care for GI patients. We are focused on the development and commercialization of innovative GI product opportunities in areas of significant unmet need, leveraging our demonstrated expertise and capabilities in GI diseases.

LINZESS® (linaclotide), our commercial product, is the first product approved by the United States Food and Drug Administration, or U.S. FDA, in a class of GI medicines called guanylate cyclase type C agonists, or GC-C agonists, and is indicated for adult men and women suffering from irritable bowel syndrome with constipation, or IBS-C, or chronic idiopathic constipation, or CIC. LINZESS is available to adult men and women suffering from IBS-C or CIC in the United States, or the U.S., and Mexico, IBS-C or chronic constipation in Japan, and IBS-C in China. Linaclotide is available under the trademarked name CONSTELLA® to adult men and women suffering from IBS-C or CIC in Canada, and to adult men and women suffering from IBS-C in certain European countries.

We have strategic partnerships with leading pharmaceutical companies to support the development and commercialization of linaclotide throughout the world, including with AbbVie Inc. (together with its affiliates), or AbbVie, in the U.S. and all countries worldwide other than China (including Hong Kong and Macau) and Japan, AstraZeneca AB (together with its affiliates), or AstraZeneca, in China (including Hong Kong and Macau) and Astellas Pharma Inc., or Astellas, in Japan. We also aim to leverage our leading development and commercialization capabilities in GI to bring additional treatment options to GI patients; for example, in November 2021, we entered into a collaboration and license option agreement, or the COUR Collaboration Agreement, with COUR Pharmaceutical Development Company, Inc., or COUR, that grants us an option to acquire an exclusive license, or the License, to research, develop, manufacture and commercialize, in the U.S., products containing CNP-104, a tolerizing immune modifying nanoparticle for the treatment of primary biliary cholangitis, or PBC.

We are also advancing IW-3300, a GC-C agonist, for the potential treatment of visceral pain conditions, such as interstitial cystitis / bladder pain syndrome, or IC/BPS, and endometriosis.

In 2022, our GI-focused strategy, building on our commercial success and GI development capabilities, continued to focus on three core priorities: maximize LINZESS, strengthen our innovative GI pipeline, and deliver sustained profits and generate cash flow.

We were incorporated in Delaware on January 5, 1998 as Microbia, Inc. On April 7, 2008, we changed our name to Ironwood Pharmaceuticals, Inc. To date, we have dedicated a majority of our activities to the research, development and commercialization of linaclotide, as well as to the research and development of our other product candidates.

Performance Against 2022 Core Priorities

1. <u>Maximize LINZESS</u>

- We recognized $398.8 million in collaborative arrangements revenue related to sales of LINZESS in the U.S. during the year ended December 31, 2022, a slight decrease compared to the year ended December 31, 2021. The slight decrease was primarily driven by net price erosion and inventory channel fluctuations, partially offset by an increase in LINZESS prescription demand.

- In September 2022, we announced positive topline data from a Phase III clinical trial evaluating linaclotide 72 mcg in pediatric patients aged 6-17 years with functional constipation, or FC. The trial met its primary and secondary endpoints, demonstrating that linaclotide 72 mcg improved frequency of spontaneous bowel movements and stool consistency. Linaclotide was generally well-tolerated, and the safety profile is consistent with previously reported studies with linaclotide in FC and irritable bowel syndrome in pediatric patients. In December 2022, we and AbbVie submitted a Supplemental New Drug Application, or sNDA,

to the U.S. FDA seeking approval of a new indication of linaclotide for FC in pediatric patients aged 6-17 years. In February 2023, the U.S. FDA granted priority review to our sNDA and assigned a Prescription Drug User Free Act, or PDUFA, date of June 14, 2023. Additional clinical pediatric programs in IBS-C and FC are ongoing. There are currently no U.S. FDA approved prescription therapies for FC.

2. Strengthen Innovative GI Pipeline

- Through the COUR Collaboration Agreement, we and COUR are developing CNP-104 for the potential treatment of PBC, a rare autoimmune disease targeting the liver that affects approximately 130,000 people in the U.S., according to a study published in Clinical Gastroenterology and Hepatology in 2018. If successful, CNP-104 has the potential to be the first approved PBC disease modifying therapy. In December 2021, the U.S. FDA granted Fast Track Designation to CNP-104. COUR is currently conducting a clinical study to evaluate the safety, tolerability, pharmacodynamic effects and efficacy of CNP-104 in PBC patients, with early data assessing T-cell response from patients enrolled in the clinical study expected in the second half of 2023. We expect that such early data will inform timing of topline data readout.

- We are advancing IW-3300, a GC-C agonist, for the potential treatment of visceral pain conditions, including interstitial cystitis/bladder pain syndrome, or IC/BPS, and endometriosis. IC/BPS affects an estimated 4 to 12 million people in the U.S., according to the Interstitial Cystitis Association as of 2022. An estimated 4 million reproductive-age women in the U.S. have been diagnosed with endometriosis, according to a study published in Gynecologic and Obstetric Investigation in 2017. Both diseases have a limited number of treatment options available. We successfully completed Phase I studies to evaluate the safety and tolerability of IW-3300 in healthy volunteers and expect to begin patient dosing for the Phase II proof of concept study in IC/BPS patients in early 2023.

3. Deliver Sustained Profits and Generate Cash Flow

- Delivered net income of $175.1 million during the year ended December 31, 2022.

- We generated $273.8 million in cash from operations during the year ended December 31, 2022, ending the year with $656.2 million in cash and cash equivalents.

Impact of the COVID-19 Pandemic on our Business

There continue to be significant uncertainties surrounding the extent and duration of the impact of the COVID-19 pandemic on our business and operations and the COVID-19 pandemic may have a material adverse impact on our business and financial condition in the future. We continue to evaluate the impact of the COVID-19 pandemic on our operating results and financial condition. The impact of COVID-19 on our business and financial condition is more fully described below in Part II, Item 7: *Management's Discussion and Analysis of Financial Condition and Results of —Trends and Uncertainties.*

GI Programs – IBS-C and CIC

IBS-C and CIC are chronic, functional GI disorders that afflict millions of sufferers worldwide. As many as 11.5 million adults suffer from IBS-C and as many as 28.5 million adults suffer from CIC in the U.S., based on Rome II criteria from the Lieberman GI Patient Landscape Survey performed in 2010, or the Lieberman Survey. Symptoms of IBS-C include abdominal pain, discomfort and/or bloating and constipation symptoms (e.g., incomplete evacuation, infrequent bowel movements, hard/lumpy stools), while CIC is primarily characterized by constipation symptoms. Greater than 65% of IBS-C patients suffer from bloating and/or discomfort at least one time per week, according to the Lieberman Survey.

Linaclotide—U.S. In August 2012, the U.S. FDA approved LINZESS as a once-daily treatment for adult men and women suffering from IBS-C (290 mcg dose) or CIC (145 mcg dose). We and AbbVie began commercializing LINZESS in the U.S. in December 2012. In January 2017, the U.S. FDA approved a 72 mcg dose of linaclotide for the treatment of adult men and women with CIC.

We and AbbVie continue to explore ways to enhance the clinical profile of linaclotide by studying linaclotide in additional indications, populations, and formulations to assess its potential to treat various conditions. In September 2020, based on Phase IIIb data demonstrating the efficacy and safety of LINZESS 290 mcg on the overall abdominal symptoms of bloating, pain and discomfort, in adult patients with IBS-C, the U.S. FDA approved our sNDA to include a more comprehensive description of the effects of LINZESS in its approved label.

In addition, we and AbbVie have established a nonclinical and clinical post-marketing plan with the U.S. FDA to understand the safety and efficacy of LINZESS in pediatric patients. In August 2021, the U.S. FDA approved a revised label for LINZESS based on clinical safety data that had been generated thus far in pediatric studies. The updated label modified the boxed warning for risk of serious dehydration and contraindication against use in children to those less than two years of age. The boxed warning and contraindication previously applied to all children less than 18 years of age and less than 6 years of age, respectively. In September 2022, we announced positive topline data from a Phase III clinical trial evaluating linaclotide 72 mcg in pediatric patients aged 6-17 years with FC. The trial met its primary and secondary endpoints, demonstrating that linaclotide 72 mcg improved frequency of spontaneous bowel movements and stool consistency. Linaclotide was generally well-tolerated, and the safety profile is consistent with previously reported studies with linaclotide in FC and irritable bowel syndrome in pediatric patients. In December 2022, we and AbbVie submitted an sNDA to the U.S. FDA seeking approval of a new indication of linaclotide for FC in pediatric patients aged 6-17 years. In February 2023, the U.S. FDA granted priority review to our sNDA and assigned a PDUFA date of June 14, 2023. There are currently no U.S. FDA approved prescription pediatric therapies for FC. The safety and effectiveness of LINZESS in patients less than 18 years of age have not been established. Additional clinical pediatric programs in IBS-C and FC are ongoing.

Linaclotide—Global. AbbVie has rights to develop and commercialize linaclotide in all countries worldwide other than China (including Hong Kong and Macau) and Japan. In November 2012, the European Commission granted marketing authorization to CONSTELLA for the symptomatic treatment of moderate to severe IBS-C in adults. CONSTELLA is the first, and to date, only drug approved in the European Union, or E.U., for IBS-C. CONSTELLA first became commercially available in certain European countries beginning in the second quarter of 2013. AbbVie is commercializing CONSTELLA in a number of European countries, including the United Kingdom, Italy and Spain.

In December 2013 and February 2014, linaclotide was approved in Canada and Mexico, respectively, as a treatment for adult men and women suffering from IBS-C or CIC. AbbVie has exclusive rights to commercialize linaclotide in Canada as CONSTELLA and in Mexico as LINZESS. In May 2014, CONSTELLA became commercially available in Canada and in June 2014, LINZESS became commercially available in Mexico.

Astellas has rights to develop, manufacture and commercialize linaclotide in Japan. In December 2016, the Japanese Ministry of Health, Labor and Welfare approved LINZESS for the treatment of adults with IBS-C in Japan. In March 2017, Astellas began commercializing LINZESS for the treatment of adults with IBS-C in Japan. In August 2018, the Japanese Ministry of Health, Labor and Welfare approved LINZESS for the treatment of adults with chronic constipation in Japan. In September 2018, Astellas began commercializing LINZESS for the treatment of adult patients with chronic constipation in Japan.

AstraZeneca has rights to develop, manufacture and commercialize linaclotide in China (including Hong Kong and Macau). In January 2019, the Chinese National Medical Products Administration approved the marketing application for LINZESS for adults with IBS-C in China. AstraZeneca began commercializing LINZESS in China in November 2019.

IW-3300

We are advancing IW-3300, a GC-C agonist, for the potential treatment of visceral pain conditions, including IC/BPS and endometriosis. IC/BPS affects an estimated 4 to 12 million Americans, according to the Interstitial Cystitis Association as of 2022. An estimated 4 million reproductive-age women in the U.S. have diagnosed endometriosis, according to a study published in Gynecologic and Obstetric Investigation in 2017. Both diseases have a limited number of treatment options available. We successfully completed Phase I studies to evaluate the safety and tolerability of IW-3300 in healthy volunteers and expect to begin patient dosing for the Phase II proof of concept study in IC/BPS in early 2023.

CNP-104

Through the COUR Collaboration Agreement, we and COUR are developing CNP-104 for the potential treatment of PBC, a rare autoimmune disease targeting the liver that affects approximately 130,000 people in the U.S., according to a study published in Clinical Gastroenterology and Hepatology in 2018. If successful, CNP-104 has the potential to be the first approved PBC disease modifying therapy. In December 2021, the U.S. FDA granted Fast Track Designation to CNP-104. COUR is currently conducting a clinical study for CNP-104 to evaluate the safety, tolerability, pharmacodynamic effects and efficacy of CNP-104 in PBC patients, with early data assessing T-cell response expected from patients enrolled in the clinical study in the second half of 2023. We expect that such early data will inform timing of topline data readout.

Collaborations and Partnerships

As part of our GI-focused strategy, we have established development and commercial capabilities that we plan to leverage as we seek to bring multiple medicines to patients. We intend to play an active role in the development and commercialization of our products in the U.S., either independently or with partners that have strong capabilities. We also intend to establish strong global brands by out-licensing development and commercialization rights to our products in other key territories to high-performing partners. We plan to seek collaborations that increase the value of our products by providing meaningful economics and incentives for us and any potential partner. We intend to continue to expand our expertise in GI by accessing innovative externally developed products and to leverage our existing capabilities to develop and commercialize these products in the U.S.

We have pursued a partnering strategy for commercializing linaclotide that has allowed us to focus our commercialization efforts in the U.S. and enabled partners with strong global capabilities to commercialize linaclotide in territories outside of the U.S.

The following chart shows our revenue for the U.S. and the rest of the world as a percentage of our total revenue for each of the years ended December 31, 2022, 2021, and 2020.

	Year Ended December 31,		
	2022	2021	2020
U.S.	98.1 %	97.8 %	95.8 %
Rest of world	1.9 %	2.2 %	4.2 %
	100.0 %	100.0 %	100.0 %

Revenue attributable to our linaclotide partnerships comprised substantially all of our revenue for each of the years indicated. Further, we currently derive a significant portion of our revenue from our LINZESS collaboration with AbbVie for the U.S. and believe that the revenues from this collaboration will continue to constitute a significant portion of our total revenue for the foreseeable future. Our revenue from our LINZESS collaboration with AbbVie for the U.S. is highly dependent on the responsiveness of patients to fill prescriptions and other factors such as retail chains' and wholesalers' buying patterns and inventory levels. Our collaborative arrangements revenue may continue to fluctuate as a result of the timing and amount of royalties from sales of linaclotide in the markets in which it is currently approved, or any other markets where linaclotide receives approval, as well as clinical and commercial milestones received and recognized under our strategic partnerships outside of the U.S.

Collaboration Agreement for North America with AbbVie

In September 2007, we entered into a collaboration agreement with AbbVie to develop and commercialize linaclotide for the treatment of IBS-C, CIC and other GI conditions in North America. Under the terms of the collaboration agreement, we and AbbVie are jointly and equally funding the development and commercialization of LINZESS in the U.S., with equal share of any profits or losses. Additionally, we granted AbbVie exclusive rights to develop and commercialize linaclotide in Canada and Mexico for which we receive royalties in the mid-teens percent on net sales in those countries. AbbVie is solely responsible for the further development, regulatory approval and commercialization of linaclotide in those countries and funding any costs.

License Agreement with AbbVie (All countries other than the countries and territories of North America, China (including Hong Kong and Macau), and Japan)

In April 2009, we entered into a license agreement with Almirall, S.A., or Almirall, or the European License Agreement, to develop and commercialize linaclotide in Europe (including the Commonwealth of Independent States and Turkey) for the treatment of IBS-C, CIC and other GI conditions. In October 2015, Almirall transferred its exclusive license to develop and commercialize linaclotide in Europe to AbbVie. In January 2017, we and AbbVie entered into an amendment to the European License Agreement. The European License Agreement, as amended, extended the license to develop and commercialize linaclotide in all countries other than China (including Hong Kong and Macau), Japan, and the countries and territories of North America. We refer to the additional licensed countries as the Expanded Territory. Under the European License agreement, AbbVie is obligated to pay us (i) certain commercial milestones totaling up to $42.5 million, (ii) royalties based on sales volume in Europe, beginning in the mid-single digits percent and escalating to the upper-teens percent, and (iii) on a country-by-country and product-by-product basis in the Expanded Territory, a royalty as a percentage of net sales of products containing linaclotide as an active ingredient in the upper-single digits for five years following the first commercial sale of a linaclotide product in a country, and in the low-double digits thereafter. The royalty rate for products in the Expanded Territory will decrease, on a country-by-country basis, to the lower-single digits, or cease entirely, following the occurrence of certain events.

License Agreement for Japan with Astellas

In November 2009, we entered into a license agreement with Astellas to develop and commercialize linaclotide for the treatment of IBS-C, CIC and other GI conditions in Japan. Pursuant to this license agreement, as amended, we were responsible for the supply of linaclotide active pharmaceutical ingredient, or API, to Astellas. On August 1, 2019, we and Astellas amended and restated the license agreement. Under the terms of the amended and restated license agreement, we are no longer responsible for the supply of linaclotide API to Astellas and Astellas is responsible for its own supply of linaclotide API in Japan. Astellas is obligated to pay royalties to us at rates beginning in the mid-single-digits percent and escalating to low-double-digits percent, based on aggregate annual net sales in Japan of products containing linaclotide API.

Collaboration Agreement for China (including Hong Kong and Macau), with AstraZeneca

In October 2012, we entered into a collaboration agreement with AstraZeneca to co-develop and co-commercialize linaclotide in China (including Hong Kong and Macau). In September 2019, we and AstraZeneca amended and restated the collaboration agreement, under which AstraZeneca obtained the exclusive right to develop, manufacture and commercialize products containing linaclotide in the territory. Under the terms of the amended and restated agreement, we transferred all manufacturing responsibilities in China (including Hong Kong and Macau) to AstraZeneca, and we are entitled to receive non-contingent payments totaling $35.0 million in three installments through 2024, of which $25.0 million remained outstanding at December 31, 2022. In addition, AstraZeneca may be required to make milestone payments totaling up to $90.0 million contingent on the achievement of certain sales targets and is required to pay tiered royalties to us at rates beginning in the mid-single-digits percent and increasing up to twenty percent based on the aggregate annual net sales of products containing linaclotide in the territory.

Collaboration and License Option Agreement with COUR

In November 2021, we entered into the COUR Collaboration Agreement with COUR, pursuant to which we have been granted an option to acquire an exclusive license to research, develop, manufacture and commercialize, in the U.S., products containing CNP-104 for the treatment of PBC. In December 2021, the U.S. FDA granted Fast Track Designation to CNP-104. COUR has initiated a clinical study to evaluate the safety, tolerability, and pharmacodynamic effects and efficacy of CNP-104 in PBC patients, with early data assessing T-cell response from patients enrolled in the clinical study expected in the second half of 2023. We expect that such early data will inform timing of topline data readout.

Pursuant to the terms of the COUR Collaboration Agreement, we made an upfront, non-refundable payment of $6.0 million to COUR during the year ended December 31, 2021 and agreed to pay a non-contingent payment and milestone payments to COUR totaling $13.5 million in connection with certain development activities and regulatory milestones. After reviewing the data from the clinical study for CNP-104, if we exercise the option, we will pay COUR $35.0 million in exchange for the exclusive license. Upon commercialization, we will pay royalties to COUR in the

high-single digits to low-double digits percentage of the aggregated annual net sales in the U.S. of products containing CNP-104, and COUR will be eligible to receive commercial milestone payments of up to $440.0 million over the term of the agreement.

Our Strategy

Our vision is to become the leading U.S. GI-focused healthcare company. To achieve this vision, we assembled a team with demonstrated success in creating, acquiring and partnering, developing, and commercializing medicines that can make a difference in patients' lives. We are dedicated to leveraging our development and commercial expertise to advance the treatment of GI diseases and redefine the standard of care for patients suffering from GI diseases. Our strategy is focused on three core priorities: maximize LINZESS, strengthen and progress our innovative GI portfolio, and deliver sustained profits and generate cash flow. Key elements of our strategy include:

Maximize LINZESS

- Leveraging our U.S.-focused commercial capabilities in marketing, reimbursement, patient engagement, and sales to expand the commercial potential of LINZESS.
- Exploring development opportunities to enhance the clinical profile of LINZESS by studying linaclotide in additional indications, populations, and formulations.
- Collaborating with global partners who share our vision, values, culture, and processes to develop and commercialize linaclotide outside of the U.S.

Strengthen and progress our innovative GI portfolio

- Evaluating innovative, externally developed clinical and commercial products for in-licensing, or acquisition opportunities. We are prioritizing assets that address serious GI diseases in areas primarily managed by gastroenterologists/hepatologists and provide scientific innovation. In addition, we are pursuing assets that we believe have a sound mechanistic rationale, a strong clinical safety profile, and a clear development path towards potential regulatory approval and commercialization.
- Progressing our current pipeline, including LINZESS in a pediatric population, CNP-104 for the potential treatment of PBC, and progressing our wholly owned GC-C agonist, IW-3300, for the potential treatment of IC/BPS and endometriosis.

Deliver sustained profits and cash flow

- Executing our strategy with our stockholders' long-term interests in mind by delivering sustainable profits and cash flows.
- Applying a thoughtful and disciplined capital allocation strategy to deliver value for our shareholders over the long-term.

Competition

Linaclotide competes globally with certain branded and generic prescription therapies and over the counter, or OTC, products for the treatment of IBS-C and CIC, or their associated symptoms.

OTC laxatives make up the majority of the treatments in the U.S. for IBS-C and CIC, according to our internal research. LINZESS is the number one prescribed branded treatment in the U.S. for adults with IBS-C and CIC, according to 2021 data from IQVIA Inc. National Prescription Audit.

Until the launch of LINZESS, the only available branded prescription therapy for IBS-C and CIC in the U.S. was AMITIZA® (lubiprostone), which was approved for the treatment of CIC in 2006, for the treatment of IBS-C in 2008, and for the treatment of opioid induced constipation in 2013. AMITIZA is being commercialized in the U.S. by Takeda Pharmaceuticals Limited. AMITIZA also is being commercialized for the treatment of adults with CIC in certain European countries, including the United Kingdom and Switzerland by Sucampo AG, and for the treatment of chronic constipation in Japan by Mylan N.V. Authorized generic versions of AMITIZA became available in the U.S. by Endo International plc and Dash Pharmaceuticals LLC in January 2021 and in October 2022, respectively, and we expect additional generic versions of AMITIZA may become available. TRULANCE® (plecanatide) was approved in the U.S. for the treatment of CIC in adults in January 2017 and for the treatment of IBS-C in adults in January 2018 and is being commercialized in the U.S. by Bausch Health Companies. Shire plc obtained approval of MOTEGRITY™

(prucalopride) in the U.S. for the treatment of CIC in adults in December 2018. In April 2022, Ardelyx, Inc., or Ardelyx, launched IBSRELA™ (tenapanor), a U.S. FDA approved treatment for IBS-C in adults.

Manufacturing and Supply

It is our objective that the supply of linaclotide be safe and effective, with redundancy built into critical steps of the supply chain, and that each of our collaboration partners are in a position to manage the supply and distribution of linaclotide in their respective territories through a combination of contract manufacturers and in-house manufacturing capabilities. Linaclotide production consists of three phases—manufacture of the API (sometimes referred to as drug substance), manufacture of finished drug product and manufacture of finished goods. We and/or our partners have commercial supply agreements with multiple third-party manufacturers for the production of linaclotide API. We believe the current commercial suppliers have the capabilities to produce linaclotide API in accordance with current good manufacturing practices, or GMP, on a sufficient scale to meet the worldwide development and commercial needs for linaclotide. The commercial suppliers of linaclotide API are subject to routine inspections by regulatory agencies worldwide and also undergo periodic audit and certification by our partners' or our own quality department.

Each of AbbVie, Astellas and AstraZeneca is responsible for linaclotide API, finished drug product and finished goods manufacturing (including bottling and packaging) and distributing the finished goods to wholesalers in its respective territories.

Prior to linaclotide, there was no precedent for long-term room temperature shelf storage formulation for an orally dosed peptide to be produced in millions of capsules per year. Our efforts to date have led to formulations that are both cost effective and able to meet the stability requirements for commercial pharmaceutical products.

Sales and Marketing

For the foreseeable future, we intend to develop and commercialize our drugs in the U.S. alone or with partners, and expect to rely on partners to develop and commercialize our drugs in territories outside the U.S. In executing our strategy, our goal is to retain oversight over the worldwide development and commercialization of our products by playing an active role in their commercialization or finding partners who share our vision, values, culture and processes.

To date, we have established a high-quality commercial organization dedicated to supporting our vision of becoming the leading GI healthcare company in the U.S. Our GI commercial capabilities, including marketing, patient engagement and sales, are designed to support our existing product as well as potential future internally and externally developed products.

We are also coordinating efforts with our linaclotide partners to launch and maintain an integrated, global linaclotide brand. By leveraging the knowledge base and expertise of our experienced commercial team and the insights of each of our linaclotide commercialization partners, we continually improve our collective marketing strategies.

Patents and Proprietary Rights

We actively seek to protect the proprietary technology that we consider important to our business, including pursuing patents that cover our products, compositions, and formulations, their methods of use and the processes for their manufacture, as well as any other relevant inventions and improvements that are commercially important to the development of our business. We also rely on trade secrets that may be important to the development of our business.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for the technology, inventions and improvements we consider important to our business; defend our patents; preserve the confidentiality of our trade secrets; and operate without infringing the patents and proprietary rights of third parties.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the date of filing the non-provisional application. We expect to apply, and have applied, for patent term extension in countries where it is available.

Linaclotide Patent Portfolio

Our linaclotide patent portfolio is currently composed of 14 patents in the U.S., including 12 U.S. patents listed in the U.S. FDA publication, Approved Drug Products with Therapeutic Equivalence Evaluations, or the Orange Book, eight granted European patents, most of which have been validated in available European countries, ten granted Japanese patents, five granted Chinese patents, 80 issued patents in other foreign jurisdictions, and numerous pending U.S., foreign and Patent Cooperation Treaty, or PCT, patent applications. We and our partners own, either jointly or individually, all of the issued patents and pending applications.

The issued U.S. patents, which will expire between 2024 and 2033, contain claims directed to the linaclotide molecule, pharmaceutical compositions thereof, methods of using linaclotide to treat GI disorders, processes for making the molecule, and room temperature stable formulations of linaclotide and methods of use thereof. The 72 mcg, 145 mcg and 290 mcg LINZESS doses are covered by various composition of matter patents in the U.S., the latest of which expires in 2026. In addition, the commercial formulations of the 72 mcg, 145 mcg and 290 mcg LINZESS doses are covered by patents in the U.S. that expire in the early 2030s. The granted European patents, which will expire between 2024 and 2036, some of which are subject to potential patent term extension, contain claims directed to the linaclotide molecule, pharmaceutical compositions thereof, uses of linaclotide to prepare medicaments for treating GI disorders, and room temperature stable formulations of linaclotide and their use in treating IBS-C and chronic constipation. The granted Chinese patents, which will expire between 2024 and 2032, the granted Japanese patents, which will expire between 2025 and 2036, some of which are subject to granted and potential patent term extension, and the granted patents in other foreign jurisdictions, which will expire between 2024 and 2034, some of which may be subject to potential patent term extension, contain claims directed to the linaclotide molecule, pharmaceutical compositions of linaclotide for use in treating GI disorders, and room temperature stable formulations of linaclotide.

We have pending patent applications in certain countries worldwide that, if issued, will expire between 2024 and 2040 and which include claims covering the linaclotide molecule, methods of using linaclotide to treat GI disorders, the current commercial formulations of linaclotide and uses thereof to treat GI disorders and delayed release and other potential formulations of linaclotide.

The patent term of a patent that covers a U.S. FDA approved drug is also eligible for patent term extension, which permits patent term extension as compensation for some of the patent term lost during the U.S. FDA regulatory review process. The Hatch Waxman Act permits a patent term extension of a single patent applicable to an approved drug for up to five years beyond the expiration of the patent but the extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval by the U.S. FDA. The United States Patent and Trademark Office has issued a Certificate of Patent Term Extension for U.S. Patent 7,304,036, which covers linaclotide and methods of use thereof. As a result, the patent term of this patent was extended to August 30, 2026, 14 years from the date of linaclotide's approval by the U.S. FDA. Similar provisions are available in Europe and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug. We have received patent term extensions in Japan for several of our linaclotide patents. We have also received patent term extensions, called supplementary protection certificates, for certain linaclotide patents from several national patent offices in Europe.

We and AbbVie received Paragraph IV certification notice letters regarding ANDAs submitted to the U.S. FDA by five generic drug manufacturers requesting approval to engage in commercial manufacture, use, sale and offer for sale of linaclotide capsules (72 mcg, 145 mcg and 290 mcg), proposed generic versions of LINZESS. All five manufacturers requested approval for their 145 mcg and 290 mcg generic doses of LINZESS and two requested additional approval for their 72 mcg generic doses of LINZESS. We and AbbVie have entered into settlement agreements with all five of these generic drug manufacturers providing for licenses to market their 72 mcg (if applicable),145 mcg and 290 mcg generic versions of LINZESS, beginning as early as March 2029 (subject to U.S. FDA Approval), unless certain limited circumstances, customary for settlement agreements of this nature, occur.

Government Regulation

Our business is subject to government regulation in both the U.S. and in other countries. In the U.S., pharmaceutical products are subject to extensive regulation by the U.S. FDA. The Federal Food, Drug, and Cosmetic Act and other federal and state statutes and regulations, as well as similar foreign regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-marketing requirements and assessments, post-approval monitoring and reporting,

sampling, and import and export of pharmaceutical products. The U.S. FDA and other regulatory authorities have very broad enforcement authority and failure to abide by applicable regulatory requirements can result in administrative or judicial sanctions being imposed on us, including warning letters, refusals of government contracts, clinical holds, civil penalties, injunctions, restitution, disgorgement of profits, recall or seizure of products, total or partial suspension of production or distribution, withdrawal of approval, refusal to approve pending applications, and civil or criminal prosecution.

U.S. FDA Approval Process

No company may market a new drug in the U.S. until it has submitted an NDA to the U.S. FDA, and the U.S. FDA has approved it. The steps required before the U.S. FDA may approve an NDA generally include:

- conducting nonclinical laboratory tests and animal tests in compliance with U.S. FDA's good laboratory practice, or GLP, requirements;
- development, manufacture and testing of active pharmaceutical product and dosage forms suitable for human use in compliance with current GMP;
- conducting adequate and well-controlled human clinical trials that establish the safety and efficacy of the product for its specific intended use(s);
- in order to evaluate a drug in humans in the U.S., an IND must be submitted and come into effect before human clinical trials may begin;
- the submission to the U.S. FDA of an NDA;
- satisfactory completion of one or more U.S. FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current GMP requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- inspections of other sources of data in the NDA, such as inspection of clinical trial sites to assess compliance with good clinical practice, or GCP, requirements are also generally required; and
- U.S. FDA review and approval of the NDA.

Nonclinical tests include laboratory evaluation of the product candidate, as well as animal studies to assess the potential safety and efficacy of the product candidate. The conduct of the nonclinical tests must comply with federal regulations and requirements including GLP. We must submit the results of the nonclinical tests, together with manufacturing information, analytical data and a proposed clinical trial protocol to the U.S. FDA as part of an IND, which must become effective before we may commence human clinical trials in the U.S. The IND will automatically become effective 30 days after its receipt by the U.S. FDA, unless the U.S. FDA raises concerns or questions before that time about the conduct of the proposed trial. In such a case, we must work with the U.S. FDA to resolve any outstanding concerns before the clinical trial can proceed. We cannot be sure that submission of an IND will result in the U.S. FDA allowing clinical trials to begin, or that, once begun, issues will not arise that will cause us or the U.S. FDA to modify, suspend or terminate such trials. The study protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board, or IRB, for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB requirements or if the trial has been associated with unexpected serious harm to subjects. An IRB may also impose other conditions on the trial. For studies conducted outside of the U.S., similarly, we are subject to local regulations which may differ from the U.S. and local regulations must be followed appropriately.

Clinical trials involve the administration of the product candidate to humans under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control. Clinical trials are typically conducted in three sequential phases, though the phases may overlap or be combined. In Phase I, the initial introduction of the drug into healthy human subjects, the drug is usually tested for safety (adverse effects), dosage tolerance and

pharmacologic action, as well as to understand how the drug is taken up by and distributed within the body. Phase II usually involves studies in a limited patient population (individuals with the disease under study) to:

- evaluate preliminarily the efficacy of the drug for specific, targeted conditions;
- determine dosage tolerance and appropriate dosage as well as other important information about how to design larger Phase III trials; and
- identify possible adverse effects and safety risks.

Phase III trials generally further evaluate clinical efficacy and test for safety within an expanded patient population. The conduct of clinical trials is subject to extensive regulation, including compliance with GCP regulations and guidance, and regulations designed to protect the rights and safety of subjects involved in investigations.

The U.S. FDA may order the temporary or permanent discontinuation of a clinical trial at any time or impose other sanctions if it believes that the clinical trial is not being conducted in accordance with U.S. FDA requirements or presents an unacceptable risk to the clinical trial patients. We may also suspend clinical trials at any time on various grounds.

The results of the nonclinical and clinical studies, together with other detailed information, including the manufacture and composition of the product candidate, are submitted to the U.S. FDA in the form of an NDA requesting approval to market the drug. The U.S. FDA approval of the NDA is required before marketing of the product may begin in the U.S. If the NDA contains all pertinent information and data, the U.S. FDA will “file” the application and begin review. The review process, however, may be extended by U.S. FDA requests for additional information, nonclinical or clinical studies, clarification regarding information already provided in the submission, or submission of a risk evaluation and mitigation strategy. The U.S. FDA may refer an application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The U.S. FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. Before approving an NDA, the U.S. FDA will typically inspect the facilities at which the product candidate is manufactured and will not approve the product candidate unless current GMP compliance is satisfactory. The U.S. FDA also typically inspects facilities responsible for performing animal testing, as well as clinical investigators who participate in clinical trials. The U.S. FDA may refuse to approve an NDA if applicable regulatory criteria are not satisfied or may require additional testing or information. The U.S. FDA may also limit the indications for use and/or require post-marketing testing and surveillance to monitor the safety or efficacy of a product. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

The testing and approval process requires substantial time, effort and financial resources, and our product candidates may not be approved on a timely basis, if at all. The time and expense required to perform the clinical testing necessary to obtain U.S. FDA approval for regulated products can frequently exceed the time and expense of the research and development initially required to create the product. The results of nonclinical studies and initial clinical trials of our product candidates are not necessarily predictive of the results from large-scale clinical trials, and clinical trials may be subject to additional costs, delays or modifications due to a number of factors, including difficulty in obtaining enough patients, investigators or product candidate supply. Failure by us or our collaborators, licensors or licensees, including AbbVie, Astellas and AstraZeneca, to obtain, or any delay in obtaining, regulatory approvals or in complying with requirements could adversely affect commercialization and our ability to receive product or royalty revenues.

Hatch-Waxman Act

The Hatch-Waxman Act established abbreviated approval procedures for generic drugs. Approval to market and distribute these drugs is obtained by submitting an ANDA with the U.S. FDA. The application for a generic drug is “abbreviated” because it need not include nonclinical or clinical data to demonstrate safety and effectiveness and may instead rely on the U.S. FDA’s previous finding that the brand drug, or reference drug, is safe and effective. In order to obtain approval of an ANDA, an applicant must, among other things, establish that its product is bioequivalent to an existing approved drug and that it has the same active ingredient(s), strength, dosage form, and route of administration. A generic drug is considered bioequivalent to its reference drug if testing demonstrates that the rate and extent of

absorption of the generic drug is not significantly different from the rate and extent of absorption of the reference drug when administered under similar experimental conditions.

The Hatch-Waxman Act also provides incentives by awarding, in certain circumstances, certain legal protections from generic competition. This protection comes in the form of a non-patent exclusivity period, during which the U.S. FDA may not accept, or approve, an application for a generic drug, whether the application for such drug is submitted through an ANDA or a through another form of application, known as a 505(b)(2) application.

The Hatch-Waxman Act grants five years of exclusivity when a company develops and gains NDA approval of a new chemical entity that has not been previously approved by the U.S. FDA. This exclusivity provides that the U.S. FDA may not accept an ANDA or 505(b)(2) application for five years after the date of approval of previously approved drug, or four years in the case of an ANDA or 505(b)(2) application that challenges a patent claiming the reference drug (see discussion below regarding Paragraph IV Certifications). The Hatch-Waxman Act also provides three years of exclusivity for approved applications for drugs that are not new chemical entities, if the application contains the results of new clinical investigations (other than bioavailability studies) conducted or sponsored by the applicant that were essential to approval of the application. Examples of applications that may require new clinical investigations essential to approval and receive three-year exclusivity include applications for new indications, dosage forms (including new drug delivery systems), strengths, or conditions of use for an already approved product. This three-year exclusivity period only protects against U.S. FDA approval of ANDAs and 505(b)(2) applications for generic drugs for the conditions of approval (for example, indication or dosage form) that required new clinical investigations that were essential to approval; it does not prohibit the U.S. FDA from accepting or approving ANDAs or 505(b)(2) NDAs for generic drugs that do not include such conditions of approval.

Paragraph IV Certifications. Under the Hatch-Waxman Act, NDA applicants and NDA holders must provide information about certain patents claiming their drugs, or methods of use of the drug that is the subject of the NDA, for listing in the Orange Book. When an ANDA or 505(b)(2) application is submitted, it must contain one of several possible certifications regarding each of the patents listed in the Orange Book for the reference drug. A certification that a listed patent is invalid, unenforceable or will not be infringed by the sale of the proposed product is called a "Paragraph IV" certification. A certification that provides the date a listed patent will expire, but does not challenge the validity, enforceability or infringement of the patent, is called a "Paragraph III" certification. FDA can approve the ANDA or 505(b)(2) application containing the Paragraph III certification upon expiration of the patent.

Within 20 days of the acceptance by the U.S. FDA of an ANDA or 505(b)(2) application containing a Paragraph IV certification, the applicant must notify the NDA holder and patent owner that the application has been submitted, and provide the factual and legal basis for the applicant's opinion that the patent is invalid, unenforceable, or not infringed. The NDA holder or patent holder may then initiate a patent infringement suit in response to the Paragraph IV notice. If this is done within 45 days of receiving notice of the Paragraph IV certification, a 30-month stay of the U.S. FDA's ability to approve the ANDA or 505(b)(2) application is triggered. The U.S. FDA may approve the proposed product before the expiration of the 30-month stay only if a court finds the patent invalid or not infringed, and the court may shorten or lengthen the 30-month stay under certain limited circumstances.

Patent Term Extension. Under the Hatch-Waxman Act, a portion of the patent term lost during product development and U.S. FDA review of an NDA or 505(b)(2) application is extended if approval of the application is the first permitted commercial marketing of a drug containing the active ingredient. The patent term extension period is generally one-half the time between the effective date of the IND and the date of submission of the NDA, plus the time between the date of submission of the NDA and the date of U.S. FDA approval of the product. The maximum period of patent term extension is five years, and the patent cannot be extended to more than 14 years from the date of U.S. FDA approval of the product. Only one unexpired patent claiming the drug product, a method of using the product or a method of manufacturing the product is eligible for extension and the patent holder must apply for extension within 60 days of approval. The U.S. Patent and Trademark Office, in consultation with the U.S. FDA, reviews and approves the application for patent term extension.

Other Regulatory Requirements

After approval, finished drug products are subject to extensive continuing regulation by the U.S. FDA, which include company obligations to manufacture products in accordance with current GMP, maintain and provide to the U.S.

FDA updated safety and efficacy information, report adverse experiences with the product, keep certain records and submit periodic reports, obtain U.S. FDA approval of certain manufacturing or labeling changes, and comply with U.S. FDA promotion and advertising requirements and restrictions. Failure to meet these obligations can result in various adverse consequences, both voluntary and U.S. FDA-imposed, including product recalls, withdrawal of approval, restrictions on marketing, and the imposition of civil fines and criminal penalties against the NDA holder. In addition, later discovery of previously unknown safety or efficacy issues may result in restrictions on the product, manufacturer or NDA holder.

We and our partners and any third-party manufacturers we or our partners engage are required to comply with applicable U.S. FDA manufacturing requirements contained in the U.S. FDA's current GMP regulations. Current GMP regulations require, among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation. The manufacturing facilities for our products must meet current GMP requirements to the satisfaction of the U.S. FDA pursuant to a pre-approval inspection before we can use them to manufacture our products. We and any third-party manufacturers are also subject to periodic inspections of facilities by the U.S. FDA and other authorities, including procedures and operations used in the testing and manufacture of our products to assess our compliance with applicable regulations.

With respect to post-market product advertising and promotion, the U.S. FDA imposes a number of complex regulations on entities that advertise and promote pharmaceuticals, which include, among others, standards for direct-to-consumer advertising, prohibitions on promoting drugs for uses, conditions or diseases, or in patient populations that are not consistent with the drug's approved labeling (known as "off-label use"), and principles governing industry-sponsored scientific and educational activities. Failure to comply with U.S. FDA requirements can have negative consequences, including adverse publicity, warning or untitled letters from the U.S. FDA, mandated corrective advertising or communications with doctors or patients, and civil or criminal penalties. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and U.S. FDA approval of a new NDA or sNDA before the change can be implemented. An sNDA for a new indication typically requires clinical data similar in type and quality to the clinical data supporting the original application for the original indication, and the U.S. FDA uses similar procedures and actions in reviewing such sNDAs as it does in reviewing NDAs.

Adverse event reporting and submission of periodic reports is required following U.S. FDA approval of an NDA. The U.S. FDA also may require post-marketing testing, known as Phase IV testing, risk evaluation and mitigation strategies, and surveillance to monitor the effects of an approved product or to place conditions on an approval that restrict the distribution or use of the product.

Outside the U.S., our and our collaborators' abilities to market a product are contingent upon receiving marketing authorization from the appropriate regulatory authorities. The requirements governing the conduct of clinical trials, marketing authorization, pricing and reimbursement vary widely from jurisdiction to jurisdiction. At present, foreign marketing authorizations are applied for at a national level, although within the E.U. registration procedures are available to companies wishing to market a product in more than one E.U. member state. We are subject to U.S. federal and foreign anti-corruption laws. Those laws include the U.S. Foreign Corrupt Practices Act, or FCPA, which prohibits U.S. corporations and their representatives from offering, promising, authorizing, or making payments to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business abroad. The scope of the FCPA encompasses certain healthcare professionals in many countries. We are also subject to similar laws of other countries that have enacted anti-corruption laws and regulations.

Pricing and Reimbursement

Within the U.S., significant uncertainty exists regarding the coverage and reimbursement status of products approved by the U.S. FDA. Sales of our products depend, in part, on the extent to which our products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. The process for determining whether a third-party payor will provide coverage for a finished drug product typically is separate from the process for setting the price of a finished drug product or for establishing the reimbursement rate that the payor will pay for the finished drug product once coverage is approved. Third-party payors may limit coverage to specific finished drug products on an approved list, also known as a formulary, which might not include all of the U.S.

FDA-approved drugs for a particular indication. A decision by a third-party payor not to cover our products or to restrict coverage of our products could reduce utilization of our products. Moreover, a third-party payor's decision to provide coverage for a finished drug product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Additionally, coverage and reimbursement for finished drug products can differ significantly from payor to payor. One third-party payor's decision to cover a particular finished drug product or service does not ensure that other payors will also provide coverage for the medical product or service or will provide coverage at an adequate reimbursement rate.

The containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. Federal and state governments have shown significant interest in implementing cost-containment programs, including restrictions on reimbursement and requirements for substitution of generic products. Adoption of new or enhanced cost-containment measures could limit our net revenue and results. Third party payors are increasingly challenging the prices charged for medical products and services and examining the medical necessity and cost effectiveness of medical products and services, in addition to their safety and efficacy. Restrictions in coverage or decreases in third-party reimbursement for our products could have a material adverse effect on our sales, results of operations and financial condition. We expect that the pharmaceutical industry will experience pricing pressures due to the increasing influence of managed care (and related implementation of managed care strategies to control utilization), additional federal and state legislative and regulatory proposals to regulate pricing of drugs, limit coverage of drugs or reduce reimbursement for drugs, and public scrutiny of drug pricing. While we cannot predict what executive, legislative and regulatory proposals will be adopted or other actions will occur, such events could have a material adverse effect on our business, financial condition and profitability. For additional information relating to pricing and reimbursement and legislative and other reform initiatives that may affect coverage, pricing and reimbursement, see Item 1A, Risk Factors, elsewhere in this Annual Report on Form 10-K.

Sales and Marketing

The marketing and sale of pharmaceutical products are subject to comprehensive governmental regulation both within and outside the U.S.

Within the U.S., numerous federal, state and local authorities have jurisdiction over, or enforce laws related to, such activities, including the U.S. FDA, U.S. Drug Enforcement Agency, Centers for Medicare & Medicaid Services, the U.S. Department of Health and Human Services Office of Inspector General, the U.S. Department of Justice, state Attorneys General, state departments of health and state pharmacy boards.

We are subject to the requirements of the Federal Food, Drug, and Cosmetic Act and accompanying regulations that prohibit pharmaceutical companies from promoting a drug prior to approval from the U.S. FDA and from promoting an approved drug in a manner inconsistent with the approved label.

We are also subject to various federal and state laws pertaining to health care "fraud and abuse," including anti-kickback laws and false claims laws, for activities related to sales of any of our products or product candidates that may in the future receive marketing approval. Anti-kickback laws generally prohibit persons from soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid or, in some cases, private third-party payors. Although the specific provisions of these laws vary, their scope is generally broad and there may not be regulations, guidance or court decisions that apply the laws to particular industry practices. False claims laws prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, information or claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent. Violations of fraud and abuse laws may be punishable by criminal or civil sanctions, including fines and civil monetary penalties, and/or exclusion from federal health care programs (including Medicare and Medicaid).

Laws and regulations have been enacted by the federal government and various states to regulate the sales and marketing practices of pharmaceutical manufacturers with marketed products. The laws and regulations generally limit financial interactions between manufacturers and health care providers, require disclosure to the government and public of such interactions and/or require reporting of pricing information or marketing expenditures. Many of these laws and regulations contain ambiguous requirements or require administrative guidance for implementation.

Human Capital

As of December 31, 2022, we had 219 employees. Of these employees, 45 were on our drug development team, 125 were on our sales and commercial team, and 49 were in general and administrative functions. We consider our employee relations to be good.

Diversity, Equity and Inclusion (DE&I)

Creating a diverse, equitable, and inclusive culture is essential to attracting, motivating and retaining the talent necessary to deliver on our corporate mission. To establish and maintain this culture, we have a simple vision in mind: to make Ironwood an environment rooted in valuing each employee for who they are.

This begins with ensuring our workforce represents the diverse populations we serve and reflecting our DE&I principles in our employee-related trainings and policies. Women represent approximately 52% of our employee base, 27% of our leadership team (vice president and above) and 33% of our board of directors (including our board and audit committee chairs). Additionally, approximately 18% of our employees are racially or ethnically diverse and in 2022, approximately 28% of our new hires were racially or ethnically diverse.

We are focused on fostering an environment where employees feel included and empowered. This approach includes DE&I initiatives such as learning and development opportunities, strengthened talent acquisition strategies, the support of equality programs in our local communities, and added metrics related to retention and career advancement of diverse populations. We are also proud to have three strong and growing employee resource groups: W@IRWD (Women at Ironwood), ISTAR (Ironwood Stands Together Against Racism), and PRIDE.

In 2022, we continued to advance our DE&I initiatives with strong advocacy from our leadership team and board of directors. We incorporated DE&I metrics into our corporate goals. Over the course of the year, we achieved our target level of performance on these metrics.

Compensation and Benefits

All our employees receive equity and are encouraged to think and act as owners of Ironwood. We strive to provide pay, benefits, and services that are competitive to market and to create incentives to attract, motivate and retain our employees. We are focused on pay equity and regularly monitor our pay practices among similar roles and responsibilities throughout our organization.

Communication and Engagement

We strongly believe that our success depends on employees understanding how their work contributes to our ability to execute on our vision, mission and strategy. Our communication and engagement efforts seek to offset competitive talent challenges in the biopharmaceutical industry and employees' higher expectations of their employers. To this end, we utilize a variety of channels to facilitate open and direct communication, including frequent town hall meetings, Ironwood intranet, CEO blog, leadership engagement opportunities, regular communications regarding business updates, and employee engagement surveys.

Health, Wellness and Safety in the Face of the COVID-19 Pandemic

The health and safety of all our employees is a top priority for us. We have augmented certain healthcare, childcare and leave benefits in an effort to support our employees and their families in the face of the continuing challenges brought on by the COVID-19 pandemic. We maintain a working group focused on creating and keeping employees well informed about the company's latest plans and guidance around COVID-19. We also provided personal protective equipment, at-home COVID-19 test kits and safety trainings for field-based employees, a home supply stipend to create home office space, and extended additional wellness benefits including backup childcare, among other efforts.

Available Information

You may obtain free copies of our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, and amendments to those reports, as soon as reasonably practicable after they are electronically filed or furnished to the SEC, on the Investors section of our website at www.ironwoodpharma.com or by contacting our

Investor Relations department at (617) 621-8395. The contents of our website are not incorporated by reference into this report and you should not consider information provided on our website to be part of this report.

PART II OTHER INFORMATION

Item 1A. *Risk Factors*

In addition to the other information in this Annual Report on Form 10-K, any of the factors described below could significantly and negatively affect our business, financial condition, results of operations or prospects. The trading price of our Class A Common Stock may decline due to these risks.

Risks Related to Commercializing LINZESS and Other Product Candidates

We are highly dependent on the commercial success of LINZESS (linaclotide) in the U.S. for the foreseeable future.

We and our partner, AbbVie, began selling LINZESS in the U.S. in December 2012. Revenues from our LINZESS collaboration constitute a significant portion of our total revenue, and we believe they will continue to do so for the foreseeable future. The commercial success of LINZESS depends on a number of factors, including:

- the effectiveness of LINZESS as a treatment for adult patients with irritable bowel syndrome with constipation, or IBS-C, or chronic idiopathic constipation, or CIC, and, if approved, as a treatment for pediatric patients aged 6-17 years with functional constipation, or FC;
- the size of the treatable patient population;
- the effectiveness of the sales, managed markets and marketing efforts by us and AbbVie, including our ability to adapt our commercial model and market strategy to the evolving landscape;
- the adoption of LINZESS by physicians, which depends on whether physicians view it as safe and effective treatment for adult patients with IBS-C and CIC and, if approved, for pediatric patients aged 6-17 years with FC;
- our success in educating and activating adult IBS-C and CIC patients to enable them to more effectively communicate their symptoms and treatment history to their physicians;
- our ability to both secure and maintain adequate reimbursement for, and optimize patient access to, LINZESS and our ability to demonstrate that LINZESS is safer, more efficacious and/or more cost-effective than alternative therapies;
- the effectiveness of our partners' distribution networks;
- the occurrence of any side effects, adverse reactions or misuse, or any unfavorable publicity in these or other areas, associated with linaclotide; and
- the development or commercialization of competing products or therapies for the treatment of IBS-C or CIC, or their associated symptoms.

Our revenues from the commercialization of LINZESS are subject to these and other factors, and therefore may be unpredictable from quarter-to-quarter.

Our products may cause undesirable side effects or have other properties that could limit their commercial potential.

Linaclotide has been prescribed to millions of patients since its launch in the U.S. and other territories beginning in December 2012. The most commonly reported adverse reaction since linaclotide became commercially available, as well as in the clinical trials for linaclotide in IBS-C and CIC, has been diarrhea. In the linaclotide Phase III IBS-C and CIC trials, severe diarrhea was reported in 2% or less of the linaclotide-treated patients and its incidence was similar between the IBS-C and CIC populations.

The number and type of patients treated with linaclotide could continue to grow if physicians prescribe linaclotide to more patients and as we and our partners conduct clinical trials, including in new indications, populations or formulations, as well as explore potential combination products, in existing and new territories. As patient experience increases and expands, we and others may identify previously unknown side effects, known side effects may be found to be more frequent and/or severe than in the past, and we and others may detect unexpected safety signals for our products or any products perceived to be similar to our products. The foregoing, or the perception of the foregoing, may have the following effects, among others:

- sales of our products may be impaired;
- regulatory approvals for our products may be delayed, denied, restricted or withdrawn;
- we or our partners may decide to, or be required to, change the products' label or send product warning letters or field alerts to physicians, pharmacists or hospitals;
- reformulation of the products, additional nonclinical or clinical studies, changes in labeling or changes to or re-approvals of manufacturing facilities may be required;
- we or our partners may be precluded from pursuing approval of linaclotide in new territories or from studying additional development opportunities to enhance our products' clinical profiles, including within new or existing indications, populations or formulations, as well as in potential combination products;
- our or our products' reputation in the marketplace may suffer; and
- government investigations or lawsuits, including class action suits, may be brought against us or our partners.

Any of the above occurrences would harm or prevent sales of our products, increase expenses and impair our and our partners' ability to successfully commercialize our products.

In addition, the U.S. FDA-approved label for LINZESS contains a boxed warning describing the risk of serious dehydration in pediatric patients less than two years of age and a contraindication against its use in these patients. The safety and effectiveness of LINZESS in patients less than 18 years of age have not been established. These and other restrictions could limit the commercial potential of LINZESS. We and AbbVie have established a nonclinical and clinical post-marketing plan with the U.S. FDA to understand the safety and efficacy of LINZESS in pediatric patients. In September 2022, we announced positive topline data from a Phase III clinical trial evaluating linaclotide 72 mcg in pediatric patients aged 6-17 years with FC, and in December 2022, we and AbbVie submitted a Supplemental New Drug Application, or sNDA, to the U.S. FDA seeking approval of a new indication of linaclotide for FC in pediatric patients aged 6-17 years. In February 2023, the U.S. FDA granted priority review to our sNDA and assigned a Prescription Drug User Free Act, or PDUFA, date of June 14, 2023. The Phase III clinical trial demonstrated acceptable safety in the pediatric population aged 6-17 years. The most common adverse event in the study was diarrhea, which occurred in 4.3% of linaclotide-treated patients versus 1.8% in the placebo group. Additional clinical pediatric programs in IBS-C and FC are ongoing. There can be no assurances, however, that the sNDA will be approved by the U.S. FDA, and if approved, whether there may be any significant unknown side effects that could limit the commercial potential of LINZESS in this pediatric population.

We are subject to uncertainty relating to pricing and reimbursement policies in the U.S. which, if not favorable for our products, could hinder or prevent our products' commercial success.

Our and our partner's ability to commercialize our products successfully depends in part on the coverage and reimbursement levels set by governmental authorities, private health insurers and other third-party payors. In determining whether to approve reimbursement for our products and at what level, we expect that third-party payors will consider factors that include the efficacy, cost effectiveness and safety of our products, as well as the availability of other treatments including generic prescription drugs and over-the-counter alternatives. Further, in order to obtain and maintain acceptable reimbursement levels and access for patients at copay levels that are reasonable and customary, we have offered, and expect to continue to face increasing pressure to offer, discounts or rebates from list prices or discounts

to third-party payors or other unfavorable pricing modifications. Obtaining and maintaining favorable reimbursement can be a time consuming and expensive process, and there is no guarantee that we or AbbVie will be able to negotiate or continue to negotiate pricing terms with third-party payors at levels that are profitable to us, or at all. Certain third-party payors also require prior authorization for, or even refuse to provide, reimbursement for our products, and others may do so in the future. Our business would be materially adversely affected if we and our partners are not able to receive approval for reimbursement of our products from third-party payors on a broad, timely or satisfactory basis; if reimbursement is subject to overly broad or restrictive prior authorization requirements; or if reimbursement is not maintained at satisfactory levels or becomes subject to prior authorization. In addition, our business could be adversely affected if government healthcare programs, private health insurers, including managed care organizations, or other reimbursing bodies or payors limit or reduce the indications for or conditions under which our products may be reimbursed. Moreover, as discussed further below, changes in insurance coverage or reimbursement levels by governmental authorities, private health insurers and other third-party payors, or in the type of such coverage held by patients, as well as the impacts to healthcare access or administration (including, for example, limitations on medications or procedures deemed "non-essential," reduced interaction between patients and physicians, and increased unemployment), due to the COVID-19 pandemic or otherwise may materially harm our business and commercialization efforts.

We may experience pricing pressures in connection with the sale of our current and future products due to the healthcare reforms discussed below, as well as the trend toward initiatives aimed at reducing healthcare costs, the increasing influence of managed care, the scrutiny of pharmaceutical pricing, the ongoing debates on reducing government spending and additional legislative proposals. There has been significant scrutiny of pharmaceutical pricing and the resulting costs of pharmaceutical products that could cause significant operational and reimbursement changes for the pharmaceutical industry. There have been a number of federal and state efforts to address drug costs, which generally have focused on increasing transparency around drug costs or limiting drug prices, price increases or other related costs. Certain of these efforts have resulted in legislative and regulatory reforms. For example, and as discussed further below, the Inflation Reduction Act, or IRA, of 2022, which could have the effect of reducing the prices we can charge and increasing the discounts we provide for our products and product candidates.

Healthcare reform efforts or any future legislation or regulatory actions aimed at controlling and reducing healthcare costs, including through measures designed to limit reimbursement, restrict access or impose unfavorable pricing modifications on pharmaceutical products, could impact our and our partners' ability to obtain or maintain reimbursement for our products at satisfactory levels, or at all, which could materially harm our business and financial results.

We and our linaclotide partners are subject to uncertainty relating to pricing and reimbursement policies outside the U.S., as well as risks relating to the improper importation of linaclotide and sale of counterfeit versions of linaclotide. If such policies are not favorable, or if linaclotide is improperly imported or is counterfeited, our business and financial results could be adversely affected.

In some foreign countries, particularly Canada, the countries of Europe, Japan and China, the pricing and payment of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take 6 to 12 months or longer after the receipt of regulatory approval and product launch. Reimbursement sources are different in each country, and each country may include a combination of distinct potential payors, including private insurance and governmental payors. Some countries may restrict the range of medicinal products for which their national health insurance systems provide reimbursement and control the prices of medicinal products for human use. To obtain favorable reimbursement for the indications sought or pricing approval in some countries, we and our partners may be required to conduct a clinical trial that compares the cost and clinical effectiveness of linaclotide to other available therapies. Further, several countries have implemented government measures to either freeze or reduce pricing of pharmaceutical products. Many third-party payors and governmental authorities also consider the price for which the same product is being sold in other countries to determine their own pricing and reimbursement strategy, so if linaclotide is priced low or gets limited reimbursement in a particular country, this could result in similarly low pricing and reimbursement in other countries. If reimbursement for linaclotide is unavailable in any country in which reimbursement is sought, limited in scope or amount, or if pricing is set at or reduced to unsatisfactory levels, our and our partners' ability to successfully commercialize linaclotide in such country would be impacted negatively. Furthermore, if these measures prevent us or any of our partners from selling linaclotide on a profitable basis in a particular country, they could prevent the commercial launch or continued sale of linaclotide in that country.

CONSTELLA was first launched in certain European countries for the symptomatic treatment of moderate to severe IBS-C in adults in the second quarter of 2013 and our partner, AbbVie, is currently commercializing CONSTELLA in a number of European countries, including the United Kingdom, Italy and Spain. LINZESS was first launched in Japan for the treatment of IBS-C in adults in the first quarter of 2017, and for the treatment of chronic constipation in adults in the third quarter of 2018, and our partner Astellas Pharma, Inc., or Astellas, is currently commercializing LINZESS in Japan. In addition, LINZESS was first launched in China for the treatment of IBS-C in adults in November 2019, and our partner AstraZeneca AB (together with its affiliates), or AstraZeneca, is currently commercializing LINZESS in China (including Hong Kong and Macau). The pricing and reimbursement strategy is a key component of our partners' commercialization plans for CONSTELLA in Europe and LINZESS in Japan and China. Our revenues may suffer if our partners are unable to successfully and timely conclude reimbursement, price approval or funding processes and market CONSTELLA in key member states of the E.U. or LINZESS in Japan or China, or if coverage and reimbursement for either CONSTELLA or LINZESS is limited or reduced. If our partners are not able to obtain or maintain coverage, pricing or reimbursement on acceptable terms or at all, or if such terms change in any countries in its territory, our partners may not be able to, or may decide not to, sell either CONSTELLA or LINZESS in such countries.

We and our partners also face the risk that linaclotide is imported or reimported into markets with relatively higher prices from markets with relatively lower prices, which would result in a decrease of sales and any payments we receive from the affected market. Additionally, third parties may illegally produce, distribute and/or sell counterfeit or otherwise unfit or adulterated versions of linaclotide. In either case, we and our partners may not be able to detect or, if detected, prevent or prohibit the sale of such products, which could result in dangerous health consequences for patients, loss of confidence in us, our partners and our products, and adverse regulatory or legal consequences. Any of the foregoing or other consequences could adversely impact our reputation, financial results and business.

We must work effectively and collaboratively with AbbVie to market and sell LINZESS in the U.S., and we must adapt our commercial model and market strategy to the evolving landscape for LINZESS to achieve its maximum commercial potential.

We are working closely with AbbVie to execute our joint commercialization plan for LINZESS. The commercialization plan includes an agreed upon marketing campaign that targets the physicians who see patients who could benefit from LINZESS treatment. Our marketing campaign also targets the adult men and women who suffer from IBS-C or CIC. Our commercialization plan also includes an integrated call plan for our sales forces in an effort to optimize the education of specific gastroenterologists and primary care physicians on whom our and AbbVie's sales representatives call, and the frequency with which the representatives meet with them.

In order to optimize the commercial potential of LINZESS, we and AbbVie must execute upon this commercialization plan effectively and efficiently. In addition, we and AbbVie must continually assess, modify and adapt our commercialization plan in a coordinated and integrated fashion, including evaluating and adjusting as necessary the level and mix of marketing and promotion efforts, in response to changing business, market or other factors in order to advance the commercial potential of LINZESS, such as the potential approval of LINZESS in pediatric patients aged 6-17 years for FC. Further, we and AbbVie must continue to focus our marketing campaign on the importance of treating both constipation and overall abdominal symptoms in adults with IBS-C and support an effective physician-patient dialogue around IBS-C, CIC and the potential for LINZESS as an appropriate therapy for such symptoms. In addition, we and AbbVie must provide our sales forces with the highest quality support, guidance and oversight for them to continue to effectively promote LINZESS to gastroenterologists and primary care physicians. If we and AbbVie fail to evolve with the changing commercial landscape successfully and perform these commercial functions in the highest quality manner and in accordance with our joint commercialization plan and related agreements, LINZESS will not achieve its maximum commercial potential and we may suffer financial harm. Our commercial efforts to further target and engage adult patients with IBS-C or CIC may not effectively increase appropriate patient awareness or patient/physician dialogue and may not increase the revenues that we generate from LINZESS.

During 2022, in-person work practices for customer-facing employees returned to near pre-COVID 19 levels. However, new strains or variants of the virus that cause outbreaks of COVID-19 may present in the future risks to successful execution of the commercial operating plan for LINZESS due in part to limitations on in-person work practices for our customer-facing employees. The virtual support we may provide to customers may not be as effective as in-person efforts, and our in-person efforts may be limited and/or limited in their effectiveness. If this were to occur,

or if we, AbbVie or any of our partners were unable to align on our strategy and development and commercial efforts as a result of the COVID-19 pandemic or otherwise, we may not be able to maintain or increase the revenues that we generate or our business may be otherwise materially harmed.

We face competition and new products may emerge that provide different or better alternatives for treatment of the conditions that our products are approved to treat.

The pharmaceutical industry and the markets in which we operate are intensely competitive. We compete in the marketing and sale of our products, the development of new products or product candidates and the acquisition of rights to new products with commercial potential. Certain of our competitors have substantially greater financial, technical and human resources than us. Mergers and acquisitions in the pharmaceutical industry may result in even more resources being concentrated in our competitors and enable them to compete more effectively. Competition may also increase further as a result of advances made in the commercial applicability of technologies and greater availability of capital for investment in these fields. Additionally, new developments, including the development of other drug technologies and methods of preventing the incidence of disease, occur in the pharmaceutical and medical technology industries at a rapid pace. These developments may render our products obsolete or noncompetitive.

Linaclotide competes with certain prescription therapies and over-the-counter products, including with products that have attained significant levels of market acceptance. The availability of prescription competitors and over-the- counter products could limit the demand, and the price we are able to charge, for LINZESS unless we are able to achieve and maintain market acceptance among the medical community and patients and differentiate LINZESS on the basis of its cost and/or actual or perceived benefits. For example, Takeda's AMITIZA (lubiprostone) is approved by the U.S. FDA for sale in the U.S. for the treatment of IBS-C, CIC and opioid-induced constipation; Bausch Health's TRULANCE (plecanatide) is approved by the U.S. FDA for sale in the U.S. for the treatment of adults with IBS-C and CIC; Takeda's MOTEGRITY (prucalopride) is approved by the U.S. FDA for sale in the U.S. for the treatment of CIC in adults; and in April 2022, Ardelyx launched in the U.S. IBSRELA™ (tenapanor), a U.S. FDA-approved treatment for IBS-C in adults. Over-the-counter laxatives such as MiraLAX® and DULCOLAX®, and lactulose, a prescription laxative treatment, are also available for the treatment of constipation. Additionally, we believe other companies are developing products that could compete with linaclotide, should they be approved by the U.S. FDA or foreign regulatory authorities and become commercially available. In addition, there are other compounds in late-stage development and other potential competitors that are in earlier stages of development that, if approved, may compete with linaclotide. If our current or potential competitors are successful in completing drug development for their drug candidates and obtain approval from the U.S. FDA or foreign regulatory authorities, they could limit the demand for linaclotide. In addition to competition from such prescription and over-the-counter products, we may also face competition from multiple low-cost generic versions of such products when available in the U.S. For example, authorized generic versions of AMITIZA became available in the U.S. by Endo International and Dash Pharmaceuticals in January 2021 and in October 2022, respectively, and we expect additional generic versions of AMITIZA to become available as early as 2023.

Even though LINZESS is approved by the U.S. FDA for use in adult patients, post-approval development and regulatory requirements still remain, which present additional challenges, and we may not be successful in obtaining approval for additional indications for LINZESS that we are seeking or may seek in the future.

In August 2012, the U.S. FDA approved LINZESS as a once-daily treatment for adult men and women suffering from IBS-C or CIC. Although we and AbbVie completed additional nonclinical and clinical studies in adults that were required by the U.S. FDA in connection with the approval of LINZESS, LINZESS remains subject to ongoing U.S. FDA requirements, including those governing the testing, manufacturing, labeling, packaging, storage, advertising, promotion, sale, distribution, recordkeeping and submission of safety and other post-market information.

The U.S. FDA-approved label for LINZESS contains a boxed warning describing the risk of serious dehydration in pediatric patients less than two years of age and a contraindication against its use in these patients. The safety and effectiveness of LINZESS in patients less than 18 years of age have not been established. We and AbbVie have established a nonclinical and clinical post-marketing plan with the U.S. FDA to understand the safety and efficacy of LINZESS in pediatric patients. In September 2022, we announced positive topline data from a Phase III clinical trial evaluating linaclotide 72 mcg in pediatric patients aged 6-17 years with FC, and in December 2022, we and AbbVie submitted an sNDA to the U.S. FDA seeking approval of a new indication of linaclotide for FC in pediatric patients aged 6-17 years. In February 2023, the U.S. FDA granted priority review to our sNDA and assigned a PDUFA date of June 14, 2023. We may not be successful in obtaining U.S. FDA approval for this new indication of linaclotide for FC in

pediatric patients aged 6-17 years or any additional indications for linaclotide that we may seek in the future. Additional clinical pediatric programs in IBS-C and FC are ongoing. Our ability to expand the indication or label information for LINZESS to pediatrics will depend on, among other things, our successful completion of pediatric clinical programs.

These post-approval requirements impose burdens and costs on us. Failure to effectively, appropriately and timely conduct and complete the required studies relating to our products, monitor and report adverse events and meet our other post-approval commitments would lead to negative regulatory action at the U.S. FDA, which could include withdrawal of regulatory approval of our products for their currently approved indications and patient populations.

Manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the U.S. FDA and other regulatory authorities for compliance with current good manufacturing practices, or GMP, and other applicable regulations. If we or a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with a facility where the product is manufactured, a regulatory agency may impose restrictions on that product or the manufacturer, including withdrawal of the product from the market or suspension of manufacturing. If we, our partners or the manufacturing facilities for our products fail to comply with applicable regulatory requirements, a regulatory agency may take the following actions, among others:

- issue warning letters or untitled letters;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications submitted by us or our partners;
- impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products or require us to initiate a product recall.

Even though linaclotide is approved for marketing in the U.S. and in a number of other countries, we or our partners may never receive approval to commercialize linaclotide in additional parts of the world.

In order to market any products outside of the countries where linaclotide is currently approved, we or our partners must comply with numerous and varying regulatory requirements of other jurisdictions regarding, among other things, safety and efficacy. Approval procedures vary among jurisdictions and can involve product testing and administrative review periods different from, and greater than, those in the U.S. and the other countries where linaclotide is approved. Potential risks include that the regulatory authorities:

- may not deem linaclotide safe and effective;
- may not find the data from nonclinical studies and clinical trials sufficient to support approval;
- may not approve of manufacturing processes and facilities;
- may not approve linaclotide for any or all indications or patient populations for which approval is sought;
- may require significant warnings or restrictions on use to the product label for linaclotide; or
- may change their approval policies or adopt new regulations.

If any of the foregoing were to occur, our or our partners' receipt of regulatory approval in the applicable jurisdiction could be delayed or we or our partners may never receive approval at all. Additionally, we or our partners cannot be certain of the duration or extent to which the COVID-19 pandemic may impact operations of regulatory authorities in jurisdictions around the world, and any reduction in resources dedicated to review and approval of products in applicable jurisdictions could delay or otherwise impact approval or other regulatory decisions or actions.

Further, regulatory approval in one jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory processes in others. If linaclotide is not approved for all indications or patient populations or with the label requested, this would limit the uses of linaclotide and have an adverse effect on its commercial potential or require costly post-marketing studies.

Risks Related to Our Growth Strategy

If we are unable to execute on our strategy to in-license or acquire externally developed products or product candidates, or engage in other transactions with value creation potential, our business and prospects would be materially adversely affected.

Our future success is largely dependent on our ability to successfully execute on our growth strategy, which includes in-licensing or otherwise acquiring the rights to externally developed gastrointestinal products or product candidates or engaging in other transactions with value creation potential. The success of this strategy depends upon our ability to identify, select and acquire promising assets, platforms or other opportunities. For example, in November 2021, we entered into a collaboration and license option agreement with COUR Pharmaceutical Development Company, Inc., or COUR, relating to COUR's investigational therapy CNP-104, a potential treatment of primary biliary cholangitis, or PBC. Under this agreement, COUR will conduct an initial clinical trial for CNP-104 in PBC patients, and we have been granted an option to acquire an exclusive license to research, develop, manufacture and commercialize products containing CNP-104 in the U.S. for the treatment of PBC after reviewing the data from this study. There is no assurance that we will exercise this option following COUR's completion of this initial study, or that CNP-104 will be successful for the treatment of PBC. In addition, the process of proposing, negotiating and implementing a license or acquisition is lengthy and complex and there is no assurance we will be able to enter into similar transactions in the future. Pursuit of external opportunities is also a highly competitive area and a number of other companies, including some with substantially greater financial, development, marketing and sales resources, may compete with us for license or acquisition opportunities. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, product candidates, businesses or technologies and integrate them into our current infrastructure. Moreover, we expect to incur a variety of costs and devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. If we are unable to successfully acquire the rights to additional products or product candidates on terms that we find acceptable, or at all, or execute other value creating transactions, we will remain smaller, less diversified and highly dependent on the commercial success of LINZESS, and our business and prospects would be materially and adversely affected.

In addition, such in-licenses, acquisitions or other transactions may entail numerous operational and financial risks, including:

- development, regulatory and commercialization challenges;
- exposure to unknown liabilities;
- disruption of our business and diversion of our management's time and attention to develop acquired products, product candidates, businesses or technologies;
- incurrence of substantial debt, dilutive issuances of securities or depletion of cash to pay for acquisitions;
- higher than expected acquisition and integration costs;
- difficulty in combining the operations and personnel of any acquired businesses with our operations and personnel;
- increased amortization expenses;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to motivate key employees of any acquired businesses.

The development of product candidates in particular is a highly uncertain process, as we discuss further below. Any product candidate that we in-license or acquire may require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the U.S. FDA and applicable foreign regulatory authorities. We may also rely on our licensors and collaboration partners to conduct development activities for certain of our product candidates, and while we may have oversight of such development activities, such licensees or collaboration partners may not effectively develop any such product candidates. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities or competitors may develop alternatives that render our potential product candidates obsolete or less attractive. It is possible that none of the product candidates we may in-license or acquire will be approved for commercial sale or be otherwise commercially viable, which would impair our ability to grow. Furthermore, we may have little or no insight or control over the development and commercialization of any product that we in-license outside the licensed territory. If other licensees do not effectively develop or commercialize any such product outside the licensed territory, our reputation or the reputation of any such product may be impacted.

Our failure to successfully develop and commercialize additional product candidates or approved products would impair our ability to grow and/or adversely affect our business.

As part of our growth strategy, we intend to explore further linaclotide development opportunities. We and AbbVie are exploring development opportunities to enhance the clinical profile of LINZESS by studying linaclotide in new or existing indications, populations and formulations to assess its potential to treat various conditions. For example, we and AbbVie have established a nonclinical and clinical post-marketing plan with the U.S. FDA to understand the safety and efficacy of LINZESS in pediatric patients. In September 2022, we announced positive topline data from a Phase III clinical trial evaluating linaclotide 72 mcg in pediatric patients aged 6-17 years with FC, and in December 2022, we and AbbVie submitted an sNDA to the U.S. FDA seeking approval of a new indication of linaclotide for FC in that age group. In February 2023, the U.S. FDA granted priority review to our sNDA and assigned a PDUFA date of June 14, 2023. Additional clinical pediatric programs in IBS-C and FC are ongoing. These development efforts may fail or may not increase the revenues that we generate from LINZESS. Furthermore, they may result in adverse events, or perceived adverse events, in certain patient populations that are then attributed to the currently approved patient population, which may result in adverse regulatory action at the U.S. FDA or in other countries or harm linaclotide's reputation in the marketplace, each of which could materially harm our revenues from linaclotide.

The strength of our company's pipeline will depend in large part on the outcomes of studies of assets in our pipeline, such as IW-3300 for the potential treatment of interstitial cystitis/bladder pain syndrome, and any other assets that we may acquire or license from third parties, including CNP-104 for the treatment of PBC, for which we have been granted an option to acquire an exclusive license to research, develop, manufacture and commercialize, in the U.S., following COUR's completion of the initial study of CNP-104. We may spend several years and make significant investments in developing any current or future product candidate, and failure may occur at any point. Our product candidates must satisfy rigorous standards of safety and efficacy before they can be approved for sale by the U.S. FDA. To satisfy these standards, we must allocate resources among development programs and we must engage in costly and lengthy research and development efforts, which are subject to unanticipated delays and other significant uncertainties. Despite our efforts, our product candidates may not offer therapeutic or other improvement over existing competitive drugs, be proven safe and effective in clinical trials, or meet applicable regulatory standards. It is possible that none of the product candidates we develop will be approved for commercial sale, which would impair our ability to grow.

We have ongoing or planned nonclinical and clinical trials, including for linaclotide, and our product candidates. Many companies in the pharmaceutical industry have suffered significant setbacks in clinical trials even after achieving promising results in earlier nonclinical or clinical trials. Findings from completed nonclinical studies may not be replicated in later clinical trials, and clinical trials may not be predictive of the results we may obtain in later-stage clinical trials or of the likelihood of regulatory approval. Results from clinical trials and findings from nonclinical studies could lead to abrupt changes in development activities, including the possible limitation or cessation of development activities associated with a particular product candidate or program. Furthermore, our analysis of data obtained from nonclinical and clinical activities is subject to confirmation and interpretation by the U.S. FDA and other applicable regulatory authorities, which could delay, limit or prevent regulatory approval. The U.S. FDA or other regulatory authorities also may require additional clinical trials, which may be costly or delay, limit, prevent or otherwise impact regulatory submission or approval. Satisfaction of U.S. FDA or other applicable regulatory requirements is costly, time-consuming, uncertain and subject to unanticipated delays.

If we are unable to successfully partner with other companies to develop and commercialize products and/or product candidates, our ability to grow would be impaired and our business would be adversely affected.

As part of our business strategy, we may partner with pharmaceutical, biotechnology or other companies to develop and commercialize products or product candidates. Although we have entered into such arrangements with respect to the development and commercialization of linaclotide worldwide, there can be no assurance that we will be able to do so in the future with respect to other products or product candidates that we either develop internally or in- license or that we will be able to gain the interest of potential partners; establish and maintain development, manufacturing, marketing, sales or distribution relationships on acceptable terms; that such relationships, if established, will be successful or on favorable terms; or that we will gain market acceptance for such products or product candidates. The process of proposing, negotiating and implementing a partnership arrangement is lengthy and complex. If we enter into any partnering arrangements with third parties, any revenues we receive will depend upon the efforts of such third parties. If we are unable to establish successful partnering arrangements when advantageous, we may not gain access to the financial resources and industry experience necessary to develop, commercialize or successfully market our products or product candidates, may be forced to curtail, delay or stop a development program or one or more of our other development programs, delay commercialization, reduce the scope of our planned sales or marketing activities or undertake development or commercialization activities at our own expense, and therefore may be unable to generate revenue from products or product candidates or do so to their full potential.

Delays in the completion of clinical testing of any of our products or product candidates could result in increased costs and delay or limit our ability to generate revenues.

Delays in the completion of clinical testing could significantly affect our product development costs and timing of data readouts and regulatory submissions and potential approvals We do not know whether planned clinical trials will be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- the ongoing COVID-19 pandemic, including restrictions on activities imposed by government authorities in response;
- obtaining regulatory approval to commence a clinical trial;
- reaching agreement on acceptable terms with prospective CROs and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- manufacturing sufficient quantities of a product candidate for use in clinical trials;
- obtaining institutional review board approval to conduct a clinical trial at a prospective site;
- recruiting and enrolling patients to participate in clinical trials for a variety of reasons, including competition from other clinical trial programs for the treatment of similar conditions; and
- maintaining patients who have initiated a clinical trial but may be prone to withdraw due to side effects from the therapy, lack of efficacy or personal issues, or who are lost to further follow-up.

The COVID-19 pandemic has impacted enrollment in our clinical trials and may impact clinical trial enrollment or participation in the future, for example due to suspension of in-person procedures required for enrollment or lower or discontinued patient participation compared to pre-COVID-19 pandemic levels as a result of new strains or variants. Clinical trials may also be delayed or discontinued as a result of ambiguous or negative interim results or assessments. In addition, a clinical trial may be suspended or terminated by us, an institutional review board overseeing the clinical trial at a clinical trial site (with respect to that site), the U.S. FDA, or other regulatory authorities due to a number of factors, including:

- failure to conduct the clinical trial in accordance with regulatory requirements or the study protocols;

- inspection of the clinical trial operations or trial sites by the U.S. FDA or other regulatory authorities resulting in the imposition of a clinical hold;
- unforeseen safety issues; or
- lack of adequate enrollment or funding to continue the clinical trial.

Additionally, changes in regulatory requirements and guidance may occur, and we may need or otherwise determine to amend clinical trial protocols to reflect these changes. Each protocol amendment would require institutional review board review and approval, which may adversely impact the costs, timing or successful completion of the associated clinical trials. If we or our partners terminate or experience delays in the completion of any clinical trials, the commercial prospects for our products or product candidates may be harmed, and our ability to generate product revenues will be delayed. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval.

Risks Related to Our Dependence on Third Parties

Because we work with partners to develop, manufacture and commercialize linaclotide, we and our partners are dependent upon third parties, and our and our partners' relationships with those third parties, in our and our partners' efforts to obtain regulatory approval for, and to commercialize, linaclotide, as well as to comply with regulatory and other obligations with respect to linaclotide.

AbbVie played a significant role in the conduct of the clinical trials for linaclotide and in the subsequent collection and analysis of data, and AbbVie holds the new drug application, or NDA, for LINZESS. AbbVie also continues to play a significant role in the conduct of our pediatric program for linaclotide. In addition, we are commercializing LINZESS in the U.S. with AbbVie. AbbVie is also responsible for the development, regulatory approval and commercialization of linaclotide in countries worldwide other than Japan and China (including Hong Kong and Macau). AbbVie is commercializing LINZESS in Mexico and CONSTELLA in Canada as well as in certain countries including in Europe. Astellas and AstraZeneca are responsible for development and commercialization of LINZESS in Japan and China (including Hong Kong and Macau), respectively. Each of our partners for linaclotide also is responsible for active pharmaceutical ingredient, or API, finished drug product and finished goods manufacturing (including bottling and packaging) for its respective territories and distributing the finished goods to wholesalers. We and/or our partners have commercial supply agreements with independent third parties to manufacture the linaclotide API.

The integration of our efforts with our partners' efforts is subject to the uncertainty of the markets for pharmaceutical products in each partner's respective territories, and accordingly, these relationships must evolve to meet any new challenges, including those arising out of the COVID-19 pandemic, that arise in those regions. These integrated functions may not be carried out effectively and efficiently if we fail to communicate and coordinate with our linaclotide partners, and vice versa. Our linaclotide partnering strategy imposes obligations, risks and operational requirements on us as the central node in our global network of partners. If we do not effectively communicate with each partner and ensure that the entire network is making integrated and cohesive decisions focused on the global brand for linaclotide, linaclotide will not achieve its maximum commercial potential. Further, we have limited ability to control the amount or timing of resources that our partners devote to linaclotide, particularly in light of the impact of the COVID-19 pandemic on our partners' operations. If any of our partners fails to devote sufficient time and resources to linaclotide, or if its performance is substandard or otherwise hindered, it will delay the potential submission or approval of regulatory applications for linaclotide, as well as the manufacturing and commercialization of linaclotide in the particular territory. A material breach by any of our partners of our collaboration or license agreement with such partner, or a significant disagreement between us and a partner, could also delay the regulatory approval and commercialization of linaclotide, potentially lead to costly litigation, and could have a material adverse impact on our financial condition. Moreover, although we have non-compete restrictions in place with each of our linaclotide partners, they may have competitive products or relationships with other commercial entities, some of which may compete with us. If any of our partners competes with us or assists our competitors, it could harm our competitive position.

In addition, adverse event reporting requires significant coordination with our partners and third parties. We are the holder of the global safety database for linaclotide responsible for coordinating the safety surveillance and adverse event reporting efforts worldwide with respect to linaclotide; each of Astellas, AstraZeneca and AbbVie is responsible

for reporting adverse event information from its territory to us. If we fail to perform such activities and maintain the global safety database for linaclotide or if our partners do not report adverse events related to linaclotide, or fail to do so in a timely manner, we may not receive the information that we or our partners are required to report to the U.S. FDA or a foreign regulatory authority regarding such products. Furthermore, we or our partners may fail to adequately monitor, identify or investigate adverse events, or to report adverse events to the U.S. FDA or foreign regulatory authority accurately and within the prescribed timeframe. If we or our partners are unsuccessful in any of the foregoing due to poor process, execution, systems, oversight, communication, adjudication or otherwise, then we may suffer any number of consequences, including the imposition of additional restrictions on the use of linaclotide, removal of linaclotide from the market, criminal prosecution, the imposition of civil monetary penalties, seizure of such products, or delay in approval of future products.

We rely entirely on contract manufacturers, our partners and other third parties to manufacture linaclotide and our other product candidates and distribute linaclotide. If they are unable to comply with applicable regulatory requirements, unable to source sufficient raw materials, experience manufacturing or distribution difficulties, or are otherwise unable to manufacture and distribute sufficient quantities to meet demand, our development and commercialization efforts may be materially harmed.

We have no internal manufacturing or distribution capabilities. Instead, we rely on a combination of contract manufacturers and our partners to manufacture API, finished drug product and finished goods for linaclotide and our other product candidates. Each of our partners for linaclotide is responsible for API, finished drug product and finished goods manufacturing (including bottling and packaging) for its respective territories and distributing the finished goods to wholesalers. Should we, or any of our partners or any third-party manufacturers we or our partners engage, experience setbacks or challenges in our manufacturing efforts, including setbacks related to the COVID-19 pandemic described further below, our development and commercialization efforts may be materially harmed. We and/or our partners have commercial supply agreements with independent third parties to manufacture linaclotide API.

Each of our partners and the third-party manufacturers we or our partners engage must comply with GMP and other stringent regulatory requirements enforced by the U.S. FDA and foreign regulatory authorities in other jurisdictions. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation, which occur in addition to our and our partners' own quality assurance releases. Manufacturers of our products may be unable to comply with these GMP requirements and with other regulatory requirements. We have little control over compliance with these regulations and standards by our partners and the third-party manufacturers we or our partners engage.

Our partners and the third-party manufacturers we or our partners engage may experience problems with their respective manufacturing and distribution operations and processes, including, for example, quality issues, such as product specification and stability failures, procedural deviations, improper equipment installation or operation, utility failures, contamination, natural disasters and public health epidemics, including the COVID-19 pandemic. In addition, the raw materials necessary to make API for our products and product candidates are acquired from a limited number of sources. Any delay or disruption in the availability of raw materials or a change in raw material suppliers could result in production disruptions, delays or higher costs with consequent adverse effects on us.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in commercial production. These problems include difficulties with production costs and yields, quality control, including stability of the product and quality assurance testing, and shortages of qualified personnel, as well as compliance with federal, state and foreign regulations and the challenges associated with complex supply chain management. Even if our partners or the third-party manufacturers we or our partners engage do not experience problems and commercial manufacturing is achieved, their maximum or available manufacturing capacities may be insufficient to meet commercial demand. Finding alternative manufacturers or adding additional manufacturers requires a significant amount of time and involves significant expense. New manufacturers would need to develop and implement the necessary production techniques and processes, which along with their facilities, would need to be inspected and approved by the regulatory authorities in each applicable territory.

If our partners or the third-party manufacturers we or our partners engage fail to adhere to applicable GMP or other regulatory requirements, experience delays or disruptions in the availability of raw materials or experience manufacturing or distribution problems, we will suffer significant consequences, including product seizures or recalls,

loss of product approval, fines and sanctions, reputational damage, shipment delays, inventory shortages, inventory write-offs and other product-related charges and increased manufacturing costs. If we experience any of these results, or if maximum or available manufacturing capacities are insufficient to meet demand, our and our partners' development or commercialization efforts may be materially harmed.

If any of our linaclotide partners undergoes a change of control or in management, this may adversely affect our collaborative relationship or the success of the commercialization of linaclotide in the U.S. or in the other countries where it is approved, or the ability to achieve regulatory approval, launch and commercialize linaclotide in other territories.

We work jointly and collaboratively with partners on many aspects of the development, manufacturing and/or commercialization of linaclotide. In doing so, we have established relationships with several key members of the management teams of our linaclotide partners in functional areas such as development, quality, regulatory, drug safety and pharmacovigilance, operations, marketing, sales, field operations and medical science. Further, the success of our collaborations is highly dependent on the resources, efforts and skills of our partners and their key employees. As we and our partners develop and commercialize linaclotide in the U.S. and the other countries where it is approved, and develop, launch and commercialize linaclotide in other parts of the world, the drug's success becomes more dependent on us maintaining highly collaborative and well aligned partnerships. In May 2020, AbbVie announced the completion of its acquisition of Allergan plc. Our collaboration, now with AbbVie, for the development and commercialization of linaclotide in North America, and our license, now to AbbVie, to develop and commercialize linaclotide in all countries worldwide other than China (including Hong Kong and Macau) and Japan, remain in effect. In connection with this transaction, we continue to engage with AbbVie to reestablish relationships and confirm alignment, including on our development and commercialization strategy for linaclotide. Any failure to do so could adversely affect the development and commercialization of linaclotide. If any of our linaclotide partners undergoes a change of control or in management, we would similarly need to reestablish many relationships and confirm alignment, including on our development and commercialization strategy for linaclotide. Further, in connection with any change of control or change in management, there is inherent uncertainty and disruption in operations, which could result in distraction, inefficiencies, and misalignment of priorities. As a result, in the event of a change of control or in management at one of our linaclotide partners, we cannot be sure that we will be able to successfully execute on our development and commercialization strategy for linaclotide in an effective and efficient manner and without disruption or reduced performance. Finally, any change of control or in management may result in a reprioritization of linaclotide within a partner's portfolio, or such partner may fail to maintain the financial or other resources necessary to continue supporting its portion of the development, manufacturing or commercialization of linaclotide.

If any of our linaclotide partners undergoes a change of control and the acquirer either (i) is unable to perform such partner's obligations under its collaboration or license agreement with us or (ii) does not comply with the divestiture or certain other provisions of the applicable agreement, we have the right to terminate the collaboration or license agreement and reacquire that partner's rights with respect to linaclotide. If we elect to exercise these rights in such circumstances, we will need to either establish the capability to develop, manufacture and commercialize linaclotide in that partnered territory on our own or we will need to establish a relationship with a new partner. We have assembled a team that represents the functional areas necessary to support the commercialization of LINZESS in the U.S. If AbbVie was subject to a change of control that allowed us to further commercialize LINZESS in the U.S. on our own, and we chose to do so, we would need to enhance each of these functional aspects, as well as develop others, to replace the capabilities that AbbVie was previously providing to the collaboration. Any such transition might result in a period of reduced efficiency or performance by our operations and commercialization teams, which could adversely affect our ability to commercialize LINZESS.

We do not have certain operational capabilities outside of the U.S. If AbbVie, Astellas or AstraZeneca was subject to a change of control that allowed us to continue linaclotide's development or commercialization anywhere outside of the U.S. on our own, and we chose to do so rather than establishing a relationship with a new partner, we would need to build operational capabilities in the relevant territory. In any of these situations, the development and commercialization of linaclotide could be negatively impacted.

Risks Related to Regulatory, Legal and Compliance Matters

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

The use of our product candidates in clinical trials and the sale of our approved products, including the sale of linaclotide, expose us to product liability claims. If we do not successfully defend ourselves against product liability claims, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- decreased demand for approved products;
- impairment of our business reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- litigation costs;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- loss of revenues; and
- the inability to commercialize our product candidates.

We currently have product liability insurance coverage for the commercial sale of our products and for the clinical trials of our product candidates which is subject to industry-standard terms, conditions and exclusions. Our insurance coverage may not be sufficient to reimburse us for expenses or losses associated with claims. 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. On occasion, large judgments have been awarded in lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims could cause our stock price to decline and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

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

Physicians are permitted to prescribe drug products and medical devices for uses that are not described in the product's labeling and that differ from those approved by the U.S. FDA or other applicable regulatory agencies. Such "off-label" uses are common across medical specialties. Although the U.S. FDA and other regulatory agencies do not regulate a physician's choice of treatments, the U.S. FDA and other regulatory agencies do restrict manufacturer communications on off-label use. Companies are not permitted to promote drugs or medical devices for off-label uses or to promote unapproved drugs or medical devices. Accordingly, we do not permit promotion of any product that we develop, license, commercialize, promote, co-promote or otherwise partner prior to approval or for any indication, population or use not described in or consistent with such product's label. The U.S. FDA and other regulatory and enforcement authorities actively enforce laws and regulations prohibiting promotion of off-label uses and the promotion of products for which marketing approval has not been obtained. A company that is found to have promoted off-label uses will be subject to significant liability, including civil and administrative remedies as well as criminal sanctions. Even if it is later determined that we were not in violation of these laws, we may be faced with negative publicity, incur significant expenses defending our actions and have to divert significant management resources from other matters.

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

in place a robust compliance program, which is designed to ensure that all such activities are performed in a legal and compliant manner, we cannot be certain that our program will address all areas of potential exposure and the risks in this area cannot be entirely eliminated.

If we fail to comply with healthcare and other regulations, we could face substantial penalties and our business, operations and financial condition could be adversely affected.

The products that we promote are marketed in the U.S. and/or covered by federal healthcare programs, and, as a result, certain federal and state healthcare laws and regulations pertaining to product promotion, fraud and abuse, privacy and price reporting and payment are applicable to, and may affect, our business. These laws and regulations include:

- federal healthcare program anti-kickback laws, which prohibit, among other things, persons from offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual for, or the purchasing or ordering of, a good or service for which payment may be made under federal healthcare programs such as Medicare and Medicaid;

- federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, information or claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent, and which may apply to us for reasons including providing coding and billing advice to customers;

- the federal Health Insurance Portability and Accountability Act of 1996, which prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters and which also imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information on certain types of entities, which include many healthcare providers with whom we interact and health plans with which we may interact;

- the Federal Food, Drug, and Cosmetic Act, which among other things, strictly regulates drug product and medical device marketing, prohibits manufacturers from marketing such products prior to approval or for off-label use and regulates the distribution of samples;

- federal laws, including the Medicaid Drug Rebate Program, that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under government healthcare programs;

- the so-called "federal sunshine" law, which requires pharmaceutical and medical device companies to monitor and report certain financial interactions with physicians, certain non-physician practitioners and teaching hospitals to the federal government for re-disclosure to the public; and

- state law equivalents of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, state transparency laws, state laws limiting interactions between pharmaceutical manufacturers and members of the healthcare industry, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by federal laws, thus complicating compliance efforts.

We also are subject to the U.S. Foreign Corrupt Practices Act which prohibits corporations and individuals from paying, offering to pay, or authorizing the payment of anything of value to any foreign government official, government staff member, political party, or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity, related to any ex-U.S. activities, as well as other similar anti-bribery laws in any other country in which we may do business.

In addition, we may be subject to privacy and security laws in the various jurisdictions, both inside and outside the U.S., in which we operate, obtain or store personally identifiable information. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. For example, we are subject to the California Consumer

Privacy Act, or CCPA, as amended by the California Privacy Rights Act, or CPRA, which became effective on January 1, 2023 (the CPRA, together with CCPA, the California Privacy Law). The California Privacy Law gives California consumers (defined to include all California residents) certain rights regarding personal information collected about them; the California Privacy Law also imposes certain obligations and limitations on companies regarding the collection, use, selling or sharing (as defined in the California Privacy Law) of personal information collected from or about California consumers.

The compliance obligations imposed by the California Privacy Law, and other applicable privacy laws, have required us to revise our operations. Breaches of applicable data protection requirements may result in substantial fines and other regulatory penalties, as well as confer a private right of action on consumers and their representatives for breaches of certain data protection requirements. We expect to be subject to additional privacy laws at both the U.S. state level and abroad as many jurisdictions either recently have data privacy legislation or are considering enacting such legislation to which we may become subject. Achieving and sustaining compliance with applicable international, federal and state privacy, security, fraud and reporting laws may prove time-consuming and costly.

If our operations are found to be in violation of any of the laws described above or any other laws, rules or regulations that apply to us, we will be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could 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, rules or regulations, we cannot be certain that our program will address all areas of potential exposure and the risks in this area cannot be entirely eliminated, particularly because the requirements and government interpretations of the requirements in this space are constantly evolving. Any action against us for violation of these laws, rules or regulations, 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, as well as damage our business or reputation.

Healthcare reform and other governmental and private payor initiatives may have an adverse effect upon, and could prevent, our products' or product candidates' commercial success.

The U.S. government and individual states have been aggressively pursuing healthcare reform designed to impact delivery of, and/or payment for, healthcare, which include initiatives intended to reduce the cost of healthcare. For example, in March 2010, the U.S. Congress enacted the Patient Protection and Affordable Care Act, as modified by the Health Care and Education Reconciliation Act, or the ACA, which, among other things, expanded healthcare coverage through Medicaid expansion and the implementation of the individual health insurance mandate; included changes to the coverage and reimbursement of drug products under government healthcare programs; imposed an annual fee on manufacturers of branded drugs; and expanded government enforcement authority. We face uncertainties because there have been, and may be additional, federal legislative and administrative efforts to repeal, substantially modify or invalidate some or all of the provisions of the ACA. Such efforts may lead to fewer Americans having more comprehensive health insurance compliant with the ACA, even in the absence of legislative repeal. For example, tax reform legislation was enacted at the end of 2017 that eliminated the tax penalty for individuals who do not maintain sufficient health insurance coverage beginning in 2019. The ACA has also been subject to judicial challenge. Beyond the ACA, there have been ongoing legislative and administrative and other health care reform efforts. Some healthcare reform efforts affect pricing or payment for drug products or the healthcare industry more generally. Drug pricing and payment reform was a focus of the Trump Administration and has been a focus of the Biden Administration. For example, federal legislation enacted in 2021 eliminates a statutory cap on Medicaid drug rebate program rebates effective January 1, 2024. As another example, the IRA contains various drug pricing and payment provisions. Among other provisions, the IRA imposes a yearly cap ($2,000 in 2025) on out-of-pocket prescription drug costs in Medicare Part D, implements a new Medicare Part D manufacturer discount drug program in 2025, requires manufacturers to pay a rebate to the federal government if prices for single-source drugs and biologicals covered under Medicare Part B and nearly all covered drugs under Part D increase faster than the rate of inflation and, in 2026, creates a drug price negotiation program under which the prices for certain high Medicare spend drugs and biologicals without generic or biosimilar competition will be limited by a cap that is defined by reference to, among other things, a specified non-federal average manufacturer price. The effect of IRA on our business and the healthcare industry in general is not yet known.

Some of the health care reform changes have been and may continue to be subject to revisions to regulations under the federal anti-kickback statute that would remove protection for traditional Medicare Part D discounts offered by

pharmaceutical manufacturers to pharmacy benefit managers and health plans. Pursuant to court order, the removal was delayed, and the IRA further delayed implementation of the rule until January 1, 2032. Adoption of new healthcare reform legislation at the federal or state level could negatively affect demand for, or pricing of, our products or product candidates if approved for sale.

In addition, other legislative changes have been adopted that could have an adverse effect upon, and could prevent, our products' or product candidates' commercial success. For example, the Budget Control Act of 2011, as amended, or the Budget Control Act, includes provisions intended to reduce the federal deficit, including reductions in Medicare payments to providers through 2031 (except May 1, 2020 to March 31, 2022). Any significant spending reductions affecting Medicare, Medicaid or other publicly funded or subsidized health programs, or any significant taxes or fees imposed as part of any broader deficit reduction effort or legislative replacement to the Budget Control Act, or otherwise, could have an adverse impact on our anticipated product revenues.

In addition to governmental efforts in the U.S., foreign jurisdictions as well as private health insurers and managed care plans are likely to continue challenging manufacturers' ability to obtain reimbursement, as well as the level of reimbursement, for pharmaceuticals and other healthcare-related products and services. These cost-control initiatives could significantly decrease the available coverage and the price we might establish for our products, which would have an adverse effect on our financial results.

The Food and Drug Administration Amendments Act of 2007 also provides the U.S. FDA enhanced post- marketing authority, including the authority to require post-marketing studies and clinical trials, labeling changes based on new safety information, and compliance with risk evaluation and mitigation strategies approved by the U.S. FDA. We and AbbVie have established a nonclinical and clinical post-marketing plan with the U.S. FDA to understand the safety and efficacy of LINZESS in pediatrics. The U.S. FDA's exercise of this authority has resulted (and is expected to continue to result) in increased development-related costs following the commercial launch of our products, and could result in potential restrictions on the sale and/or distribution of our products, even in such products' approved indications and patient populations.

Risks Related to the Separation of Cyclerion

We may be exposed to claims and liabilities as a result of the separation of Cyclerion.

On April 1, 2019, we distributed all of the outstanding shares of Cyclerion Therapeutics, Inc., or Cyclerion, common stock to Ironwood stockholders in connection with the separation of our soluble guanylate cyclase business, or the Separation. In connection with the distribution, we entered into a separation agreement and various other agreements, including a tax matters agreement and an employee matters agreement. These agreements governed the separation and distribution as well as the relationship between us and Cyclerion, including with respect to potential tax-related losses associated with the separation and distribution.

The separation agreement provides for indemnification obligations designed to make Cyclerion financially responsible for many liabilities that may exist relating to its business activities, whether incurred prior to or after the distribution, including any pending or future litigation, but we cannot guarantee that Cyclerion will be able to satisfy its indemnification obligations. It is also possible that a court would disregard the allocation agreed to between us and Cyclerion and require us to assume responsibility for obligations allocated to Cyclerion. Third parties could also seek to hold us responsible for any of these liabilities or obligations, and the indemnity rights we have under the separation agreement may not be sufficient to fully cover all of these liabilities and obligations. Even if we are successful in obtaining indemnification, we may have to bear costs temporarily. In addition, our indemnity obligations to Cyclerion, including those related to assets or liabilities allocated to us, may be significant. These risks could negatively affect our business, financial condition or results of operations.

If the distribution of the shares of Cyclerion common stock in connection with the Separation is not generally tax- free for U.S. federal income tax purposes, we and our stockholders could be subject to significant tax liabilities.

The distribution, together with certain related transactions, is intended to qualify for tax-free treatment to us and our stockholders for U.S. federal income tax purposes. We received a favorable private letter ruling from the Internal Revenue Service, or IRS, under the pilot program established in Revenue Procedure 2017-52 relating to the U.S. federal income tax treatment of the distribution. Consistent with the guidelines set forth in Revenue Procedure 2017-52, the IRS private letter ruling does not cover all of the issues that are relevant to determining whether the distribution is generally

tax free for U.S. federal income tax purposes. Accordingly, completion of the distribution was conditioned upon, among other things, our receipt of an opinion from an outside tax advisor that the distribution will qualify as a transaction that is generally tax-free to both us and our stockholders for U.S. federal income tax purposes under Sections 355 and 368(a)(1)(D) of the Internal Revenue Code. The private letter ruling and opinion were based on and relied on, among other things, certain facts and assumptions, as well as certain representations, statements and undertakings from us and Cyclerion (including those relating to the past and future conduct of us and Cyclerion). If any of these facts, assumptions, representations, statements or undertakings is, or becomes, inaccurate or incomplete, or if we or Cyclerion breach any of our respective covenants relating to the distribution, the IRS private letter ruling and any tax opinion may be invalid. Moreover, the opinion is not binding on the IRS or any courts. Accordingly, notwithstanding receipt of the IRS private letter ruling and the opinion, the IRS could determine that the distribution and certain related transactions should be treated as taxable transactions for U.S. federal income tax purposes.

If the distribution, together with certain related transactions, fails to qualify as a transaction that is generally tax-free under Sections 355 and 368(a)(1)(D) of the Internal Revenue Code, in general, for U.S. federal income tax purposes, we would recognize taxable gain with respect to Cyclerion's distributed common stock and our stockholders who received shares of Cyclerion common stock in the distribution would be subject to tax as if they had received a taxable distribution equal to the fair market value of such shares.

Risks Related to Intellectual Property

Limitations on our ability to obtain patent protection and/or the patent rights relating to our products and our product candidates may limit our ability to prevent third parties from competing against us.

Our success depends on our ability to obtain and maintain sufficient patent protection for our products and product candidates, preserve our trade secrets, prevent third parties from infringing upon our proprietary rights and operate without infringing upon the proprietary rights of others.

The strength of patents in the pharmaceutical industry involves complex legal and scientific questions and can be uncertain. Patent applications in the U.S. and most other countries are confidential for a period of time until they are published, and publication of discoveries in scientific or patent literature typically lags actual discoveries by several months or more. As a result, we cannot be certain that we were the first to conceive inventions covered by our patents and pending patent applications or that we were the first to file patent applications for such inventions. In addition, we cannot be certain that our patent applications will be granted, that any issued patents will adequately protect our intellectual property, or that such patents will not be challenged, narrowed, invalidated or circumvented.

We have several issued patents in the U.S. related to LINZESS, including a LINZESS composition of matter and methods of use patent (U.S. Patent 7,304,036) expiring in 2026. Additional U.S. patents related to LINZESS include multiple patents relating to our commercial, room temperature stable formulations of the 72 mcg, 145 mcg and 290 mcg doses of linaclotide and methods of using these formulations, the latest of which expires in the early 2030s, as well as other patents covering processes for making LINZESS, formulations thereof, and molecules related to LINZESS. Although none of these issued patents currently is subject to a patent reexamination or review, we cannot guarantee that they will not be subject to reexamination or review by the U.S. Patent and Trademark Office, or the USPTO, in the future. We believe in the strength of our LINZESS patent portfolio and that we have sufficient freedom to operate; however, if any of our present or future patents is challenged, narrowed, invalidated or circumvented, or our pending patent applications are not granted, our ability to prevent third parties from competing with LINZESS could be limited and our business and financial results may be materially harmed.

Furthermore, the America Invents Act, which was signed into law in 2011, has made several major changes in the U.S. patent statutes. These changes permit third parties to challenge our patents more easily and create uncertainty with respect to the interpretation and practice of U.S. patent law. Moreover, the U.S. Supreme Court has ruled on several patent cases that narrow the scope of patent protection available and weakening the rights of patent owners in certain circumstances. Depending on the impact of these decisions and other actions by the U.S. Congress, the federal courts, the USPTO, and their foreign counterparts, the laws and regulations governing patents may change, or their interpretation or implementation may change, in unpredictable ways that could impact, potentially adversely, our ability to obtain new patents or to enforce and defend patents that we have already obtained or that we might obtain in the future. For example, such changes may increase the costs and complexity associated with obtaining, enforcing or defending our patents, including in abbreviated new drug application, or ANDA, litigation.

We also rely upon unpatented trade secrets, unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our employees and our partners and consultants. We also have agreements with our employees and selected consultants that obligate them to assign their inventions to us. It is possible, however, that technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees and consultants that are parties to these agreements breach or violate the terms of these agreements, we may not have adequate remedies, and we could lose our trade secrets through such breaches or violations. Additionally, our trade secrets could otherwise become known or be independently discovered by our competitors.

In addition, the laws of certain foreign countries do not protect proprietary rights to the same extent or in the same manner as the U.S., and, therefore, we or our partners may encounter problems in protecting and defending our intellectual property in certain foreign jurisdictions.

If we are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in such litigation could have a material adverse effect on our business.

Our commercial success depends on our ability, and the ability of our partners, to develop, manufacture, market and sell our products and use our proprietary technologies without infringing the proprietary rights of third parties. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we and our partners are developing products. As the biotechnology and pharmaceutical industry expands and more patents are issued, the risk increases that our potential products may give rise to claims of infringement of the patent rights of others. There may be issued patents of third parties of which we are currently unaware that may be infringed by LINZESS or our product candidates. Because patent applications can take many years to issue, there may be currently pending applications which may later result in issued patents that LINZESS or our product candidates may infringe.

We may be exposed to, or threatened with, litigation by third parties alleging that LINZESS or our product candidates infringe their intellectual property rights. If LINZESS or one of our product candidates is found to infringe the intellectual property rights of a third party, we or our partners could be enjoined by a court and required to pay damages and could be unable to develop or commercialize LINZESS or the applicable product candidate unless we obtain a license to the intellectual property rights. A license may not be available to us on acceptable terms, if at all. In addition, during litigation, the counterparty could obtain a preliminary injunction or other equitable relief which could prohibit us from making, using or selling our products, pending a trial on the merits, which may not occur for several years.

There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries generally. If a third party claims that we or our partners infringe its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business;

- substantial damages for infringement, which we may have to pay if a court decides that the product at issue infringes on or violates the third party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees;

- a court prohibiting us from selling our product unless the third party licenses its rights to us, which it is not required to do;

- if a license is available from a third party, we may have to pay substantial royalties, fees or grant cross- licenses to our intellectual property rights; and

- redesigning our products so they do not infringe, which may not be possible or may require substantial monetary expenditures and time.

We have received notices of Paragraph IV certifications related to LINZESS in conjunction with ANDAs filed by generic drug manufacturers, and we may receive additional notices from others in the future. We have, and may continue to, become involved in legal proceedings to protect or enforce intellectual property rights relating to our products and our product candidates, which could be expensive and time consuming, and unfavorable outcomes in such proceedings could have a material adverse effect on our business.

Competitors may infringe the patents relating to our products and our product candidates or may assert that such patents are invalid. To counter ongoing or potential infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. Litigation with generic manufacturers has become increasingly common in the biotechnology and pharmaceutical industries. In addition, in an infringement or invalidity proceeding, a court or patent administrative body may determine that a patent of ours is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question.

Generic drug manufacturers were first able to file ANDAs for generic versions of LINZESS in August 2016. When filing an ANDA for one of our products, a generic drug manufacturer may choose to challenge one or more of the patents that cover such product and seek to commercialize generic versions of one or more LINZESS doses. As such, we have brought, and may bring in the future, legal proceedings against generic drug manufacturers.

We and AbbVie have received Paragraph IV certification notice letters regarding ANDAs submitted to the U.S. FDA by generic drug manufacturers requesting approval to engage in commercial manufacture, use, sale and offer for sale of linaclotide capsules (72 mcg, 145 mcg and 290 mcg), proposed generic versions of our U.S. FDA-approved drug LINZESS. We filed patent infringement lawsuits against five companies making such ANDA filings and subsequently entered into settlement agreements with each of these filers. Frequently, innovators receive multiple ANDA filings. Consequently, we may receive additional notice letters regarding ANDAs submitted to the U.S. FDA (and we may receive amendments to those notice letters), but we may not become aware of these filings for several months after any such submission due to procedures specified under applicable U.S. FDA regulations.

After evaluation, we have in the past filed, and may, in the future, file patent infringement lawsuits or take other action against companies making ANDA filings. If a patent infringement suit has been filed within 45 days of receipt of a notice letter, the U.S. FDA is not permitted to approve any ANDA that is the subject of such lawsuit for 30 months from the date of the NDA holder's and patent owner's receipt of the ANDA filer's notice letter, or until a court decides that the relevant patents are invalid, unenforceable and/or not infringed. Additionally, the validity of the patents relating to our products and our product candidates may be challenged by third parties pursuant to administrative procedures introduced by the America Invents Act, specifically *inter partes* review, or IPR, and/or post grant review, or PGR, before the USPTO. Generic drug manufacturers may challenge our patents through IPRs or PGRs instead of or in addition to ANDA legal proceedings.

Patent litigation (including any lawsuits that we file against generic drug manufacturers in connection with the receipt of a notice letter), IPRs and PGRs involve complex legal and factual questions and we may need to devote significant resources to such legal proceedings. We can provide no assurance concerning the duration or the outcome of any such patent-related lawsuits or administrative proceedings, including any settlements or other resolutions thereof which could, in addition to other risks, result in a shortening of exclusivity periods. An adverse result in any litigation or defense proceedings could put one or more of the patents relating to our products and our product candidates at risk of being invalidated or interpreted narrowly, or could otherwise result in a loss of patent protection for the product or product candidate at issue, and could put our patent applications at risk of not issuing, which would materially harm our business. Upon any loss of patent protection for one of our products, or upon an "at-risk" launch (despite pending patent infringement litigation, before any court decision or while an appeal of a lower court decision is pending) by a manufacturer of a generic version of one of our patented products, our revenues for that product could be significantly reduced in a short period of time, which would materially and adversely affect our business.

Interference or derivation proceedings brought by the USPTO may be necessary to determine the priority of inventions with respect to the patents relating to our products and our product candidates and patent applications or those of our partners. An unfavorable outcome could require us to cease using the technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if a prevailing party does not offer us a license on terms that are acceptable to us. Litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distraction of our management and other employees. In addition, we may not be able to prevent, alone or with

our partners, misappropriation of our proprietary rights, particularly in countries where the laws may not protect those rights as fully as in the U.S.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, as well as the potential for public announcements of the results of hearings, motions or other interim proceeding or developments, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Risks Related to Our Finances and Capital Requirements

We incurred significant losses from our inception in 1998 through the year ended December 31, 2018, and we may incur losses in future periods.

In recent years, we have focused primarily on developing, manufacturing and commercializing linaclotide, as well as developing our other product candidates. We have financed our business to date primarily through the issuance of equity, our collaboration and license arrangements, and debt issuances, including our June 2015 issuance of our 2.25% Convertible Senior Notes that matured and were repaid in full on June 15, 2022, or the 2022 Convertible Notes, and our August 2019 issuance of our 0.75% Convertible Senior Notes due 2024, or the 2024 Convertible Notes, and our 1.50% Convertible Senior Notes due 2026, or the 2026 Convertible Notes (together with the 2024 Convertible Notes, the Convertible Senior Notes). We currently derive a significant portion of our revenue from our LINZESS collaboration with AbbVie for the U.S. We believe that the revenues from the LINZESS collaboration will continue to constitute a significant portion of our total revenue for the foreseeable future. Such revenue is highly dependent on LINZESS demand and other factors such as fluctuations in retail chains' and wholesalers' buying patterns and inventory levels, pricing and reimbursement. Our collaborative arrangements revenue outside of the U.S. has and may continue to fluctuate as a result of the timing and amount of royalties from sales of linaclotide in the markets in which it is currently approved, or any other markets where linaclotide receives approval, as well as clinical and commercial milestones received and recognized under our current and future strategic partnerships outside of the U.S.

Prior to the year ended December 31, 2019, we incurred net losses in each year since our inception in 1998. As of December 31, 2022, we had an accumulated deficit of $696.4 million. We cannot be certain that sales of our products, and the revenue from our other commercial activities will not fall short of our projections or be delayed. Further, we expect to continue to incur substantial expenses in connection with our efforts to commercialize linaclotide, research and develop our product candidates, and access externally developed products or product candidates. Because of the numerous risks and uncertainties associated with developing and commercializing pharmaceutical products, as well as those related to our expectations for our products and our other activities, we are unable to predict the extent of any future losses. Failure to achieve sustainable net income and maintain positive cash flows would have an adverse effect on stockholders' equity and working capital.

We may need additional funding and may be unable to raise capital when needed, which could cause us to delay, reduce or eliminate our corporate or product development or commercialization efforts.

We have previously raised funds to finance our operations through capital raising activities, including the sale of shares of our Class A Common Stock in public offerings and convertible and other debt issuances. However, marketing and selling gastrointestinal drugs, purchasing commercial quantities of pharmaceutical products, developing product candidates, conducting clinical trials and accessing externally developed products or product candidates are expensive and uncertain. Circumstances, our strategic imperatives, or opportunities to create or acquire new programs, as well as maturities, redemptions or repurchases of our outstanding debt securities, could require us to, or we may choose to, seek to raise additional funds. The amount and timing of our future funding requirements will depend on many factors, including, but not limited to:

- the level of underlying demand for our products by prescribers and patients in the countries in which they are approved;
- the costs associated with commercializing our products in the U.S.;
- the costs of establishing, maintaining and/or expanding sales, marketing, distribution, and market access capabilities for our products;

- the regulatory approval of linaclotide within new indications, populations and formulations, as well as the associated development and commercial milestones and royalties;
- the rate of progress, the cost of our clinical trials and the other costs associated with our development programs, including our post-approval nonclinical and clinical studies of linaclotide in pediatrics and our investment to enhance the clinical profile of LINZESS within IBS-C and CIC, as well as to study linaclotide in additional indications, populations and formulations to assess its potential to treat various conditions;
- the costs and timing of in-licensing additional products or product candidates or acquiring other complementary companies or assets;
- the achievement and timing of milestone payments and royalties due or payable under our collaboration and license agreements;
- the status, terms and timing of any collaboration, licensing, co-commercialization or other arrangements;
- the timing of any regulatory approvals of our product candidates;
- whether the holders of our Convertible Senior Notes hold the notes to maturity without conversion into our Class A Common Stock or cash and whether we are required to repurchase any of our Convertible Senior Notes prior to maturity upon a fundamental change, as defined in each of the indentures governing the Convertible Senior Notes; and
- whether we seek to redeem, repurchase or retire all or part of our outstanding debt through cash purchases and/or exchanges, in open market purchases, privately negotiated transactions, by tender offer or otherwise.

Additional funding may not be available on acceptable terms or at all. If adequate funds are not available, we may be required to delay or reduce the scope of our commercialization efforts, delay, reduce or eliminate one or more of our development programs or delay or abandon potential strategic opportunities.

Our ability to pay principal of and interest on our outstanding debt securities will depend in part on the receipt of payments from AbbVie under our collaboration agreement for North America.

In August 2019, we issued $200.0 million aggregate principal amount of our 2024 Convertible Notes bearing an annual interest rate of 0.75% and $200.0 million aggregate principal amount of our 2026 Convertible Notes bearing an annual interest rate of 1.50%, and we used a portion of the proceeds from this offering to repurchase $215.0 million aggregate principal amount of the 2022 Convertible Notes. The 2022 Convertible Notes matured and were repaid in full on June 15, 2022. Semi-annual payments on each of our 2024 Convertible Notes and 2026 Convertible Notes began on December 15, 2019. We expect that for the next few years, at a minimum, the net quarterly payments from AbbVie will be a significant source of cash flows from operations. If the cash flows derived from the net quarterly payments that we receive from AbbVie under the collaboration agreement for North America are insufficient on any particular payment date to fund the interest payment on our outstanding indebtedness, at a minimum, we will be obligated to pay the amounts of such shortfall out of our general funds. The determination of whether AbbVie will be obligated to make a net quarterly payment to us in respect of a particular quarterly period is a function of the revenue generated by LINZESS in the U.S. as well as the development, manufacturing and commercialization expenses incurred by each of us and AbbVie under the collaboration agreement for North America. Accordingly, since we cannot guarantee that our company will maintain net income or positive cash flows, we cannot provide assurances for any particular quarterly period that (i) we will have the available funds to fund the interest payment on our outstanding indebtedness, at a minimum, in the event that there is a deficiency in the net quarterly payment received from AbbVie, (ii) there will be a net quarterly payment from AbbVie at all or (iii) we will not also be required to make a true-up payment to AbbVie under the collaboration agreement for North America.

Our indebtedness could adversely affect our financial condition or restrict our future operations.

As of December 31, 2022, we had total indebtedness of $400.0 million and available cash and cash equivalents of $656.2 million. Our indebtedness, combined with our other financial obligations and contractual commitments, could have important consequences on our business, including:

- limiting our ability to obtain additional financing to fund future working capital, capital expenditures or other general corporate purposes, including product development, commercialization efforts, research and development activities, strategic arrangements, acquisitions and refinancing of our outstanding debt;
- requiring a substantial portion of our cash flows to be dedicated to debt service payments instead of other purposes, thereby reducing the amount of cash flows available for working capital, capital expenditures, corporate transactions and other general corporate purposes;
- increasing our vulnerability to adverse changes in general economic, industry and competitive conditions;
- limiting our flexibility in planning for and reacting to changes in the industry in which we compete;
- placing us at a disadvantage compared to other, less leveraged competitors or competitors with comparable debt at more favorable interest rates; and
- increasing our cost of borrowing.

If we do not generate sufficient cash flows from operations or if future borrowings are not available to us in an amount sufficient to pay our indebtedness, including payments of principal when due on our outstanding indebtedness or, in the case of our Convertible Senior Notes, in connection with a transaction involving us that constitutes a fundamental change under the indentures governing the Convertible Senior Notes, or to fund our liquidity needs, we may be forced to refinance all or a portion of our indebtedness on or before the maturity dates thereof, sell assets, reduce or delay currently planned activities or curtail operations, seek to raise additional capital or take other actions. We may not be able to execute any of these actions on commercially reasonable terms or at all. This, together with any of the factors described above, could materially and adversely affect our business, financial condition and results of operations.

In addition, while none of the indentures governing our Convertible Senior Notes includes covenants restricting the operation of our business except in certain limited circumstances, in the event of a default under any of the Convertible Senior Notes, the applicable noteholders or the trustee under the indenture governing the applicable Convertible Senior Notes may accelerate our payment obligations under such Convertible Senior Notes, which could have a material adverse effect on our business, financial condition and results of operations. We are also required to offer to repurchase the Convertible Senior Notes upon the occurrence of a fundamental change, which could include, among other things, any acquisition of our company (other than an acquisition in which at least 90% of the consideration is Class A Common Stock listed on The Nasdaq Global or Global Select Market or The New York Stock Exchange), subject to the terms of each of the indenture governing the Convertible Senior Notes. The repurchase price must be paid in cash, and this obligation may have the effect of discouraging, delaying or preventing an acquisition of our company that would otherwise be beneficial to our security holders.

Each of the indentures governing our Convertible Senior Notes also includes cross-default features providing that certain failures to pay for outstanding indebtedness would result in a default under the indentures governing our Convertible Senior Notes. In the event of such default, the trustee or noteholders could elect to declare all amounts outstanding to be immediately due and payable under the applicable indenture, which could have a material adverse effect on our business, financial condition and results of operations.

The note hedge warrant transactions entered into in connection with our 2022 Convertible Notes and capped call transactions entered into in connection with our 2024 Convertible Notes and our 2026 Convertible Notes may affect the value of our Class A Common Stock.

In connection with the issuance of our 2022 Convertible Notes, we entered into convertible note hedge transactions, or the Convertible Note Hedges, and separate note hedge warrant transactions, or the Note Hedge Warrants, with certain financial institutions. In June 2022, the Convertible Note Hedges terminated unexercised upon expiry. The

Note Hedge Warrants are exercisable at a strike price of $18.82 over the 150 trading day period beginning on September 15, 2022. Additionally, in connection with the issuance of our 2024 Convertible Notes and our 2026 Convertible Notes, we entered into capped call transactions, or the Capped Calls, with certain financial institutions. These transactions are expected generally to reduce the potential dilution upon any conversion of our 2024 Convertible Notes or our 2026 Convertible Notes, as applicable, or offset any cash payments we are required to make in excess of the principal amount of converted Convertible Senior Notes, as the case may be.

In connection with these transactions, the financial institutions likely purchased our Class A Common Stock in secondary market transactions and entered into various over-the-counter derivative transactions with respect to our Class A Common Stock. These entities or their affiliates are likely to modify their hedge positions from time to time prior to conversion or maturity of the 2024 Convertible Notes and the 2026 Convertible Notes, as applicable, by purchasing and selling shares of our Class A Common Stock or other instruments they may wish to use in connection with such hedging. Any of these activities could adversely affect the value of our Class A Common Stock and, as a result, the number of shares and the value of the Class A Common Stock noteholders will receive upon conversion of the 2024 Convertible Notes, or the 2026 Convertible Notes, as applicable. In addition, under certain circumstances the counterparties have the right to terminate the Capped Calls and settle the Note Hedge Warrants on terms set forth in the applicable confirmations, which may result in us not receiving all or any portion of the anticipated benefit of the Capped Calls. If the price of our Class A Common Stock increases such that the hedge transactions settle in our favor, we could also be exposed to credit risk related to the counterparties to the Capped Calls, which would limit or eliminate the benefit of such transactions to us.

Our quarterly and annual operating results may fluctuate significantly.

We expect our operating results to be subject to frequent fluctuations. Our net income (loss) and other operating results will be affected by numerous factors, including:

- the level of underlying demand and price for our products in the countries in which they are approved;
- retail chains' and wholesalers' buying patterns and inventory levels with respect to our products;
- the costs associated with commercializing our products in the U.S.;
- the achievement and timing of milestone payments and royalties due or payable under our collaboration and license agreements;
- our execution of any collaboration, partnership, licensing or other strategic arrangements, and the timing of payments we may make or receive under these arrangements;
- any impairments of assets or goodwill, and associated write-downs;
- any variations in the level of expenses related to our development programs;
- addition or termination of clinical trials;
- any impact on taxes or changes in tax rules;
- regulatory developments affecting our products and product candidates;
- any material lawsuit in which we may become involved; and
- the impact of the COVID-19 pandemic or other public health epidemics, including containment or mitigation measures, or natural disasters.

If our operating results fall below the expectations of investors or securities analysts for any of the foregoing reasons or otherwise, the price of our Class A Common Stock could decline substantially. Furthermore, any quarterly or annual fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially.

Our ability to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future tax payments is limited by provisions of the Internal Revenue Code, and it is possible that our net operating loss and tax credit carryforwards may expire before we generate sufficient taxable income to use such carryforwards, or that certain transactions or a combination of certain transactions may result in material additional limitations on our ability to use our net operating loss and tax credit carryforwards.

Prior to the year ended December 31, 2019, we incurred significant net losses since our inception. To the extent that we do not generate federal and state taxable income in the future, unused net operating loss and tax credit carryforwards will carry forward to offset future taxable income, if any, until the date, if any, on which such unused carryforwards expire. Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, contain rules that limit the ability of a company that undergoes an ownership change, which is generally any change in ownership of more than 50% of its stock over a three-year period, to utilize its net operating loss and tax credit carryforwards and certain built-in losses recognized in years after the ownership change. These rules generally operate by focusing on ownership changes involving stockholders owning directly or indirectly 5% or more of the stock of a company and any change in ownership arising from a new issuance of stock by the company. Generally, if an ownership change occurs, the yearly taxable income limitation on the use of net operating loss and tax credit carryforwards and certain built-in losses is equal to the product of the applicable long term tax exempt rate and the value of the company's stock immediately before the ownership change. Certain future equity offerings or strategic transactions, if any, could potentially result in a 50% or greater change of control.

If we do not generate sufficient taxable income prior to the expiration, if any, of the applicable carryforwards or if the carryforwards are subject to the limitations described above, we may be unable to offset our taxable income with losses, or our tax liability with credits, before such losses and credits expire and therefore would incur larger federal or state income tax liability. We have completed several financings since our inception which may have resulted in a change in control as defined by Section 382, or could result in a change in control in the future.

General Risk Factors

Public health emergencies, epidemics, or pandemics, such as the COVID-19 pandemic, impact our business.

The COVID-19 pandemic has impacted, and may continue to impact, our business and operations in a number of ways. Factors that will influence the impact on our business and operations include the duration and extent of the pandemic, the duration and extent of imposed or recommended containment and mitigation measures, periodic spikes in infection rates, new strains or variants of the virus that cause outbreaks of COVID-19, the rate of vaccinations, the availability and efficacy of vaccines for new strains or variants and vaccine mandates and the general economic consequences of the pandemic. Addressing the impacts of the COVID-19 pandemic has required, and may continue to require significant time and has diverted, and may divert in the future, the attention of our management, other employees and our board of directors.

During 2022, in-person work practices for customer-facing employees returned to near pre-COVID 19 levels. However, new strains or variants of the virus that cause outbreaks of COVID-19 may present risks to successful execution of the commercial operating plan for LINZESS due in part to limitations on in-person work practices for our customer facing employees. Should we be unable to evolve with any further changes in the commercial landscape, we may be unable to maintain or grow our revenues from the commercialization of LINZESS or successfully commercialize future products. In addition, headquarters employees have the option to work primarily remotely. If our employees are unable to work from home effectively, or if the COVID-19 pandemic otherwise impacts employees' ability to work, for example due to containment and mitigation measures related to the COVID-19 pandemic, illness, lack of resources or inadequate technology, or restrictions, closures or other limits on school and other childcare options, our business will be materially harmed. Specifically, new or continuing limits on the ability of our customer-facing employees to meet with physicians and patients to visit healthcare providers and pharmacists (including due to continued or future remote working arrangements, containment and mitigation measures that limit access to customers or other restrictions related to the COVID-19 pandemic) may have an extended negative impact on LINZESS sales.

In addition, changes in insurance coverage or reimbursement levels by governmental authorities, private health insurers and other third-party payors, or changes in the type of such coverage held by patients (including changes from commercial insurance to Medicaid) or the loss of coverage by some patients, due to the impacts of the COVID-19

pandemic (including the related increase in unemployment in the U.S.) may negatively impact our revenue from LINZESS. Moreover, continuing impacts to healthcare access or administration (including, for example, limitations on medications or procedures deemed "non-essential" and reduced interaction between patients and physicians) due to the COVID-19 pandemic may impact demand for LINZESS and materially harm our business and commercialization efforts.

Revenue from LINZESS sales or the progression of our trials will be affected should the COVID-19 pandemic cause significant disruptions to manufacturing operations or supply of LINZESS to the U.S. or API, finished drug product or finished goods for linaclotide or our product candidates, for example due to impacts of the COVID-19 pandemic on personnel involved in the manufacturing and supply chain, international travel and shipping restrictions, inability of vendors to provide services, closed manufacturing sites, or any other disruptions in the international supply chain. In addition, the COVID-19 pandemic has impacted enrollment in our clinical trials, and may impact clinical trial enrollment or participation in the future compared to pre-COVID-19 pandemic levels. In addition, the COVID-19 pandemic has impacted enrollment in our clinical trials and may impact clinical trial enrollment or participation in the future, for example, due to suspension of in-person procedures required for enrollment or lower or discontinued patient participation compared to pre-COVID-19 pandemic levels as a result of new strains or variants

The spread of COVID-19 continues to disrupt the U.S. healthcare and healthcare regulatory system. Capital markets in the U.S. and around the world may be negatively impacted and can potentially harm our business, including our ability to obtain future financing. The COVID-19 pandemic, including containment and mitigation measures, has impacted our business and operations, and could have a material adverse impact on our financial condition and results of operations in the future, including for an extended period of time.

We may not be able to manage our business effectively if we lose any of our current management team or if we are unable to attract, motivate and retain key personnel.

We may not be able to attract, motivate or retain qualified management and scientific, clinical, operations and commercial personnel due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the greater-Boston area. If we are not able to attract, motivate and retain necessary personnel to accomplish our business objectives, we will experience constraints that will significantly impede the achievement of our objectives.

We are highly dependent on the drug research, development, regulatory, commercial, financial and other expertise of our management, particularly Thomas A. McCourt, our chief executive officer; Sravan K. Emany, our senior vice president, chief financial officer; Andrew Davis, our senior vice president, chief business officer; John Minardo, our senior vice president, chief legal officer and secretary; Jason Rickard, our senior vice president, chief operating officer; and Michael Shetzline, our senior vice president, chief medical officer and head of research and drug development. Transitions in our senior management team or other key employees, or the unavailability of any such persons for any reason, can be inherently difficult to manage and may disrupt our operations or business or otherwise harm our business, for example due to the diversion of our board and management's time and attention and a decline in employee morale. In addition to the competition for personnel, the Boston area in particular is characterized by a high cost of living. As such, we could have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment efforts, which may or may not be successful.

We also have scientific and clinical advisors who assist us in formulating our product development, clinical strategies and our global supply chain plans, as well as sales and marketing advisors who have assisted us in our commercialization strategy and brand plan for our products. 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, or may have arrangements with other companies to assist in the development and commercialization of products that may compete with ours.

Security breaches and other disruptions to our information technology structure could compromise our information, disrupt our business and expose us to liability, which would cause our business and reputation to suffer.

In the ordinary course of our business, we collect, process and store sensitive data, including intellectual property, our proprietary business information and that of our suppliers and business partners, as well as personally identifiable information of our patients, clinical trial participants and employees. We also rely to a large extent on

information technology systems to operate our business, including to deliver our products. We have outsourced elements of our confidential information processing and information technology structure, and as a result, we are managing independent vendor relationships with third parties who may or could have access to our confidential information. Similarly, our business partners and other third-party providers possess certain of our sensitive data. The secure maintenance of this information is critical to our operations and business strategy. Despite our security measures, our large and complex information technology and infrastructure (and those of our partners, vendors and third-party providers) may be vulnerable to attacks by hackers or breached due to employee, partner, vendor or third-party error, malfeasance or other disruptions. We, our partners, vendors and other third-party providers could be susceptible to third party attacks on our, and their, information security systems, which attacks are of ever-increasing levels of sophistication and are made by groups and individuals with a wide range of motives and expertise, including organized criminal groups, hacktivists, nation states and others. While we have invested in information technology and security and the protection of confidential information, there can be no assurance that our efforts will prevent service interruptions or security breaches. Further, while some or all of our workforce, and those of our partners, vendors and other third-party providers, work remotely as a result of the COVID-19 pandemic or otherwise, we may have greater vulnerability to cyberattacks or other losses of confidential information, as well as interruptions in information technology systems. Any such interruptions, losses or breaches would substantially impair our ability to operate our business and would compromise our, or our partners, vendors and other third-party providers, networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, disrupt our operations, negatively impact our financial condition and damage our reputation, any of which could adversely affect our business. While we maintain cyber liability insurance, this insurance may not be sufficient to cover the financial or other losses that may result from an interruption or breach of our (or our partners', vendors' and third-party providers') systems.

Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control which could negatively impact the market price of our Class A Common Stock.

Provisions in our certificate of incorporation and bylaws may have the effect of delaying or preventing a change of control. These provisions include the following:

- Our board of directors has the right to elect directors to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors.

- Our board of directors may issue, without stockholder approval, shares of preferred stock. The ability to authorize preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to acquire us.

- Stockholders must provide advance notice to nominate individuals for election to the board of directors or to propose matters that can be acted upon at a stockholders' meeting. These provisions may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect such acquirer's own slate of directors or otherwise attempting to obtain control of our company.

- Our stockholders may not act by written consent. As a result, a holder, or holders, controlling a majority of our capital stock are not able to take certain actions outside of a stockholders' meeting.

- Special meetings of stockholders may be called only by the chairman of our board of directors, our chief executive officer or a majority of our board of directors. As a result, a holder, or holders, controlling a majority of our capital stock are not able to call a special meeting.

- A super-majority (80%) of the outstanding shares of Class A Common Stock are required to amend our bylaws, which make it more difficult to change the provisions described above.

In addition, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These and other provisions in our certificate of incorporation and our bylaws and in the Delaware General Corporation

Law could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors.

If we identify a material weakness in our internal control over financial reporting, it could have an adverse effect on our business and financial results and our ability to meet our reporting obligations could be negatively affected, each of which could negatively affect the trading price of our Class A Common Stock.

A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. Accordingly, a material weakness increases the risk that the financial information we report contains material errors.

We regularly review and update our internal controls, disclosure controls and procedures, and corporate governance policies. In addition, we are required under the Sarbanes-Oxley Act of 2002 to report annually on our internal control over financial reporting. Our system of internal controls, however well-designed and operated, is based in part on certain assumptions and includes elements that rely on information from third parties, including our partners. Our system can provide only reasonable, not absolute, assurances that the objectives of the system are met. If we, or our independent registered public accounting firm, determine that our internal controls over financial reporting are not effective, or we discover areas that need improvement in the future, these shortcomings could have an adverse effect on our business and financial results, and the price of our Class A Common Stock could be negatively affected.

Further, we are dependent on our partners for information related to our results of operations. Our net profit or net loss generated from the sales of LINZESS in the U.S. is partially determined based on amounts provided by AbbVie and involves the use of estimates and judgments, which could be modified in the future. We are highly dependent on our linaclotide partners for timely and accurate information regarding any revenues realized from sales of linaclotide in their respective territories, and in the case of AbbVie for the U.S., the costs incurred in developing and commercializing it in order to accurately report our results of operations. Our results of operations are also dependent on the timeliness and accuracy of information from any other licensing, collaboration or other partners we may have, as well as our and our partners' use of estimates and judgments. If we do not receive timely and accurate information or if estimated activity levels associated with the relevant collaboration or partnership at a given point in time are incorrect, whether the result of a material weakness or not, we could be required to record adjustments in future periods. Such adjustments could have an adverse effect on our financial results, which could lead to a decline in our Class A Common Stock price.

If we cannot conclude that we have effective internal control over our financial reporting, or if our independent registered public accounting firm is unable to provide an unqualified opinion regarding the effectiveness of our internal control over financial reporting, investors could lose confidence in the reliability of our financial statements, which could lead to a decline in our stock price. Failure to comply with reporting requirements could also subject us to sanctions and/or investigations by the SEC, The Nasdaq Stock Market or other regulatory authorities.

We expect that the price of our Class A Common Stock will fluctuate substantially.

The market price of our Class A Common Stock may be highly volatile due to many factors, including:

- the commercial performance of our products in the countries in which they are approved, as well as the costs associated with such activities;
- any third-party coverage and reimbursement policies for our products;
- market conditions in the pharmaceutical and biotechnology sectors;
- developments, litigation or public concern about the safety of our products or our potential products;
- announcements of the introduction of new products by us or our competitors;
- announcements concerning product development, including clinical trial results or timelines, or intellectual property rights of us or others;

- actual and anticipated fluctuations in our quarterly and annual operating results;
- deviations in our operating results from any guidance we may provide or the estimates of securities analysts;
- sales of additional shares of our Class A Common Stock or sales of securities convertible into Class A Common Stock or the perception that these sales might occur;
- any conversions of our Convertible Senior Notes into Class A Common Stock, exercises of the Note Hedge Warrants or activities undertaken by the counterparties to the Capped Calls;
- additions or departures of key personnel;
- developments concerning current or future collaboration, partnership, licensing or other strategic arrangements;
- discussion of us or our stock price in the financial or scientific press or in online investor communities; and
- the impact of the COVID-19 pandemic or other public health epidemics, including containment or mitigation measures, or natural disasters.

Our business could be negatively affected as a result of a proxy contest or certain other stockholder actions.

Responding to certain stockholder actions can be costly, disruptive and time-consuming, and could also impact our ability to attract, retain and motivate our employees. For example, a proxy contest for our annual meeting of stockholders relating to stockholder proposals or director nominees would require significant time and could divert the attention of our management, other employees and our board of directors. In addition, a proxy contest would require us to incur significant costs, including legal fees and proxy solicitation expenses. The realization of any of the risks described in these "Risk Factors" could have a dramatic and material adverse impact on the market price of our Class A Common Stock. In addition, class action litigation has often been instituted against companies whose securities have experienced periods of volatility. Any such litigation brought against us could result in substantial costs and a diversion of management attention, which could hurt our business, operating results and financial condition.

Item 1B. *Unresolved Staff Comments*

None.

Item 2. *Properties*

Our corporate headquarters and operations are located in Boston, Massachusetts, where, as of December 31, 2022, we occupied approximately 39,000 square feet of office space under our lease expiring in June 2030. We believe that our facilities are suitable and adequate for our needs for the foreseeable future.

Item 3. *Legal Proceedings*

None.

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***

Shares of our Class A Common Stock are traded on the Nasdaq Global Select Market under the symbol "IRWD." Our shares have been publicly traded since February 3, 2010. As of January 31, 2023, there were 34 stockholders of record of our Class A Common Stock. The number of record holders is based upon the actual number of holders registered on the books of the company at such date and does not include holders of shares in "street names" or persons, partnerships, associations, corporations or other entities identified in security position listings maintained by depositories.

Subject to preferences that may apply to any shares of preferred stock outstanding at the time, the holders of Class A Common Stock are entitled to share equally in any dividends that our board of directors may determine to issue from time to time. In the event a dividend is paid in the form of shares of common stock or rights to acquire shares of common stock, the holders of Class A Common Stock will receive Class A Common Stock, or rights to acquire Class A Common Stock, as the case may be.

We have never declared or paid any cash dividends on our capital stock, and we do not currently anticipate declaring or paying cash dividends on our capital stock in the foreseeable future. We currently intend to retain all of our future earnings, if any, to finance operations and any acquisitions of businesses, products and technologies or other strategic transactions. Any future determination relating to our dividend policy will be made at the discretion of our board of directors and will depend on a number of factors, including future earnings, capital requirements, financial conditions, future prospects, contractual restrictions and covenants and other factors that our board of directors may deem relevant.

The information required to be disclosed by Item 201(d) of Regulation S-K, "Securities Authorized for Issuance Under Equity Compensation Plans," is referenced under Item 12 of Part III of this Annual Report on Form 10-K.

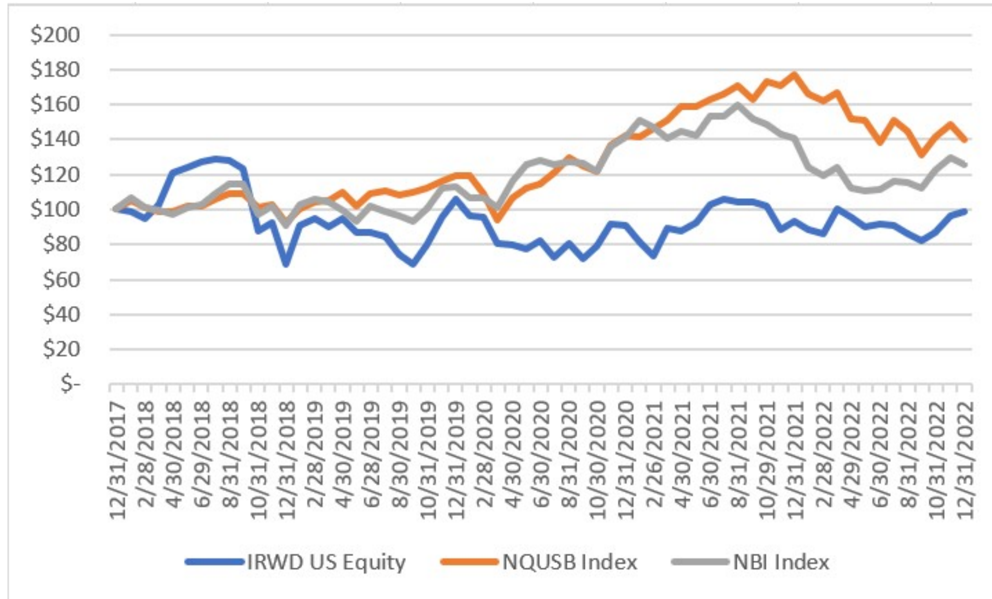
Corporate Performance Graph

The following performance graph and related information shall not be deemed to be "soliciting material" or to be "filed" with the SEC, nor shall such information be incorporated by reference into any future filing under the Securities Act of 1933, as amended, or the Securities Act, except to the extent that we specifically incorporate it by reference into such filing.

On April 1, 2019, we completed the separation, or the Separation, of our soluble guanylate cyclase, or sGC, business, and certain other assets and liabilities, into a separate, independent publicly traded company, Cyclerion Therapeutics, Inc., or Cyclerion. The Separation was effected by means of a distribution of all the outstanding shares of common stock, with no par value, of Cyclerion, through a dividend of Cyclerion's common stock to our stockholders of record as of the close of business on March 19, 2019.

The following graph compares the performance of our Class A Common Stock to the Nasdaq Benchmark TR Index (U.S.) and to the Nasdaq Biotechnology Index (U.S.) from December 31, 2017 through December 31, 2022. The comparison assumes $100 was invested after the market closed on December 31, 2017 in our Class A Common Stock and in each of the presented indices, and it assumes reinvestment of dividends, if any (other than any Cyclerion common stock distributed in connection with the Separation). Total returns reflected in the following graph for periods prior to the date of the Separation have been adjusted for the effect of the Separation to exclude the sGC business.

COMPARISON OF QUARTERLY CUMULATIVE TOTAL RETURN
Among The Nasdaq U.S. Benchmark Index,
the Nasdaq Biotechnology Index,
and Ironwood Pharmaceuticals, Inc.



Item 6. ***Selected Financial Data***

Reserved.

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

Forward-Looking Information

The following discussion of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and the notes to those financial statements appearing elsewhere in this Annual Report on Form 10-K. This discussion contains forward looking statements that involve significant risks and uncertainties. As a result of many factors, such as those set forth under "Risk Factors" in Item 1A of this Annual Report on Form 10 K, our actual results may differ materially from those anticipated in these forward-looking statements.

Discussion and analysis of our financial condition and results of operations for the fiscal year ended December 31, 2021 compared to the fiscal year ended December 31, 2020 is included in Part II, Item 7 – "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2021 filed with the Securities and Exchange Commission on February 18, 2022.

Overview

We are a gastrointestinal, or GI, healthcare company dedicated to advancing the treatment of GI diseases and redefining the standard of care for GI patients. We are focused on the development and commercialization of innovative GI product opportunities in areas of significant unmet need, leveraging our demonstrated expertise and capabilities in GI diseases.

LINZESS® (linaclotide), our commercial product, is the first product approved by the United States Food and Drug Administration, or U.S. FDA, in a class of GI medicines called guanylate cyclase type C agonists, or GC-C agonists, and is indicated for adult men and women suffering from irritable bowel syndrome with constipation, or IBS-C, or chronic idiopathic constipation, or CIC. LINZESS is available to adult men and women suffering from IBS-C or CIC in the United States, or the U.S., and Mexico, IBS-C or chronic constipation in Japan, and IBS-C in China. Linaclotide is available under the trademarked name CONSTELLA® to adult men and women suffering from IBS-C or CIC in Canada, and to adult men and women suffering from IBS-C in certain European countries.

We have strategic partnerships with leading pharmaceutical companies to support the development and commercialization of linaclotide throughout the world, including with AbbVie Inc. (together with its affiliates), or AbbVie, in the U.S. and all countries worldwide other than China (including Hong Kong and Macau) and Japan, AstraZeneca AB (together with its affiliates), or AstraZeneca, in China (including Hong Kong and Macau) and Astellas Pharma Inc., or Astellas, in Japan. We also aim to leverage our leading development and commercialization capabilities in GI to bring additional treatment options to GI patients; for example, in November 2021, we entered into a collaboration and license option agreement, or the COUR Collaboration Agreement, with COUR Pharmaceutical Development Company, Inc., or COUR, that grants us an option to acquire an exclusive license, to research, develop, manufacture and commercialize, in the U.S., products containing CNP-104, a tolerizing immune modifying nanoparticle, for the treatment of primary biliary cholangitis, or PBC.

We are also advancing IW-3300, a GC-C agonist, for the potential treatment of visceral pain conditions, such as interstitial cystitis / bladder pain syndrome, or IC/BPS, and endometriosis.

To date, we have dedicated a majority of our activities to the research, development and commercialization of linaclotide, as well as to the research and development of our other product candidates. Prior to the year ended December 31, 2019, we incurred net losses in each year since inception. For the years ended December 31, 2022, 2021 and 2020, we recorded net income of $175.1 million, $528.4 million, and $106.2 million, respectively. As of December 31, 2022, we had an accumulated deficit of $696.4 million. We are unable to predict the extent of any future losses or guarantee that our company will be able to maintain positive cash flows.

We were incorporated in Delaware on January 5, 1998 as Microbia, Inc. On April 7, 2008, we changed our name to Ironwood Pharmaceuticals, Inc. We operate in one reportable business segment – human therapeutics.

Key 2022 Financial Highlights

- We recognized $410.6 million in total revenues during the year ended December 31 2022, compared to $413.8 million during the year ended December 31, 2021. The slight decrease was primarily driven by a decrease of $1.6 million in collaborative arrangements revenue related to sales of LINZESS in the U.S.

- We recognized $398.8 million in collaborative arrangements revenue related to sales of LINZESS in the U.S. during the year ended December 31, 2022, compared to $400.4 million during the year ended December 31, 2021. The slight decrease was primarily driven by net price erosion and inventory channel fluctuations, partially offset by an increase in LINZESS prescription demand.

- We generated income from operations of $250.3 million during the year ended December 31, 2022 compared to income from operations of $232.3 million during the year ended December 31, 2021. The increase was driven primarily by the recognition of $19.5 million of research and development expense in 2021 for the up-front payment, non-contingent payment, and milestone payment obligations in connection with the COUR Collaboration Agreement.

- We generated $273.8 million in cash from operations during the year ended December 31, 2022, ending the year with $656.2 million in cash and cash equivalents.

- We completed our $150 million stock repurchase program. During the year ended December 31 2022, we repurchased 10.8 million shares of our Class A Common Stock at an aggregate purchase price of $123.4 million.

Financial Operations Overview

Revenues. Our revenues are generated primarily through our collaborative arrangements and license agreements related to research and development and commercialization of linaclotide.

The majority of our revenues are generated from the sales of LINZESS in the U.S. We record our share of the net profits and losses from the sales of LINZESS in the U.S. less commercial expenses on a net basis and present the settlement payments to and from AbbVie as collaboration expense or collaborative arrangements revenue, as applicable. Net profits or losses consist of net sales to third-party customers and sublicense income in the U.S. less the cost of goods sold as well as selling, general and administrative expenses. Although we expect net sales to increase over time, the settlement payments between AbbVie and us, resulting in collaborative arrangements revenue or collaboration expense, are subject to fluctuation based on the ratio of selling, general and administrative expenses incurred by each party. In addition, our collaborative arrangements revenue may fluctuate as a result of the timing and amount of license fees and clinical and commercial milestones received and recognized under our current and future strategic partnerships as well as timing and amount of royalties from the sales of linaclotide in the European, Canadian, Mexican, Japanese, or Chinese markets or any other markets where linaclotide receives approval and is commercialized.

Cost of Revenues. Cost of revenues primarily includes costs related to the sales of linaclotide API, finished drug product, and finished goods to our partners, which generally occurs upon shipment for sales of API, finished drug product and finished goods after the material has passed all quality testing required for acceptance by the partner to certain of our partners outside of the U.S.

Research and Development Expense. The core of our research and development strategy is to leverage our demonstrated expertise and capabilities in GI diseases to bring multiple medicines to patients. Research and development expense consists of expenses incurred in connection with the research into and development of products and product candidates. These expenses consist primarily of compensation, benefits and other employee-related expenses, research and development related facility costs, third-party contract costs relating to nonclinical study and clinical trial activities, development of manufacturing processes, regulatory registration of third-party manufacturing facilities, and licensing fees for our product candidates.

Research and development expenses include amounts owed to AbbVie on an ongoing basis under cost-sharing provisions in our collaboration agreement for linaclotide. Reimbursements received for research and development activities under this agreement are netted against research and development expenses.

Linaclotide. Our commercial product, LINZESS, is commercially available in the U.S. for the treatment of IBS-C or CIC in adults. Linaclotide is also available to adult men and women suffering from IBS-C or CIC in certain countries of the world, including China, Japan, and in a number of E.U. countries.

We and AbbVie continue to explore ways to enhance the clinical profile of LINZESS by studying linaclotide in additional indications, populations and formulations to assess its potential to treat various conditions. In September 2020, based on the Phase IIIb data of linaclotide 290 mcg on the overall abdominal symptoms of bloating, pain and discomfort in adult patients with IBS-C, the U.S. FDA approved our Supplemental New Drug Application, or sNDA, to include a more comprehensive description of the effects of LINZESS in its approved label.

In addition, we and AbbVie have established a nonclinical and clinical post-marketing plan with the U.S. FDA to understand the safety and efficacy of LINZESS in pediatric patients. In August 2021, the U.S. FDA approved a revised label for LINZESS based on clinical safety data that had been generated thus far in pediatric studies. The updated label modified the boxed warning for risk of serious dehydration and contraindication against use in children to those less than two years of age. The boxed warning and contraindication previously applied to all children less than 18 years of age and less than 6 years of age, respectively. In September 2022, we announced positive topline data from a Phase III clinical trial evaluating linaclotide 72 mcg in pediatric patients aged 6-17 with functional constipation, or FC. The trial met its primary and secondary endpoints, demonstrating that linaclotide 72 mcg improved frequency of spontaneous bowel movements and stool consistency. Linaclotide was generally well-tolerated, and the safety profile is consistent with previously reported studies with linaclotide in FC and irritable bowel syndrome in pediatric patients. In December 2022, we and AbbVie submitted an sNDA to the U.S. FDA seeking approval of a new indication of linaclotide for FC in that age group. In February 2023, the U.S. FDA granted priority review to our sNDA and assigned a Prescription Drug User Free Act, or PDUFA, date of June 14, 2023. There are currently no U.S. FDA approved prescription pediatric therapies for functional constipation. The safety and effectiveness of LINZESS in patients less than 18 years of age have not been established. Additional clinical pediatric programs in IBS-C and FC are ongoing.

IW-3718. We were developing IW-3718, a gastric retentive formulation of a bile acid sequestrant, for the potential treatment of refractory gastroesophageal reflux disease, or refractory GERD. In September 2020, we announced that one of our two identical Phase III trials evaluating IW-3718 in refractory GERD did not meet the pre-specified criteria associated with a planned early efficacy assessment and, based on these findings, we discontinued development of IW-3718.

IW-3300. We are developing IW-3300, a GC-C agonist, for the potential treatment of visceral pain conditions, including IC/BPS and endometriosis. We successfully completed Phase I studies to evaluate the safety and tolerability of IW-3300 in healthy volunteers and expect to begin patient dosing for the Phase II proof of concept study in IC/BPS in early 2023.

CNP-104. Through the COUR Collaboration Agreement, we and COUR are developing CNP-104 for the treatment of PBC, a rare autoimmune disease targeting the liver. In December 2021, the U.S. FDA granted Fast Track Designation to CNP-104. COUR is currently conducting a clinical study to evaluate the safety, tolerability, pharmacodynamic effects and efficacy of CNP-104 in PBC patients, with early data assessing T-cell response from patients enrolled in the clinical study expected in the second half of 2023. We expect that such early data will inform timing of topline data readout.

Early research and development. Our early research and development efforts have been focused on supporting our development stage GI programs, including exploring strategic options for further development of certain of our internal programs, as well as evaluating external development-stage GI programs.

The following table sets forth our research and development expenses related to our product pipeline for the years ended December 31, 2022, 2021, and 2020, respectively. These expenses relate primarily to compensation, benefits and other employee-related expenses and external costs associated with nonclinical studies and clinical trial costs for our product candidates. We allocate costs related to facilities, depreciation, share-based compensation, research and development support services and certain other costs directly to programs.

	Year Ended December 31,		
	2022	2021	2020
Linaclotide[1]	$ 17,267	$ 21,075	$ 25,531
IW-3718	461	8,002	52,183
IW-3300	15,824	11,687	3,810
CNP-104	1,022	19,500	—
Early research and development	9,691	10,141	6,538
Total research and development expenses	$ 44,265	$ 70,405	$ 88,062

(1) Includes linaclotide in all indications, populations and formulations.

The lengthy process of securing regulatory approvals for new drugs requires the expenditure of substantial resources. Any failure by us to obtain, or any delay in obtaining, regulatory approvals would materially adversely affect our product development efforts and our business overall.

We and AbbVie are exploring development opportunities to enhance the clinical profile of LINZESS by studying linaclotide in additional indications, populations and formulations to assess its potential to treat various conditions. We cannot currently estimate with any degree of certainty the amount of time or money that we will be required to expend in the future on linaclotide for additional indications, populations or formulations.

Given the inherent uncertainties that come with the development of pharmaceutical products, we cannot estimate with any degree of certainty how our programs will evolve, and therefore the amount of time or money that would be required to obtain regulatory approval to market them.

As a result of these uncertainties surrounding the timing and outcome of any approvals, we are currently unable to estimate precisely when, if ever, linaclotide's utility will be expanded within its currently approved indications; if or when linaclotide will be developed outside of its current markets, indications, populations or formulations; or when, if ever, any of our other product candidates will generate revenues and cash flows.

We invest carefully in our pipeline, and the commitment of funding for each subsequent stage of our development programs is dependent upon the receipt of clear, supportive data. In addition, we intend to access externally discovered drug candidates that fit within our core strategy. In evaluating these potential assets, we apply the same investment criteria as those used for investments in internally discovered assets.

The successful development of our product candidates is highly uncertain and subject to a number of risks including, but not limited to:

- The duration of clinical trials may vary substantially according to the type, complexity and novelty of the product candidate;
- The U.S. FDA and comparable agencies in foreign countries impose substantial and varying requirements on the introduction of therapeutic pharmaceutical products, typically requiring lengthy and detailed laboratory and clinical testing procedures, sampling activities and other costly and time-consuming procedures;
- Data obtained from nonclinical and clinical activities at any step in the testing process may be adverse and lead to discontinuation or redirection of development activity. Data obtained from these activities also are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval;
- The duration and cost of early research and development, including nonclinical studies and clinical trials may vary significantly over the life of a product candidate and are difficult to predict;

- The costs, timing and outcome of regulatory review of a product candidate may not be favorable, and, even if approved, a product may face post-approval development and regulatory requirements;

- There may be substantial costs, delays and difficulties in successfully integrating externally developed product candidates into our business operations; and

- The emergence of competing technologies and products and other adverse market developments may negatively impact us.

As a result of the factors discussed above, including the factors discussed under “Risk Factors” in Item 1A of this Annual Report on Form 10-K, we are unable to determine the duration and costs to complete current or future nonclinical and clinical stages of our product candidates or when, or to what extent, we will generate revenues from the commercialization and sale of our product candidates. Development timelines, probability of success and development costs vary widely. We anticipate that we will make determinations as to which additional programs to pursue and how much funding to direct to each program on an ongoing basis in response to the data of each product candidate, the competitive landscape and ongoing assessments of such product candidate’s commercial potential.

We expect to invest in our development programs for the foreseeable future. We will continue to invest in linaclotide, including the investigation of ways to enhance the clinical profile within its currently approved indications, and the exploration of its potential utility in other indications, populations and formulations. We will continue to invest in our GI-focused product candidates as we advance them through pre-clinical and clinical trials, in addition to funding research and development activities under our external collaboration and license agreements.

Selling, General and Administrative Expense. Selling, general and administrative expense consists primarily of compensation, benefits and other employee-related expenses for personnel in our administrative, finance, legal, information technology, business development, commercial, sales, marketing, communications and human resource functions. Other costs include legal costs of pursuing patent protection of our intellectual property, general and administrative related facility costs, insurance costs and professional fees for accounting, tax, consulting, legal and other services. As we continue to invest in the commercialization of LINZESS, we expect our selling, general and administrative expenses will be substantial for the foreseeable future.

We include AbbVie’s selling, general and administrative cost-sharing payments in the calculation of the net profits and net losses from the sale of LINZESS in the U.S. and present the net payment to or from AbbVie as collaboration expense or collaborative arrangements revenue, respectively.

Restructuring Expenses. Restructuring expenses pertain to workforce reduction and restructuring initiatives and are more fully described in Note 16, *Workforce Reduction and Restructuring*, to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Interest Expense. Interest expense consists primarily of cash and non-cash interest costs related to our convertible senior notes. Non-cash interest expense consists of amortization of the debt discount and debt issuance costs.

Interest and Investment Income. Interest and investment income consists of interest earned on our cash and cash equivalents, as well as significant financing components of payments due from collaboration partners.

Gain (Loss) on Derivatives. In June 2015, we issued 2.25% Convertible Senior Notes due June 15, 2022, or the 2022 Convertible Notes, and in August 2019, we issued 0.75% Convertible Senior Notes due 2024, or the 2024 Convertible Notes, and 1.50% Convertible Senior Notes due 2026, or the 2026 Convertible Notes (together with the 2024 Convertible Notes, the Convertible Senior Notes). In connection with the issuance of our 2022 Convertible Notes, we entered into convertible note hedge transactions, or the Convertible Note Hedges, and separate note hedge warrant transactions, or the Note Hedge Warrants, with certain financial institutions. Gain (loss) on derivatives consists of the change in fair value of the Convertible Note Hedges and Note Hedge Warrants, which are recorded at fair value at each reporting date and changes in fair value are recorded in our consolidated statements of income. The Convertible Note Hedges terminated unexercised upon expiry in June 2022. The Convertible Note Hedges and Note Hedge Warrants are more fully described in Note 9*, Notes Payable*, to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Income Taxes. We prepare our income tax provision based on our interpretation of the income tax accounting rules and each jurisdiction's enacted tax laws and regulations. For additional information refer to Note 13, *Income Taxes,* to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations is based upon our consolidated financial statements prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make certain estimates and assumptions that may affect the reported amounts of assets and liabilities, the disclosure of assets and liabilities at the date of the consolidated financial statements, and the amounts of revenues and expenses during the reported periods. We base our estimates on our historical experience and on various other assumptions that are believed to be reasonable, the results of which form the basis for making judgments about the carrying values of assets and liabilities. Actual results may differ materially from our estimates under different assumptions or conditions. Changes in estimates are reflected in reported results in the period in which they become known.

We believe that our application of the following accounting policies, each of which require significant judgments and estimates on the part of management, are the most critical to aid in fully understanding and evaluating our reported financial results. Our significant accounting policies are more fully described in Note 2, *Summary of Significant Accounting Policies*, to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Revenue Recognition

Upon executing a revenue generating arrangement, we assess whether it is probable we will collect consideration in exchange for the good or service it transfers to the customer and perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy the performance obligations. We must develop assumptions that require significant judgment to determine the standalone selling price for each performance obligation identified in the contract. The assumptions that are used to determine the standalone selling price may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success.

Our revenues are generated primarily through collaborative arrangements and license agreements related to the development and commercialization of linaclotide. The terms of the collaborative arrangements and other agreements contain multiple performance obligations which may include (i) licenses, (ii) research and development activities, including participation on joint steering committees, (iii) the manufacture of finished drug product, API, or development materials for a partner, which are reimbursed at a contractually determined rate, and (iv) education or co-promotion activities by our clinical sales specialists. Non-refundable payments to us under these agreements may include (i) up-front license fees, (ii) payments for research and development activities, (iii) payments for the manufacture of finished drug product, API, or development materials, (iv) payments based upon the achievement of certain milestones, (v) payments for sales detailing, promotional support services and medical education initiatives, and (vi) royalties on product sales. Additionally, we receive our share of the net profits or bear our share of the net losses from the sale of linaclotide in the U.S. We have adopted a policy to recognize revenue net of tax withholdings, as applicable.

Collaboration, License, and Other Agreements

Upon licensing intellectual property, we determine if the license is distinct from the other performance obligations identified in the arrangement. We recognize revenues from the transaction price, including non-refundable, up-front fees allocated to the license when the license is transferred to the customer if the license has distinct benefit to the customer. For licenses that are combined with other promises, we assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time. For performance obligations that are satisfied over time, we evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Our license and collaboration agreements include milestone payments, such as development and other milestones. We evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method at the inception of the agreement. If it is probable

that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation on a relative standalone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. We re-evaluate the probability of achievement of such milestones and any related constraint at each reporting period, and any adjustments are recorded on a cumulative catch-up basis.

Agreements that include the supply of API or drug product for either clinical development or commercial supply at the customer's discretion are generally considered as options. We assess if these options provide a material right to our partner, and if so, they are accounted for as separate performance obligations. If we are entitled to additional payments when the customer exercises these options, any additional payments are recorded as revenue when the customer obtains control of the goods, which is typically upon shipment for sales of API and finished drug product.

For agreements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize revenue when the related sales occur.

Net Profit or Net Loss Sharing

In accordance with Accounting Standards Codification, or ASC, Topic 808, *Collaborative Arrangements*, or ASC 808, we considered the nature and contractual terms of the arrangement and the nature of our business operations to determine the classification of payments under our collaboration agreements. While ASC 808 provides guidance on classification, the standard is silent on matters of separation, initial measurement, and recognition. Therefore, we apply the separation, initial measurement, and recognition principles of ASC Topic 606, *Revenue from Contracts with Customers*, to our collaboration agreements.

Our collaborative arrangements revenue generated from sales of LINZESS in the U.S. are considered akin to sales-based royalties. We recognize our share of the pre-tax commercial net profit or net loss generated from the sales of LINZESS in the U.S. in the period the product sales are earned, as reported by AbbVie, and related cost of goods sold and selling, general and administrative expenses as incurred by us and our collaboration partner. These amounts are partially determined based on amounts provided by AbbVie and involve the use of estimates and judgments, such as product sales allowances and accruals related to prompt payment discounts, chargebacks, governmental and contractual rebates, wholesaler fees, product returns, and co-payment assistance costs, which could be adjusted based on actual results in the future. We are highly dependent on AbbVie for timely and accurate information regarding any net revenues realized from sales of LINZESS in the U.S. in accordance with ASC 808, and the related costs, in order to accurately report its results of operations. If we do not receive timely and accurate information or incorrectly estimate activity levels associated with the collaboration at a given point in time, we could be required to record adjustments in future periods.

We record revenue transactions as net product revenue in our consolidated statements of income if we are deemed the principal in the transaction, which includes being the primary obligor, retaining inventory risk, and control over pricing. Given that we are not the primary obligor and do not have the inventory risks in the collaboration agreement with AbbVie for North America, we record our share of the net profits or net losses from the sales of LINZESS in the U.S. on a net basis and present the settlement payments to and from AbbVie as collaboration expense or collaborative arrangements revenue, as applicable. We and AbbVie settle the cost sharing quarterly, such that our consolidated statements of income reflect 50% of the pre-tax net profit or loss generated from sales of LINZESS in the U.S.

Sale of Active Pharmaceutical Ingredient

During the year ended December 31, 2020, we produced linaclotide API, finished drug product, finished goods, and/or development materials for certain of our partners. As of December 31, 2020, we were no longer responsible for the supply of linaclotide API, finished drug product, finished goods or development materials to such partners. After December 31, 2020, we have occasionally provided development materials from time to time to certain of

our partners and we may continue to do so. Sales of such development materials have been and are expected to continue to be immaterial.

We recognize revenue on linaclotide API, finished drug product, finished goods, and development materials when control has transferred to the partner, which generally occurs upon shipment after the material has passed all quality testing required for acceptance by the partner.

Other

Our deferred revenue balance consists of advance billings and payments received from customers in excess of revenue recognized.

Research and Development Expense

We have committed significant resources into the research and development of our product candidates and intend to continue to do so for the foreseeable future. Research and development expenses are generally expensed as incurred. We capitalize nonrefundable advance payments we make for research and development activities and defer expense recognition until the related goods are received or the related services are performed.

Research and development expenses are comprised of costs incurred in performing research and development activities, including salary, benefits, share-based compensation, and other employee-related expenses; laboratory supplies and other direct expenses; facilities expenses; overhead expenses; third-party contractual costs relating to nonclinical studies and clinical trial activities and related contract manufacturing expenses, development of manufacturing processes and regulatory registration of third-party manufacturing facilities; licensing fees for our product candidates; and other outside expenses.

Clinical trial expenses include expenses associated with contract research organizations, or CROs. The invoicing from CROs for services rendered can lag several months. We accrue the cost of services rendered in connection with CRO activities based on our estimate of site management, monitoring costs, project management costs, and investigator fees. We maintain regular communication with our CRO vendors to gauge the reasonableness of our estimates. Differences between actual clinical trial expenses and estimated clinical trial expenses recorded have not been material and are adjusted for in the period in which they become known. However, if we incorrectly estimate activity levels associated with the CRO services at a given point in time, we could be required to record material adjustments in future periods. Under our collaboration agreement with AbbVie for North America, we are reimbursed for certain research and development expenses and we net these reimbursements against our research and development expenses as incurred.

Research and development expense also includes up-front payment, non-contingent payment, and milestone payment obligations under the COUR Collaboration Agreement. Recognition of expense for such payments requires judgment with respect to when the obligation is probable.

Share-Based Compensation Expense

We grant awards under our share-based compensation programs, including stock awards, restricted stock awards, or RSAs, restricted stock units, or RSUs (including performance-based RSUs, or PSUs), stock options, and shares issued under our employee stock purchase plan, or ESPP. Share-based compensation is recognized as expense in the consolidated statements of income based on the grant date fair value over the requisite service period, net of estimated forfeitures. We estimate forfeitures over the requisite service period using historical forfeiture activity and record share-based compensation expense only for those awards that are expected to vest.

We estimate the fair value of stock options on the date of grant using the Black-Scholes option-pricing model, which requires the use of subjective assumptions including volatility and expected term, among others. The fair value of stock awards, RSAs, and RSUs is based on the market value of our Class A Common Stock on the date of grant, with the exception of PSUs with market conditions, which are measured using the Monte Carlo simulation method. Discounted stock purchases under our ESPP are valued on the first date of the offering period using the Black-Scholes option-pricing model to compute the fair value of the lookback provision plus the purchase discount.

For awards that vest based on service conditions and market conditions, we use the straight-line method to recognize compensation expense over the respective service period. For awards that contain performance conditions, we determine the appropriate amount to expense based on the anticipated achievement of performance targets, which requires judgment, including forecasting the achievement of future specified targets. At the date performance conditions are determined to be probable of achievement, we record a cumulative expense catch-up, with remaining expense amortized over the remaining service period. Throughout the performance period, we re-assess the estimated performance and update the number of performance-based awards that we believe will ultimately vest. Discounted stock purchases under our ESPP are recognized over the offering period.

Compensation expense related to modified awards is measured based on the fair value for the awards as of the modification date. Any incremental compensation expense arising from the excess of the fair value of the awards on the modification date compared to the fair value of the awards immediately before the modification date is recognized at the modification date or ratably over the remaining service period, as appropriate.

While the assumptions used to calculate and account for share-based compensation awards represent management's best estimates, these estimates involve inherent uncertainties and the application of management's judgment. As a result, if revisions are made to our underlying assumptions and estimates, our share-based compensation expense could vary significantly from period to period.

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 basis of assets and liabilities using enacted tax rates in effect for years in which the temporary differences are expected to reverse. We provide a valuation allowance when it is more likely than not that deferred tax assets will not be realized.

Prior to 2021, we maintained a valuation allowance on the majority of our net operating losses and other deferred tax assets. On a periodic basis, we reassess the valuation allowance on our deferred tax assets, weighing positive and negative evidence to assess the recoverability of the deferred tax assets. During the year ended December 31, 2021, we reassessed the valuation allowance noting the shift of positive evidence outweighing negative evidence, including: continued strong prescription demand growth of LINZESS, continued profitability of a GI-focused business since completing the tax-free spin-off of Cyclerion, and expectations regarding future profitability. After assessing both the positive evidence and negative evidence, we determined it was more likely than not that we will realize the majority of our deferred tax assets and therefore released the majority of our valuation allowance for the deferred tax assets that are expected to be utilized in future years. We will continue to maintain a valuation allowance for deferred tax assets that are unlikely to be realized, which are primarily certain tax credits that are expected to expire prior to utilization.

Significant judgment is required in making these assessments to maintain or reverse our valuation allowances and, to the extent our future expectations change we would have to assess the recoverability of these deferred tax assets at that time. If we determine that our net deferred tax assets are not realizable in a future period, we would record material changes to income tax expense or benefit in that period.

We record uncertain tax positions on the basis of a two-step process. First, we determine whether it is more likely than not that the tax positions will be sustained based on the technical merits of the position. Second, for those tax positions that meet the more-likely-than-not recognition threshold, we recognize the largest amount of tax benefit that is greater than 50 percent likely to be realized upon ultimate settlement with the relevant tax authority. Significant judgment is required in evaluating whether our tax positions meet this two-step process. The nature of the uncertain tax positions is often very complex and subject to change, and the amounts at issue can be substantial. We re-evaluate these uncertain tax positions on a quarterly basis based on a number of factors including, but not limited to, changes in facts or circumstances, changes in tax law, and effectively settled issues under audit and new audit activity. Any change in these factors could result in the recognition of a tax benefit or an additional charge to the tax provision.

Results of Operations

The following discussion summarizes the key factors our management believes are necessary for an understanding of our consolidated financial statements.

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Revenues:		
Collaborative arrangements revenue	$ 410,596	$ 412,784
Sale of active pharmaceutical ingredient	—	969
Total revenues	410,596	413,753
Operating expenses:		
Research and development	44,265	70,405
Selling, general and administrative	115,994	111,133
Restructuring expenses	—	(44)
Total operating expenses	160,259	181,494
Income from operations	250,337	232,259
Other (expense) income:		
Interest expense	(7,598)	(31,150)
Interest and investment income	9,501	726
Gain (loss) on derivatives	182	(1,178)
Other (expense) income, net	2,085	(31,602)
Income before income taxes	252,422	200,657
Income tax (expense) benefit	(77,357)	327,791
Net income	$ 175,065	$ 528,448

Year Ended December 31, 2022 Compared to Year Ended December 31, 2021

Revenues

	Year Ended December 31,		Change
	2022	2021	$
	(in thousands)		
Revenues:			
Collaborative arrangements revenue	$ 410,596	$ 412,784	$ (2,188)
Sale of active pharmaceutical ingredient	—	969	(969)
Total revenues	$ 410,596	$ 413,753	$ (3,157)

Collaborative arrangements revenue. The decrease in collaborative arrangements revenue of $2.2 million for the year ended December 31, 2022 compared to the year ended December 31, 2021 was primarily related to a $1.6 million decrease in our share of net profits from the sale of LINZESS in the U.S., which was driven by net price erosion and inventory channel fluctuations, partially offset by an increase in prescription demand.

Sale of active pharmaceutical ingredient. The decrease in sale of API of $1.0 million for the year ended December 31, 2022 compared to the year ended December 31, 2021 was primarily due to certain non-recurring, insignificant sales during the year ended December 31, 2021.

Cost and Expenses

	Year Ended December 31, 2022	2021	Change $
		(in thousands)	
Operating expenses:			
Research and development	$ 44,265	$ 70,405	$ (26,140)
Selling, general and administrative	115,994	111,133	4,861
Restructuring expenses	—	(44)	44
Total operating expenses	$ 160,259	$ 181,494	$ (21,235)

Research and development. The decrease in research and development expense of $26.1 million for the year ended December 31, 2022 compared to the year ended December 31, 2021 was primarily related to a decrease of $19.4 million of expenses recognized for up-front payment, non-contingent payment, and milestone payment obligations in connection with the COUR Collaboration Agreement; a decrease of $5.4 million in external development costs related to IW-3718; a decrease of $3.4 million related to linaclotide development; and a decrease of $1.8 million in compensation, benefits, and other employee-related expenses. These decreases in expenses were partially offset by a $3.0 million increase in external development costs related to IW-3300.

Selling, general and administrative. Selling, general and administrative expenses increased $4.9 million for the year ended December 31, 2022 compared to the year ended December 31, 2021, primarily due to a $3.4 million increase in sales and marketing activities and a $1.7 million increase in compensation, benefits, and other employee-related expenses.

Restructuring expenses. Restructuring expenses and adjustments related to the workforce reduction resulting from our decision to discontinue IW-3718 development were insignificant during the year ended December 31, 2021, as the workforce reduction was substantially completed during the fourth quarter of 2020.

Other (Expense) Income, Net

	Year Ended December 31, 2022	2021	Change $
		(in thousands)	
Other (expense) income:			
Interest expense	$ (7,598)	$ (31,150)	$ 23,552
Interest and investment income	9,501	726	8,775
Gain (loss) on derivatives	182	(1,178)	1,360
Total other (expense) income, net	$ 2,085	$ (31,602)	$ 33,687

Interest expense. Interest expense decreased by $23.6 million during the year ended December 31, 2022 compared to the year ended December 31, 2021 due to a $22.1 million decrease in non-cash interest expense associated with the Senior Convertible Notes following the adoption of ASU 2020-06 on January 1, 2022 and a $1.5 million decrease in coupon interest expense associated with the 2022 Convertible Notes, which were fully repaid upon maturity in June 2022.

Interest and investment income. Interest and investment income increased by $8.8 million in the year ended December 31, 2022 compared to the year ended December 31, 2021, resulting primarily from an increase in investment interest rates.

Gain (loss) on derivatives. For the year ended December 31, 2022, we recorded a gain on derivatives of $0.2 million resulting from a $1.1 million decrease in the fair value of the Convertible Note Hedges, which terminated unexercised upon expiry in June 2022, and a $1.3 million decrease in the fair value of the Note Hedge Warrants. For the year ended December 31, 2021, we recorded a loss on derivatives of $1.2 million resulting from a $12.0 million decrease in the fair value of the Convertible Note Hedges and a $10.8 million decrease in the fair value of the Note Hedge Warrants.

Income taxes. During the year ended December 31, 2022, we recorded income tax expense of $77.4 million, comprised of non-cash tax expense of $73.4 million and cash tax expense of $4.0 million for state income taxes in

certain states in which state taxable income exceeded available net operating losses. During the year ended December 31, 2021, we recorded income tax benefit of $327.8 million, which primarily pertained to the non-cash income tax benefit of $333.3 million related to the release of the valuation allowance on the majority of our tax attributes and other deferred tax assets, partially offset by state income taxes of $5.5 million in certain states which have temporarily disallowed or only partially allow the use of net operating losses to fully offset taxable income.

Until the second quarter of 2021, we maintained a valuation allowance on our net operating losses and other deferred tax assets. Thereafter, we have continued to utilize our net operating losses to offset federal taxable income and taxable income in many states but record a significant portion of income taxes reflecting the utilization of the deferred tax assets. The majority of this provision for income taxes will be a non-cash expense until our net operating losses are fully utilized. Further information on the release of the valuation allowance and significant judgments related to its release can be found below in Note 13, *Income Taxes*, in the accompanying notes to our financial statements appearing elsewhere in this Annual Report on Form 10-K.

Liquidity and Capital Resources

Until the year ended December 31, 2019, we had incurred losses since our inception in 1998 and had an accumulated deficit of $696.4 million as of December 31, 2022. We have financed our operations to date primarily through both the private sale of our preferred stock and the public sale of our common stock, debt financings, and cash generated from our operations. As of December 31, 2022, our debt is comprised of $400.0 million aggregate principal amount of convertible notes, due at various dates between 2024 and 2026. Refer to Note 9, *Notes Payable,* to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K, for information related to our debt obligations.

As of December 31, 2022, we had $656.2 million of unrestricted cash and cash equivalents. Our cash equivalents include amounts held in money market funds, repurchase agreements, commercial paper, and corporate bonds. We invest cash in excess of immediate requirements in accordance with our investment policy, which limits the amounts we may invest in certain types of investments and requires all investments held by us to be at least A- rated, with a remaining final maturity when purchased of less than twenty-four months, so as to primarily achieve liquidity and capital preservation objectives.

During the year ended December 31, 2022, our balances of cash and cash equivalents increased by $36.1 million. Net cash provided by operating activities totaled $273.8 million as a result of profitable operations driven primarily by the sales of LINZESS in the U.S. These cash flows were offset by financing activities totaling $237.6 million, primarily comprised of $126.4 million of share repurchases and repayment of the $120.7 million remaining aggregate principal of the 2022 Convertible Notes.

We anticipate our cash balance, which was $656.2 million as of December 31, 2022, and our expected net cash inflows from operations to allow us to meet our near-term and long-term cash obligations, which are reflected in our consolidated balance sheets. Our most significant fixed obligations are debt obligations and lease commitments, for which annual payments are disclosed in Note 9, *Notes Payable*, and Note 6, *Leases*, respectively, to our financial statements included elsewhere in this Annual Report on Form 10-K.

We may from time to time seek to retire, redeem or repurchase all or part of our outstanding debt through cash purchases and/or exchanges, in open market purchases, privately negotiated transactions, by tender offer or otherwise. Such repurchases, redemptions or exchanges, if any, of our debt will depend on prevailing market conditions, liquidity requirements, contractual restrictions and other factors, and the amounts involved may be material.

In May 2021, our board of directors authorized a program to repurchase up to $150.0 million of our Class A Common Stock. The program was completed in May 2022 and the repurchased shares were retired. Additional information regarding the repurchase program is disclosed in Note 11, *Stockholders' Equity*, to our financial statements included elsewhere in this Annual Report on Form 10-K.

Cash Flows From Operating Activities

Net cash provided by operating activities totaled $273.8 million for the year ended December 31, 2022. The cash provided by operations primarily related to cash flows from our net income of $175.1 million, net of non-cash items

of $95.9 million and net changes in operating assets and liabilities of $2.8 million. Net cash inflows are derived primarily from collaboration arrangements revenue related to sales of LINZESS in the U.S.

Net cash provided by operating activities totaled $261.9 million for the year ended December 31, 2021. The cash provided by operations primarily related to cash flows from our net income of $528.4 million, net of non-cash items of $284.4 million and net changes in operating assets and liabilities of $17.7 million. Net cash inflows are derived primarily from collaboration arrangements revenue related to sales of LINZESS in the U.S.

Cash Flows From Investing Activities

Cash used in investing activities for the year ended December 31, 2022 totaled $0.1 million and pertained to the purchase of property and equipment.

Cash used in investing activities for the year ended December 31, 2021 totaled $0.3 million and pertained to the purchase of property and equipment.

Cash Flows From Financing Activities

Cash used in financing activities for the year ended December 31, 2022 totaled $237.6 million and resulted from $126.4 million of share repurchases and repayment of the $120.7 million remaining aggregate principal on the 2022 Convertible Notes upon maturity in June 2022, partially offset by $9.5 million of proceeds from the exercise of stock options and the issuance of shares under our ESPP.

Cash provided by financing activities for the year ended December 31, 2021 totaled $4.6 million and resulted from $24.1 million of share repurchases, partially offset by $19.6 million of proceeds from the exercise of stock options and the issuance of shares under our ESPP.

Funding Requirements

We began commercializing LINZESS in the U.S. with our collaboration partner, AbbVie, in the fourth quarter of 2012, and we currently derive a significant portion of our revenue from this collaboration. In addition, we are deploying significant resources to fulfill U.S. FDA requirements for linaclotide. Our goal is to generate and maintain positive cash flows, driven by increased revenue generated through sales of LINZESS and other commercial activities and financial discipline.

Under our collaboration with AbbVie for North America, total net sales of LINZESS in the U.S., as recorded by AbbVie, are reduced by commercial costs incurred by each party, and the resulting amount is shared equally between us and AbbVie. Additionally, we receive royalties from AbbVie based on sales of linaclotide in its licensed territories outside of the U.S. We believe revenues from our LINZESS partnership for the U.S. with AbbVie will continue to constitute a significant portion of our total revenue for the foreseeable future and we cannot be certain that such revenues, as well as the revenues from our other commercial activities, will continue to enable us to generate positive cash flows, or to do so in the timeframes we expect. We also anticipate that we will continue to incur substantial expenses for the next several years as we further develop and commercialize linaclotide in the U.S., develop and commercialize other products, and invest in building our pipeline through internal or external opportunities, including potential payments associated with exercising the Option under the COUR Collaboration Agreement. We believe that our cash on hand as of December 31, 2022 will be sufficient to meet our projected operating needs at least through the next twelve months from the issuance of these financial statements.

Our forecast of the period of time through which our financial resources will be adequate to support our operations, including the underlying revenue expectations and estimates regarding the costs to develop, obtain regulatory approval for, and commercialize linaclotide in the U.S., as well as our expectations regarding revenue from Astellas for Japan and AstraZeneca for China (including Hong Kong and Macau), and our goal to generate and maintain positive cash flows, are forward-looking statements that involve risks and uncertainties. Our actual results could vary materially and negatively from these and other forward-looking statements as a result of a number of factors, including the factors discussed in the "Risk Factors" section of this Annual Report on Form 10-K. We have based our estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect.

Due to the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate precisely the amounts of capital outlays and operating expenditures necessary to develop, obtain regulatory approval for, and commercialize linaclotide and our other product candidates, in each case, for all of the markets, indications, populations and formulations for which we believe each is suited. Our funding requirements will depend on many factors, including, but not limited to, the following:

- the revenue generated by sales of LINZESS and CONSTELLA and from any other sources;
- the rate of progress and cost of our commercialization activities, including the expense we incur in marketing and selling LINZESS in the U.S. and from any other sources;
- the success of our third-party manufacturing activities;
- the time and costs involved in developing, and obtaining regulatory approvals for, our product candidates, as well as the timing and cost of any post-approval development and regulatory requirements;
- the success of our research and development efforts;
- the emergence of competing or complementary products;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- the terms and timing of any collaborative, licensing or other arrangements that we may establish, including milestones, royalties or other payments due or payable under such agreements;
- the settlement method used for our outstanding convertible notes; and
- the acquisition of businesses, products and technologies and the impact of other strategic transactions, as well as the cost and timing of evaluating, acquiring, and, if completed, integrating into our business operations any such assets.

Financing Strategy

We may, from time to time, consider additional funding through a combination of new collaborative arrangements, strategic alliances, and additional equity and debt financings or from other sources. We will continue to manage our capital structure and to consider all financing opportunities, whenever they may occur, that could strengthen our long-term liquidity profile. Any such capital transactions may or may not be similar to transactions in which we have engaged in the past. There can be no assurance that any such financing opportunities will also be available on acceptable terms, if at all.

Off-Balance Sheet Arrangements

We do not have any relationships with unconsolidated entities or financial partnerships, such as entities often referred to as structured finance or special purpose entities, that would have been established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purposes. As such, we are not exposed to any financing, liquidity, market or credit risk that could arise if we had engaged in those types of relationships. We enter into guarantees in the ordinary course of business related to the guarantee of our own performance and the performance of our subsidiaries.

New Accounting Pronouncements

For a discussion of recent accounting pronouncements, refer to Note 2, *Summary of Significant Accounting Policies*, to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K. We did not otherwise adopt any new accounting pronouncements during the fiscal year ended December 31, 2022 that had a material effect on our consolidated financial statements included in this report.

Trends and Uncertainties

Impact of the COVID-19 Pandemic

The COVID-19 pandemic, including containment and mitigation measures, has impacted, and may continue to impact, our business and operations and financial results, particularly in our day-to-day operations and our collaboration agreement for North America with AbbVie.

During 2022, in-person work practices for customer-facing employees returned to near pre-COVID 19 levels. However, new strains or variants of the virus that cause outbreaks of COVID-19 may present in the future risks to successful execution of the commercial operating plan for LINZESS due in part to limitations on in-person work practices for our customer facing employees.

We and our partner, AbbVie, are focused on maintaining the availability of LINZESS for adult men and women suffering from IBS-C or CIC. As of the date of this Annual Report on Form 10-K, the COVID-19 pandemic has not caused significant disruptions to manufacturing operations or supply of LINZESS in the U.S.

We include our and AbbVie's collaboration-related selling, general, and administrative expenses, which had previously included expenses from in-person selling activities, in the calculation of net profits from the sale of LINZESS in the U.S. and present net payments to us as collaborative arrangements revenue. As a result of the COVID-19 pandemic, since 2020, we and AbbVie agreed to include certain costs associated with remote selling activities performed by our and AbbVie's customer-facing employees in collaboration-related selling, general and administrative expenses in our calculation of net profits from the sale of LINZESS in the U.S. In 2020, we experienced fluctuations in our settlement payments based on the ratio of selling, general and administrative expenses incurred by each party throughout 2020 and may continue to experience such fluctuations in the future as a result of the reimbursement of costs associated with remote selling activities and potential limitations in the number of in-person details we or AbbVie may be able to conduct due to containment and mitigation measures related to the COVID-19 pandemic. The COVID-19 pandemic may negatively impact future net sales of LINZESS in the U.S., including as a result of reduced and/or restricted in-person promotion or potential changes in patient access to healthcare (including due to unemployment or modifications in insurance coverage) and payor reimbursement levels.

Given the uncertainties surrounding the extent and duration of the impact of the pandemic on our business and operations, we continue to evaluate the impact of the COVID-19 pandemic on our operating results and financial condition, and we may incur additional expenses in future periods as a result. Refer to "Risk Factors" in Item 1A of this Annual Report on Form 10-K for additional information on risks associated with COVID-19 that could impact our operations and results.

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

Interest Rate Risk

We are exposed to market risk related to changes in interest rates. We invest our cash in a variety of financial instruments, principally securities issued by the U.S. government and its agencies, including collateralized reverse repurchase agreements, money market instruments, as well as commercial paper and corporate bonds. The goals of our investment policy are preservation of capital, fulfillment of liquidity needs and fiduciary control of cash and investments. We also seek to maximize income from our investments without assuming significant risk.

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of interest rates, particularly because our investments are in short-term marketable securities. Due to the primarily short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 1% change in interest rates would not have a material effect on the fair market value of our portfolio. Accordingly, we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a sudden change in market interest rates on our investment portfolio.

We do not believe our cash and cash equivalents have significant risk of default or illiquidity. While we believe our cash and cash equivalents 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. Given the potential instability of financial institutions, we cannot provide assurance that we will not experience losses on these deposits.

Our Convertible Senior Notes bear interest at a fixed rate and therefore have minimal exposure to changes in interest rates; however, because these interest rates are fixed, we may be paying a higher interest rate, relative to market, in the future if our credit rating improves or other circumstances change.

Equity Price Risk

Our convertible notes include conversion and settlement provisions that are based on the price of our Class A Common Stock at conversion or maturity of the notes. The amount of cash we may be required to pay is determined by the price of our Class A Common Stock. The fair values of our convertible notes are dependent on the price and volatility of our Class A Common Stock and will generally increase or decrease as the market price of our common stock changes.

To minimize the impact of potential dilution to our common stock upon conversion of the notes, we entered into the Convertible Note Hedges and Note Hedge Warrants, with respect to the 2022 Convertible Notes, and the Capped Calls, with respect to the 2024 Convertible Notes and 2026 Convertible Notes. The Convertible Note Hedges terminated unexercised upon expiry in June 2022.

The convertible notes and derivatives are more fully described in Note 9, *Notes Payable,* in the accompanying notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Foreign Currency Risk

We have no significant monetary assets or liabilities expected to be settled in foreign currencies and we do not expect to be impacted significantly by foreign currency fluctuations.

Item 8. *Financial Statements and Supplementary Data*

Our consolidated financial statements, together with the independent registered public accounting firm, Ernst & Young LLP (PCAOB ID: 42), report thereon, appear at pages F-1 through F-50, of this Annual Report on Form 10-K.

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

As required by Rule 13a-15(b) of the Securities Exchange Act of 1934, or Exchange Act, our management, including our principal executive officer and our principal financial officer, conducted an evaluation as of the end of the period covered by this Annual Report on Form 10-K of the effectiveness of the design and operation of our disclosure controls and procedures. Based on that evaluation, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures are effective at the reasonable assurance level in ensuring that information required to be disclosed by us in the reports that we file or submit 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 us in the reports we file under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure.

Management’s Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over our financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act as the process designed by, or under the supervision of, our Chief Executive Officer and Chief Financial Officer, and

effected by our board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of our financial statements for external purposes in accordance with generally accepted accounting principles, and 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 assets;

(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 are being made only in accordance with the authorizations of management and directors; and

(3) provide reasonable assurance regarding the prevention or timely detection of unauthorized acquisition, use or disposition of assets that could have a material effect on our financial statements.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework provided in *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework). Based on this evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2022.

The effectiveness of our internal control over financial reporting as of December 31, 2022 has been audited by Ernst and Young LLP, an independent registered public accounting firm, as stated in their report, which is included herein.

Changes in Internal Control

As required by Rule 13a-15(d) of the Exchange Act, our management, including our principal executive officer and our principal financial officer, conducted an evaluation of the internal control over financial reporting to determine whether any changes occurred during the quarter ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our internal controls over financial reporting.

Based on management's evaluation, our principal executive officer and principal financial officer concluded no changes during the quarter ended December 31, 2022 materially affected, or were reasonably likely to materially affect, our internal controls over financial reporting.

Report of Independent Registered Public Accounting Firm

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

Opinion on Internal Control over Financial Reporting

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

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 income and comprehensive income, stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2022, and the related notes and our report dated February 16, 2023 expressed an unqualified opinion thereon.

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 included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and 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/ Ernst & Young LLP

Boston, Massachusetts
February 16, 2023

Item 9B. ***Other Information***

None.

PART III

Item 10. ***Directors, Executive Officers and Corporate Governance***

We have adopted a code of business conduct and ethics applicable to our directors, officers, employees, consultants and all their immediate family or other household members. A copy of that code is available on our corporate website at http://www.ironwoodpharma.com. Any amendments to the code of business conduct and ethics, and any waivers thereto involving any of our directors or executive officers, will be also available on our corporate website. A printed copy of these documents will be made available upon request. The content on our website is not incorporated by reference into this Annual Report on Form 10-K.

The other information required by this item is incorporated by reference from our proxy statement for our 2023 Annual Meeting of Stockholders.

Item 11. ***Executive Compensation***

The information required by this item is incorporated by reference from our proxy statement for our 2023 Annual Meeting of Stockholders.

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

The information relating to security ownership of certain beneficial owners of our common stock and information relating to the security ownership of our management required by this item is incorporated by reference from our proxy statement for our 2023 Annual Meeting of Stockholders.

The table below sets forth information with regard to securities authorized for issuance under our equity compensation plans as of December 31, 2022. As of December 31, 2022, we had three active equity compensation plans, each of which was approved by our stockholders:

- Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan;
- 2019 Equity Incentive Plan; and
- Amended and Restated 2010 Employee Stock Purchase Plan.

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (1)	Weighted-average exercise price of outstanding options, warrants, and rights (2)	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))
	(a)	(b)	(c)
Equity compensation plans approved by security holders	12,390,288	$ 12.34	7,366,153
Equity compensation plans not approved by security holders	—	—	—
Total	12,390,288	$ 12.34	7,366,153

(1) Amount includes the number of shares subject to issuance upon exercise of 6,931,372 outstanding stock options and vesting of 5,458,916 restricted stock units.

(2) Amount includes all outstanding stock options but does not include restricted stock units, which do not have an exercise price.

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

The information required by this item is incorporated by reference from our proxy statement for our 2023 Annual Meeting of Stockholders.

Item 14. ***Principal Accountant Fees and Services***

The information required by this item is incorporated by reference from our proxy statement for our 2023 Annual Meeting of Stockholders.

PART IV

Item 15. ***Exhibits and Financial Statement Schedules***

1. List of documents filed as part of this report

    1. Consolidated Financial Statements listed under Part II, Item 8 and included herein by reference.

    2. Consolidated Financial Statement Schedules

        No schedules are submitted because they are not applicable, not required or because the information is included in the Consolidated Financial Statements or Notes to Consolidated Financial Statements.

    3. Exhibits

		Incorporated by reference herein	
Number	**Description**	**Form**	**Date**
2.1	Separation Agreement, dated as of March 30, 2019, by and between Ironwood Pharmaceuticals, Inc. and Cyclerion Therapeutics, Inc.	Current Report on Form 8-K (File No. 001-34620)	April 4, 2019
3.1	Eleventh Amended and Restated Certificate of Incorporation	Annual Report on Form 10-K (File No. 001-34620)	March 30, 2010
3.2	Certificate of Retirement	Registration Statement on Form 8-A/A (File No. 001-34620)	January 3, 2019
3.3	Certificate of Amendment	Current Report on Form 8-K (File No. 001-34620)	May 31, 2019
3.4	Fifth Amended and Restated Bylaws	Annual Report on Form 10-K (File No. 001-34620)	March 30, 2010
4.1	Specimen Class A Common Stock certificate	Registration Statement on Form S-1, as amended (File No. 333-163275)	January 20, 2010
4.3	Indenture, dated as of August 12, 2019, by and between Ironwood Pharmaceuticals, Inc. and U.S. Bank National Association (including the form of the 0.75% Convertible Senior Note due 2024)	Current Report on Form 8-K (File No. 001-34620)	August 13, 2019
4.3.1	Form of 0.75% Convertible Senior Note due 2024	Current Report on Form 8-K (File No. 001-34620)	August 13, 2019
4.4	Indenture, dated as of August 12, 2019, by and between Ironwood Pharmaceuticals, Inc. and U.S. Bank National Association (including the form of the 1.50% Convertible Senior Note due 2026)	Current Report on Form 8-K (File No. 001-34620)	August 13, 2019
4.4.1	Form of 1.50% Convertible Senior Note due 2026	Current Report on Form 8-K (File No. 001-34620)	August 13, 2019

4.5	Description of Securities of Ironwood Pharmaceuticals, Inc.	Annual Report on Form 10-K (File No. 001-34620)	February 17, 2021
10.1#	Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan	Registration Statement on Form S-8, as amended (File No. 333-184396)	October 12, 2012
10.1.1#	Form of Stock Option Agreement under the Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan	Quarterly Report on Form 10-Q (File No. 001-34620)	November 6, 2018
10.1.2#	Form of Restricted Stock Unit Agreement under the Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan	Quarterly Report on Form 10-Q (File No. 001-34620)	November 6, 2018
10.2#	2019 Equity Incentive Plan	Quarterly Report on Form 10-Q (File No. 001-34620)	July 30, 2019
10.2.1#	Form of Non-statutory Stock Option Agreement under the 2019 Equity Incentive Plan	Quarterly Report on Form 10-Q (File No. 001-34620)	July 30, 2019
10.2.2#	Form of Restricted Stock Unit Agreement under the 2019 Equity Incentive Plan	Quarterly Report on Form 10-Q (File No. 001-34620)	July 30, 2019
10.2.3#	Form of Restricted Stock Agreement under the 2019 Equity Incentive Plan	Quarterly Report on Form 10-Q (File No. 001-34620)	July 30, 2019
10.2.4#	Form of Performance-Based Restricted Stock Unit Award Agreement under the 2019 Equity Incentive Plan	Quarterly Report on Form 10-Q (File No. 001-34620)	May 6, 2020
10.3#	Amended and Restated 2010 Employee Stock Purchase Plan	Annual Report on Form 10-K (File No. 001-34620)	February 13, 2020
10.4#	Change of Control Severance Benefit Plan, as amended and restated	Quarterly Report on Form 10-Q (File No. 001-34620)	April 29, 2014
10.5#	Form of Executive Severance Agreement	Annual Report on Form 10-K (File No. 001-34620)	February 25, 2019
10.6#	Form of Executive Severance Agreement	Current Report on Form 8-K (File No. 001-34620)	December 1, 2021
10.7#	Second Amended and Restated Executive Severance Agreement, June 22, 2021 between Ironwood Pharmaceuticals, Inc. and Thomas McCourt	Current Report on Form 8-K/A (File No. 001-34620)	June 24, 2021
10.8#*	Amended and Restated Non-employee Director Compensation Policy, effective January 1, 2023		

10.9#	Form of Indemnification Agreement with Directors and Officers	Registration Statement on Form S-1, as amended (File No. 333-163275)	December 23, 2009
10.11+	Collaboration Agreement, dated as of September 12, 2007, as amended on November 3, 2009, by and between Forest Laboratories, Inc. and Ironwood Pharmaceuticals, Inc.	Registration Statement on Form S-1, as amended (File No. 333-163275)	February 2, 2010
10.11.1	Amendment No. 2 to the Collaboration Agreement, dated as of January 8, 2013, by and between Forest Laboratories, Inc. and Ironwood Pharmaceuticals, Inc.	Annual Report on Form 10-K (File No. 001-34620)	February 21, 2013
10.12+	Commercial Agreement, dated as of January 31, 2017, by and among Allergan USA, Inc., Forest Laboratories, LLC and Ironwood Pharmaceuticals, Inc.	Quarterly Report on Form 10-Q (File No. 001-34620)	May 8, 2017
10.13+	License Agreement, dated as of April 30, 2009, by and between Allergan Pharmaceuticals International Ltd. (formerly with Almirall, S.A.) and Ironwood Pharmaceuticals, Inc.	Registration Statement on Form S-1, as amended (File No. 333-163275)	February 2, 2010
10.13.1+	Amendment No. 1 to License Agreement, dated as of June 11, 2013, by and between Allergan Pharmaceuticals International Ltd. (formerly with Almirall, S.A.) and Ironwood Pharmaceuticals, Inc.	Quarterly Report on Form 10-Q (File No. 001-34620)	August 8, 2013
10.13.2+	Amendment to the License Agreement, dated as of October 26, 2015, by and between Allergan Pharmaceuticals International Ltd. and Ironwood Pharmaceuticals, Inc.	Annual Report on Form 10-K (File No. 001-34620)	February 19, 2016
10.13.3+	Amendment to the License Agreement dated as of January 31, 2017, by and between Allergan Pharmaceuticals International Ltd., and Ironwood Pharmaceuticals, Inc.	Quarterly Report on Form 10-Q (File No. 001-34620)	May 8, 2017
10.14+	Novation Agreement, dated as of October 26, 2015, by and among Almirall, S.A., Allergan Pharmaceuticals International Ltd. and Ironwood Pharmaceuticals, Inc.	Annual Report on Form 10-K (File No. 001-34620)	February 19, 2016
10.15++	Amended and Restated License Agreement, dated as of August 1, 2019, by and between Ironwood Pharmaceuticals, Inc. and Astellas Pharma Inc.	Current Report on Form 8-K (File No. 001-34620	August 1, 2019
10.15.1+	Amendment to the Amended and Restated License Agreement, dated as of January 8, 2021, by and between Ironwood Pharmaceuticals, Inc. and Astellas Pharma Inc.	Annual Report on Form 10-K (File No. 001-34620)	February 17, 2021

10.16++	Amended and Restated License and Collaboration Agreement, dated as of September 16, 2019, by and between AstraZeneca AB and Ironwood Pharmaceuticals, Inc.	Current Report on Form 8-K (File No. 001-34620)	September 18, 2019
10.17+	Commercial Supply Agreement, dated as of June 23, 2010, by and among PolyPeptide Laboratories, Inc. and Polypeptide Laboratories (SWEDEN) AB, Forest Laboratories, Inc. and Ironwood Pharmaceuticals, Inc.	Quarterly Report on Form 10-Q (File No. 001-34620)	August 10, 2010
10.18+	Commercial Supply Agreement, dated as of March 28, 2011, by and among Corden Pharma Colorado, Inc. (f/k/a Roche Colorado Corporation), Ironwood Pharmaceuticals, Inc. and Forest Laboratories, Inc.	Quarterly Report on Form 10-Q (File No. 001-34620)	May 13, 2011
10.18.1+	Amendment No. 3 to Commercial Supply Agreement, dated as of November 26, 2013, by and between Corden Pharma Colorado, Inc. (f/k/a Roche Colorado Corporation), Ironwood Pharmaceuticals, Inc. and Forest Laboratories, Inc.	Annual Report on Form 10-K (File No. 001-34620)	February 7, 2014
10.19	Lease Agreement for facilities at 100 Summer Street, Boston, Massachusetts, dated as of June 11, 2019, by and between Ironwood Pharmaceuticals, Inc. and MA-100 Summer Street Owner, L.L.C.	Current Report on Form 8-K (File No. 001-34620)	June 13, 2019
10.20	Tax Matters Agreement, dated as of March 30, 2019, by and between Ironwood Pharmaceuticals, Inc. and Cyclerion Therapeutics, Inc.	Current Report on Form 8-K (File No. 001-34620)	April 4, 2019
10.21	Employee Matters Agreement, dated as of March 30, 2019, by and between Ironwood Pharmaceuticals, Inc. and Cyclerion Therapeutics, Inc.	Current Report on Form 8-K (File No. 001-34620)	April 4, 2019
10.24	Base Warrants Confirmation, dated as of June 10, 2015, between Ironwood Pharmaceuticals, Inc. and JPMorgan Chase Bank, National Association, London Branch	Quarterly Report on Form 10-Q (File No. 001-34620)	August 7, 2015
10.25	Base Warrants Confirmation, dated as of June 10, 2015, between Ironwood Pharmaceuticals, Inc. and Credit Suisse Capital LLC, through its agent Credit Suisse Securities (USA) LLC	Quarterly Report on Form 10-Q (File No. 001-34620)	August 7, 2015

10.28	Additional Warrants Confirmation, dated as of June 22, 2015, between Ironwood Pharmaceuticals, Inc. and JPMorgan Chase Bank, National Association, London Branch	Quarterly Report on Form 10-Q (File No. 001-34620)	August 7, 2015
10.29	Additional Warrants Confirmation, dated as of June 22, 2015, between Ironwood Pharmaceuticals, Inc. and Credit Suisse Capital LLC, through its agent Credit Suisse Securities (USA) LLC	Quarterly Report on Form 10-Q (File No. 001-34620)	August 7, 2015
10.30	Base Call Option Transaction Confirmation for the 2024 Notes, dated as of August 7, 2019, between Ironwood Pharmaceuticals, Inc. and JPMorgan Chase Bank, National Association	Current Report on Form 8-K (File No. 001-34620)	August 13, 2019
10.31	Base Call Option Transaction Confirmation for the 2026 Notes, dated as of August 7, 2019, between Ironwood Pharmaceuticals, Inc. and JPMorgan Chase Bank, National Association	Current Report on Form 8-K (File No. 001-34620)	August 13, 2019
10.32	Base Call Option Transaction Confirmation for the 2024 Notes, dated as of August 7, 2019, between Ironwood Pharmaceuticals, Inc. and Credit Suisse Capital LLC	Current Report on Form 8-K (File No. 001-34620)	August 13, 2019
10.33	Base Call Option Transaction Confirmation, for the 2026 Notes, dated as of August 7, 2019, between Ironwood Pharmaceuticals, Inc. and Credit Suisse Capital LLC	Current Report on Form 8-K (File No. 001-34620)	August 13, 2019
10.34	Additional Call Option Transaction Confirmation for the 2024 Notes, dated as of August 12, 2019, between Ironwood Pharmaceuticals, Inc. and JPMorgan Chase Bank, National Association	Current Report on Form 8-K (File No. 001-34620)	August 13, 2019
10.35	Additional Call Option Transaction Confirmation for the 2026 Notes, dated as of August 12, 2019, between Ironwood Pharmaceuticals, Inc. and JPMorgan Chase Bank, National Association	Current Report on Form 8-K (File No. 001-34620)	August 13, 2019
10.36	Additional Call Option Transaction Confirmation for the 2024 Notes, dated as of August 12, 2019, between Ironwood Pharmaceuticals, Inc. and Credit Suisse Capital LLC	Current Report on Form 8-K (File No. 001-34620)	August 13, 2019
10.37	Additional Call Option Transaction Confirmation for the 2026 Notes, dated as of August 12, 2019, between Ironwood Pharmaceuticals, Inc. and Credit Suisse Capital LLC	Current Report on Form 8-K (File No. 001-34620)	August 13, 2019

10.38	Call Spread Unwind Agreement, dated as of August 7, 2019, between Ironwood Pharmaceuticals, Inc. and JPMorgan Chase Bank, National Association	Annual Report on Form 10-K (File No. 001-34620)	February 13, 2020
10.39	Call Spread Unwind Agreement, dated as of August 7, 2019, between Ironwood Pharmaceuticals, Inc. and Credit Suisse Capital LLC	Annual Report on Form 10-K (File No. 001-34620)	February 13, 2020
21.1	Subsidiaries of Ironwood Pharmaceuticals, Inc.	Annual Report on Form 10-K (File No. 001-34620)	February 13, 2020
23.1*	Consent of Independent Registered Public Accounting Firm		
31.1*	Certification of Chief Executive Officer pursuant to Rules 13a-14 or 15d-14 of the Exchange Act		
31.2*	Certification of Chief Financial Officer pursuant to Rules 13a-14 or 15d-14 of the Exchange Act		
32.1‡	Certification of Chief Executive Officer pursuant to Rules 13a-14(b) or 15d-14(b) of the Exchange Act and 18 U.S.C. Section 1350		
32.2‡	Certification of Chief Financial Officer pursuant to Rules 13a-14(b) or 15d-14(b) of the Exchange Act and 18 U.S.C. Section 1350		
101.INS*	XBRL Instance Document – The Instance Document does not appear in the Interactive Data Files because its XBRL tags are embedded within the Inline XBRL document		
101.SCH*	XBRL Taxonomy Extension Schema Document		
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document		
101.LAB*	XBRL Taxonomy Extension Label Linkbase Database		
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document		
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document		
104*	The cover page from this Annual Report on Form 10-K, formatted in Inline XBRL		

* Filed herewith.
‡ Furnished herewith.
\+ Confidential treatment granted under 17 C.F.R. §§200.80(b)(4) and 230.406. The confidential portions of this exhibit have been omitted and are remeasured accordingly. The confidential portions have been provided separately to the SEC pursuant to the confidential treatment request.
\# Management contract or compensatory plan, contract, or arrangement.

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, in the City of Boston, Commonwealth of Massachusetts, on the 16th day of February 2023.

Ironwood Pharmaceuticals, Inc.
By: /s/ THOMAS MCCOURT
Thomas McCourt
Chief Executive Officer

Pursuant to the requirements of Section 13 or 15(d) 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 and on the date indicated.

Signature	Title	Date
/s/ THOMAS MCCOURT Thomas McCourt	Chief Executive Officer and Director (Principal Executive Officer)	February 16, 2023
/s/ SRAVAN K. EMANY Sravan K. Emany	Senior Vice President, Chief Financial Officer (Principal Financial Officer)	February 16, 2023
/s/ RONALD SILVER Ronald Silver	Vice President, Corporate Controller (Principal Accounting Officer)	February 16, 2023
/s/ JULIE H. MCHUGH Julie H. McHugh	Chair of the Board	February 16, 2023
/s/ MARK CURRIE Mark Currie	Director	February 16, 2023
Alexander Denner	Director	
/s/ ANDREW DREYFUS Andrew Dreyfus	Director	February 16, 2023
/s/ JON DUANE Jon Duane	Director	February 16, 2023
/s/ MARLA KESSLER Marla Kessler	Director	February 16, 2023
/s/ CATHERINE MOUKHEIBIR Catherine Moukheibir	Director	February 16, 2023
/s/ JAY P. SHEPARD Jay P. Shepard	Director	February 16, 2023

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Ironwood Pharmaceuticals, Inc.

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Report of Independent Registered Public Accounting Firm

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

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Ironwood Pharmaceuticals, Inc. (the Company) as of December 31, 2022 and 2021, the related consolidated statements of income and comprehensive income, stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2022, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the 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 issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated February 16, 2023 expressed an unqualified opinion thereon.

Basis for Opinion

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

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

Adoption of New Accounting Standard

As discussed in Note 2 to the consolidated financial statements, the Company changed its method of accounting for convertible senior notes in 2022 due to the adoption of ASU 2020-06.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the 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 financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the 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.

	Collaboration Agreement for North America with AbbVie Inc.
Description of the Matter	Revenue recognized from the Collaboration Agreement for North America with AbbVie Inc. (together with its affiliates, or "AbbVie") was $398.8 million for the sale of LINZESS in the U.S. for the year ended December 31, 2022. As discussed in Note 4 to the consolidated financial statements, the Company generates the majority of its revenue from a collaboration arrangement with AbbVie related to linaclotide (LINZESS). The Company records its share of the net profits or net losses from the sale of LINZESS in the U.S., less commercial expenses, and presents the

	settlement payments to and from AbbVie as collaboration expense or collaborative arrangements revenue, as applicable. Auditing revenue recognition under the AbbVie collaboration was especially challenging and required significant auditor judgment because the Company relies on AbbVie for timely and accurate information regarding net profits realized from the sale of LINZESS in the U.S. Management uses the information received from AbbVie, which includes net revenues from sales of LINZESS in the U.S. and related costs, to record its collaboration revenue. Certain of such information provided by AbbVie are determined by AbbVie by using estimates and judgments, which could be adjusted based on actual results in the future.
How We Addressed the Matter in Our Audit	We obtained an understanding, evaluated the design and tested the operating effectiveness of the Company's internal controls over its collaboration revenue process, including controls over the Company's evaluation of the completeness and accuracy of information related to net sales of LINZESS provided from AbbVie. Our audit procedures included, among others, inspecting reported information provided by AbbVie to the Company related to the net profits realized from the sale of LINZESS in the U.S. We analyzed the gross sales and certain adjustments to arrive at net sales, cost of goods sold, and related costs contributing to Ironwood's share of net profits and compared current period results to historical trends. We also tested settlement payments received by the Company throughout the year. In addition, we confirmed directly with AbbVie the collaborative arrangement revenue for the year ended December 31, 2022 related to the sale of LINZESS in the U.S. as well as the amounts due to the Company as of December 31, 2022.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 1998.

Boston, Massachusetts
February 16, 2023

Ironwood Pharmaceuticals, Inc.
Consolidated Balance Sheets
(In thousands, except share and per share amounts)

	December 31, 2022	December 31, 2021
ASSETS		
Current assets:		
Cash and cash equivalents	$ 656,203	$ 620,129
Accounts receivable, net	115,458	114,042
Prepaid expenses and other current assets	7,715	8,689
Restricted cash	1,250	1,250
Convertible note hedges	—	1,115
Total current assets	780,626	745,225
Restricted cash, net of current portion	485	485
Accounts receivable, net of current portion	14,589	23,998
Property and equipment, net	6,288	7,575
Operating lease right-of-use assets	14,023	15,350
Deferred tax assets	283,661	333,294
Other assets	847	1,000
Total assets	$ 1,100,519	$ 1,126,927
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 483	$ 935
Accrued research and development costs	5,258	15,896
Accrued expenses and other current liabilities	16,700	23,566
Current portion of operating lease liabilities	3,065	3,127
Current portion of convertible senior notes	—	116,858
Note hedge warrants	19	1,316
Total current liabilities	25,525	161,698
Operating lease obligations, net of current portion	16,599	18,484
Convertible senior notes, net of current portion	396,251	337,333
Other liabilities	9,766	3,501
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.001 par value, 75,000,000 shares authorized, no shares issued and outstanding	—	—
Class A Common Stock, $0.001 par value, 500,000,000 shares authorized and 154,026,949 shares issued and outstanding at December 31, 2022 and 500,000,000 shares authorized and 162,036,461 shares issued and outstanding at December 31, 2021	154	162
Additional paid-in capital	1,348,600	1,543,357
Accumulated deficit	(696,376)	(937,608)
Total stockholders' equity	652,378	605,911
Total liabilities and stockholders' equity	$ 1,100,519	$ 1,126,927

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

Ironwood Pharmaceuticals, Inc.
Consolidated Statements of Income and Comprehensive Income
(In thousands, except per share amounts)

	Years Ended December 31,		
	2022	2021	2020
Revenues:			
Collaborative arrangements revenue	$ 410,596	$ 412,784	$ 381,545
Sale of active pharmaceutical ingredient	—	969	7,978
Total revenues	410,596	413,753	389,523
Operating expenses:			
Cost of revenues	—	—	3,136
Research and development	44,265	70,405	88,062
Selling, general and administrative	115,994	111,133	140,003
Restructuring expenses	—	(44)	15,382
Total operating expenses	160,259	181,494	246,583
Income from operations	250,337	232,259	142,940
Other (expense) income:			
Interest expense	(7,598)	(31,150)	(29,478)
Interest and investment income	9,501	726	1,504
Gain (loss) on derivatives	182	(1,178)	(6,129)
Other income	—	—	24
Other (expense) income, net	2,085	(31,602)	(34,079)
Income before income taxes	252,422	200,657	108,861
Income tax (expense) benefit	(77,357)	327,791	(2,685)
Net income and comprehensive income	$ 175,065	$ 528,448	$ 106,176
Net income per share—basic	$ 1.13	$ 3.26	$ 0.67
Net income per share—diluted	$ 0.96	$ 3.21	$ 0.66
Weighted average shares used in computing net income per share—basic:	154,366	162,245	159,427
Weighted average shares used in computing net income per share—diluted:	186,312	164,418	160,655

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

Ironwood Pharmaceuticals, Inc.
Consolidated Statements of Stockholders' Equity (Deficit)
(In thousands, except share amounts)

	Class A Common Stock		Additional paid-in capital	Accumulated deficit	Total stockholders' equity (deficit)
	Shares	Amount			
Balance at December 31, 2019	157,535,962	$ 158	$ 1,478,823	$ (1,572,232)	$ (93,251)
Issuance of common stock related to share-based awards and employee stock purchase plan	3,080,713	3	18,537	—	18,540
Share-based compensation expense related to share-based awards and employee stock purchase plan	—	—	31,175	—	31,175
Net income	—	—	—	106,176	106,176
Balance at December 31, 2020	160,616,675	$ 161	$ 1,528,535	$ (1,466,056)	$ 62,640
Issuance of common stock related to share-based awards and employee stock purchase plan	3,776,786	3	19,678	—	19,681
Share-based compensation expense related to share-based awards and employee stock purchase plan	—	—	22,281	—	22,281
Repurchases of common stock	(2,357,000)	(2)	(27,137)	—	(27,139)
Net income	—	—	—	528,448	528,448
Balance at December 31, 2021	162,036,461	$ 162	$ 1,543,357	$ (937,608)	$ 605,911
Cumulative effect adjustment upon adoption of ASU 2020-06, net of tax	—	—	(110,217)	66,167	(44,050)
Issuance of common stock related to share-based awards and employee stock purchase plan	2,756,841	3	11,787	—	11,790
Share-based compensation expense related to share-based awards and employee stock purchase plan	—	—	27,048	—	27,048
Repurchases of common stock	(10,766,353)	(11)	(123,375)	—	(123,386)
Net income	—	—	—	175,065	175,065
Balance at December 31, 2022	154,026,949	$ 154	$ 1,348,600	$ (696,376)	$ 652,378

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

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

	Year Ended December 31,		
	2022	2021	2020
Cash flows from operating activities:			
Net income	$ 175,065	$ 528,448	$ 106,176
Adjustments to reconcile net income to net cash provided by operating activities:			
Depreciation and amortization	1,418	1,523	3,564
Loss on disposal of property and equipment	2	93	470
Share-based compensation expense	27,048	22,281	31,175
Change in fair value of note hedge warrants	(1,297)	(10,772)	(12,172)
Change in fair value of convertible note hedges	1,115	11,950	18,301
Non-cash interest expense	1,853	23,935	22,263
Deferred income taxes (including benefit from valuation allowance release)	65,739	(333,294)	—
Changes in assets and liabilities:			
Accounts receivable and related party accounts receivable, net	7,993	7,712	4,091
Prepaid expenses and other current assets	3,224	601	1,515
Inventory, net	—	—	648
Operating lease right-of-use assets	1,327	1,226	1,167
Other assets	153	(57)	(153)
Accounts payable, related party accounts payable, and accrued expenses	(8,116)	(2,644)	(7,523)
Accrued research and development costs	(10,638)	13,998	(1,058)
Operating lease liabilities	(1,947)	(1,835)	218
Deferred revenue	—	—	(875)
Other liabilities	10,824	(1,270)	1,029
Net cash provided by operating activities	273,763	261,895	168,836
Cash flows from investing activities:			
Purchases of property and equipment	(136)	(265)	(1,842)
Net cash used in investing activities	(136)	(265)	(1,842)
Cash flows from financing activities:			
Proceeds from exercise of stock options and employee stock purchase plan	9,540	19,581	18,546
Payment on 2022 Convertible Notes	(120,699)	—	—
Repurchases of common stock	(126,394)	(24,131)	—
Net cash provided by (used in) financing activities	(237,553)	(4,550)	18,546
Net increase in cash, cash equivalents and restricted cash	36,074	257,080	185,540
Cash, cash equivalents and restricted cash, beginning of period	621,864	364,784	179,244
Cash, cash equivalents and restricted cash, end of period	$ 657,938	$ 621,864	$ 364,784
Reconciliation of cash, cash equivalents, and restricted cash to the consolidated balance sheets			
Cash and cash equivalents	$ 656,203	$ 620,129	$ 362,564
Restricted cash	1,735	1,735	2,220
Total cash, cash equivalents, and restricted cash	$ 657,938	$ 621,864	$ 364,784
Supplemental cash flow disclosure:			
Cash paid for interest	$ 5,745	$ 7,216	$ 7,216
Cash paid for income taxes	$ 4,615	$ 3,452	$ 1,848
Non-cash investing and financing activities			
Stock repurchases payable in accrued expenses	$ —	$ 3,009	$ —
Stock option exercise proceeds receivable in other current assets	$ 2,351	$ 101	$ —

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

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements

1. Nature of Business

Ironwood Pharmaceuticals, Inc. (the "Company") is a gastrointestinal ("GI") healthcare company dedicated to advancing the treatment of GI diseases and redefining the standard of care for GI patients. The Company is focused on the development and commercialization of innovative GI product opportunities in areas of significant unmet need, leveraging its demonstrated expertise and capabilities in GI diseases.

LINZESS® (linaclotide), the Company's commercial product, is the first product approved by the United States Food and Drug Administration (the "U.S. FDA") in a class of GI medicines called guanylate cyclase type C agonists ("GC-C agonists") and is indicated for adult men and women suffering from irritable bowel syndrome with constipation ("IBS-C") or chronic idiopathic constipation ("CIC"). LINZESS is available to adult men and women suffering from IBS-C or CIC in the United States (the "U.S.") and Mexico and to adult men and women suffering from IBS-C in Japan and China. Linaclotide is available under the trademarked name CONSTELLA® to adult men and women suffering from IBS-C or CIC in Canada, and to adult men and women suffering from IBS-C in certain European countries.

The Company has strategic partnerships with leading pharmaceutical companies to support the development and commercialization of linaclotide throughout the world. The Company and its partner, AbbVie Inc. (together with its affiliates, "AbbVie"), began commercializing LINZESS in the U.S. in December 2012. Under the Company's collaboration for North America with AbbVie, total net sales of LINZESS in the U.S., as recorded by AbbVie, are reduced by commercial costs incurred by each party, and the resulting amount is shared equally between the Company and AbbVie. Additionally, development costs are shared equally between the Company and AbbVie. The Company and AbbVie are exploring ways to enhance the clinical profile of LINZESS by studying linaclotide in additional indications, populations and formulations to assess its potential to treat various conditions.

Outside of the U.S., the Company earns royalties as a percentage of net sales of products containing linaclotide as an active ingredient by the Company's collaboration partners. AbbVie has an exclusive license from the Company to develop and commercialize linaclotide in all countries other than China (including Hong Kong and Macau), Japan and the countries and territories of North America ("the AbbVie License Territory"). In addition, AbbVie has exclusive rights to commercialize linaclotide in Canada as CONSTELLA and in Mexico as LINZESS. Astellas Pharma Inc. ("Astellas"), the Company's partner in Japan, has an exclusive license to develop, manufacture, and commercialize linaclotide in Japan. AstraZeneca AB (together with its affiliates) ("AstraZeneca"), the Company's partner in China, has the exclusive right to develop, manufacture, and commercialize products containing linaclotide in China (including Hong Kong and Macau) (the "AstraZeneca License Territory").

The Company has a collaboration and license option agreement (the "COUR Collaboration Agreement") with COUR Pharmaceutical Development Company, Inc. ("COUR"), a biotechnology company developing novel immune-modifying nanoparticles to treat autoimmune diseases. The COUR Collaboration Agreement grants the Company an option to acquire an exclusive license to research, develop, manufacture and commercialize, in the U.S., products containing CNP-104, a potential treatment for primary biliary cholangitis, a rare autoimmune disease targeting the liver.

These and other agreements are more fully described in Note 4, *Collaboration, License, and Other Agreements,* to these consolidated financial statements.

The Company is also advancing IW-3300, a GC-C agonist, for the potential treatment of visceral pain conditions, including interstitial cystitis / bladder pain syndrome ("IC/BPS") and endometriosis.

The Company was incorporated in Delaware on January 5, 1998 as Microbia, Inc. On April 7, 2008, the Company changed its name to Ironwood Pharmaceuticals, Inc. To date, the Company has dedicated a majority of its activities to the research, development and commercialization of linaclotide, as well as to the research and development of its other product candidates.

2. Summary of Significant Accounting Policies

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of Ironwood and its wholly-owned subsidiaries, as of December 31, 2022, Ironwood Pharmaceuticals Securities Corporation and Ironwood Pharmaceuticals GmbH. All intercompany transactions and balances are eliminated in consolidation.

Segment Information

Operating segments are components of an enterprise for which separate financial information is available and is evaluated regularly by the Company's chief operating decision-maker in deciding how to allocate resources and in assessing performance. The Company currently operates in one reportable business segment – human therapeutics.

Reclassifications

Certain prior period financial statement items have been reclassified to conform to current period presentation.

Use of Estimates

The preparation of consolidated financial statements in accordance with U.S. generally accepted accounting principles requires the Company's management to make estimates and judgments that may affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements, and the amounts of revenues and expenses during the reported periods. On an ongoing basis, the Company's management evaluates its estimates, judgments and methodologies. Significant estimates and assumptions in the consolidated financial statements include those related to revenue recognition; accounts receivable; useful lives of long-lived assets, impairment of long-lived assets, including goodwill; valuation procedures for right-of-use assets and operating lease liabilities; valuation procedures for the issuance and repurchase of convertible notes; balance sheet classification of convertible notes; fair value of derivatives; income taxes, including the valuation allowance for deferred tax assets; research and development expenses; contingencies and share-based compensation. The Company bases its estimates on historical experience and on various other assumptions that are believed to be reasonable, the results of which form the basis for making judgments about the carrying values of assets and liabilities. Actual results may differ materially from these estimates under different assumptions or conditions. Changes in estimates are reflected in reported results in the period in which they become known.

Cash and Cash Equivalents

The Company considers all highly liquid investment instruments with a remaining maturity when purchased of three months or less to be cash equivalents. Investments qualifying as cash equivalents primarily consist of money market funds, repurchase agreements, commercial paper, and corporate bonds. The carrying amount of cash equivalents approximates fair value. The amount of cash equivalents included in cash and cash equivalents was $650.2 million and $595.2 million at December 31, 2022 and 2021, respectively.

Restricted Cash

The Company is contingently liable under unused letters of credit with a bank, related to the Company's facility lease and vehicle lease agreements, in the amount of $1.7 million as of December 31, 2022 and 2021. The Company records as restricted cash the collateral used to secure these letters of credit. The amount of restricted cash in current assets and non-current assets was $1.3 million and $0.5 million, respectively, at December 31, 2022 and 2021.

Concentrations of Suppliers

The Company relies on its collaboration partners and their suppliers to manufacture linaclotide API, linaclotide finished drug product, and finished goods.

If any of the Company's collaboration partners and their suppliers were to limit or terminate production or otherwise fail to meet the quality or delivery requirements needed to satisfy the supply commitments, the process of

locating and qualifying alternate sources could require up to several months, during which time production could be delayed. Such delays could have a material adverse effect on the Company's business, financial position and results of operations.

Accounts Receivable

The Company makes judgments as to its ability to collect outstanding receivables and provides an allowance for credit losses when collection becomes doubtful. Provisions are made based upon a specific review of all significant outstanding invoices and the overall quality and age of those invoices not specifically reviewed. The Company's receivables relate primarily to amounts reimbursed under its collaboration, license, and other agreements. The Company believes that credit risks associated with these partners are not significant. The Company reviews the need for an allowance for credit losses for its receivables based on various factors including payment history and historical bad debt experience. The Company had no allowance for credit losses as of December 31, 2022 or 2021.

Concentrations of Credit Risk

Financial instruments that subject the Company to credit risk primarily consist of cash and cash equivalents, restricted cash, and accounts receivable. The Company maintains its cash and cash equivalent balances with high-quality financial institutions and the Company believes that such funds are subject to minimal credit risk. The Company has adopted an investment policy which limits the amounts the Company may invest in certain types of investments, and requires all investments held by the Company to be at least A- rated, thereby reducing credit risk exposure.

Accounts receivable primarily consist of amounts due under the linaclotide collaboration agreement with AbbVie for North America (Note 4). The Company does not obtain collateral for its accounts receivable. The Company previously reflected amounts due from Allergan plc ("Allergan"), net of amounts payable to Allergan, prior to its acquisition by AbbVie as related party accounts receivable, net. Following the acquisition of Allergan by AbbVie, the Company determined that AbbVie is not a related party to the Company (Note 15).

The percentages of revenue recognized from significant collaborative partners of the Company in the years ended December 31, 2022, 2021 and 2020 as well as the account receivable balances, net of any payables due, at December 31, 2022 and 2021 are included in the following table:

	Accounts Receivable December 31,		Revenue Year Ended December 31,		
	2022	2021	2022	2021	2020
Collaborative Partner:					
AbbVie (North America and Europe)	80 %	81 %	98 %	98 %	96 %

Property and Equipment

Property and equipment, including leasehold improvements, are recorded at cost, and are depreciated when placed into service using the straight-line method based on their estimated useful lives as follows:

Asset Description	Estimated Useful Life (In Years)
Laboratory equipment	5
Computer and office equipment	3
Furniture and fixtures	7
Software	3

Included in property and equipment are certain costs of software obtained for internal use. Costs incurred during the preliminary project stage are expensed as incurred, while costs incurred during the application development stage are capitalized and amortized over the estimated useful life of the software. The Company also capitalizes costs related to specific upgrades and enhancements when it is probable the expenditures will result in additional functionality. Maintenance and training costs related to software obtained for internal use are expensed as incurred.

Leasehold improvements are amortized over the shorter of the estimated useful life of the asset or the lease term.

Costs for capital assets not yet placed into service have been capitalized as construction in process, and will be depreciated in accordance with the above guidelines once placed into service. Maintenance and repair costs are expensed as incurred.

Impairment of Long-Lived Assets

The Company regularly reviews the carrying amount of its long-lived assets to determine whether indicators of impairment may exist, which warrant adjustments to carrying values or estimated useful lives. If indications of impairment exist, projected future undiscounted cash flows associated with the asset are compared to the carrying amount to determine whether the asset's value is recoverable. If the carrying value of the asset exceeds such projected undiscounted cash flows, the asset will be written down to its estimated fair value.

Income Taxes

The Company provides for income taxes under the asset and liability method. Deferred tax assets and liabilities are determined based on differences between financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates in effect when the differences are expected to reverse. Deferred tax assets are reduced by a valuation allowance to reflect the uncertainty associated with their ultimate realization.

The Company accounts for uncertain tax positions recognized in the consolidated financial statements in accordance with the provisions of Accounting Standards Codification ("ASC") Topic 740, *Income Taxes*, by prescribing a more-likely-than-not threshold for financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. The Company evaluates uncertain tax positions on a quarterly basis and adjusts the level of the liability to reflect any subsequent changes in the relevant facts surrounding the uncertain positions. Any changes to these estimates, based on the actual results obtained and/or a change in assumptions, could impact the Company's income tax provision in future periods. Interest and penalty charges, if any, related to unrecognized tax benefits are classified as income tax expense in the Company's consolidated statements of income.

Financing Costs

Financing costs include costs directly attributable to the Company's offerings of its equity securities and its debt financings. Costs attributable to equity offerings are charged as a reduction to stockholders' equity against the proceeds of the offering once the offering is completed. Costs attributable to debt financings are deferred and amortized to interest expense over the term of the debt using the effective interest method. In accordance with ASC Topic 835, *Interest*, the Company presents debt issuance costs on the balance sheet as a direct deduction from the associated debt liability.

Leases

The Company's lease portfolio for the year ended December 31, 2022 included: an office lease for its headquarters location, vehicle leases for its salesforce representatives, and leases for computer and office equipment. The Company determines if an arrangement is a lease at the inception of the contract and determines the classification of its leases at lease commencement. The asset component of the Company's operating leases is recorded as operating lease right-of-use assets, and the liability component is recorded as current portion of operating lease liabilities and operating lease liabilities, net of current portion in the Company's consolidated balance sheets. As of December 31, 2022, the Company did not record any finance leases.

Right-of-use assets and operating lease liabilities are recognized based on the present value of lease payments over the lease term at the lease commencement date. The lease term used to measure the right-of-use asset and operating lease liability may include options to extend the lease when it is reasonably certain that the Company will exercise the option. The Company accounts for lease components and non-lease components together as a single lease component for

the asset class of right-of-use real estate assets. The Company uses an incremental borrowing rate based on the information available at lease commencement in determining the present value of lease payments, if an implicit rate of return is not readily determinable. Operating lease right-of-use assets are adjusted for prepaid rent, initial direct costs, and lease incentives.

Right-of-use assets and operating lease liabilities are remeasured upon reassessment events and modifications to leases using the present value of remaining lease payments and estimated incremental borrowing rate at the time of remeasurement, as applicable.

Operating lease cost is recognized on a straight-line basis over the lease term, and includes amounts related to short-term leases. The Company has elected to not recognize lease terms with a term of twelve months or less on its balance sheet for all classes of underlying asset types. The Company recognizes variable lease payments as operating expenses in the period in which the obligation for those payments is incurred. Variable lease payments primarily include common area maintenance, utilities, real estate taxes, insurance, and other operating costs that are passed on from the lessor in proportion to the space leased by the Company.

Derivative Assets and Liabilities

In June 2015, the Company issued 2.25% Convertible Senior Notes due June 15, 2022 (the "2022 Convertible Notes"), and in August 2019, the Company issued 0.75% Convertible Senior Notes due 2024 (the "2024 Convertible Notes"), and 1.50% Convertible Senior Notes due 2026 (the "2026 Convertible Notes", and together with the 2022 Convertible Notes and the 2024 Convertible Notes, the "Convertible Senior Notes"). In connection with the issuance of the 2022 Convertible Notes, the Company entered into convertible note hedge transactions (the "Convertible Note Hedges") and separate note hedge warrant transactions (the "Note Hedge Warrants"), with certain financial institutions (Note 9). In connection with the partial repurchase of the 2022 Convertible Notes in August 2019, the Company terminated its Convertible Note Hedges and Note Hedge Warrants proportionately. The Convertible Note Hedges terminated unexercised upon expiry in June 2022. These instruments are derivative financial instruments under ASC Topic 815, *Derivatives and Hedging* ("ASC 815").

These derivatives are recorded as assets or liabilities at fair value each reporting date and the fair value is determined using the Black-Scholes option-pricing model. The changes in fair value are recorded as a component of other (expense) income in the consolidated statements of income. Significant inputs used to determine the fair value include the price per share of the Company's Class A Common Stock, expected terms of the derivative instruments, strike prices of the derivative instruments, risk-free interest rates, and expected volatility of the Company's Class A Common Stock. Changes to these inputs could materially affect the valuation of the derivative instruments.

In August 2019, in connection with the issuance of the 2024 Convertible Notes and the 2026 Convertible Notes, the Company entered into the Capped Calls. The Capped Calls cover the same number of shares of Class A Common Stock that initially underlie the 2024 Convertible Notes and the 2026 Convertible Notes (subject to anti-dilution and certain other adjustments). These instruments meet the conditions outlined in ASC 815 to be classified in stockholders' equity (deficit) and are not subsequently remeasured as long as the conditions for equity classification continue to be met.

Share Repurchases

The Company accounts for repurchases of its Class A Common Stock on the trade date by recording the excess of the repurchase price over the par value entirely to additional paid-in capital. All repurchased shares are retired or constructively retired. Issued and outstanding shares are reduced by shares repurchased.

Revenue Recognition

The Company's revenues are generated primarily through collaborative arrangements and license agreements related to the research and development and commercialization of linaclotide. The terms of the collaborative research and development, license, co-promotion and other agreements contain multiple performance obligations which may include (i) licenses, (ii) research and development activities, including participation on joint steering committees, (iii) the manufacture of finished drug product, API, or development materials for a partner, which are reimbursed at a contractually determined rate, and (iv) education or co-promotion activities by the Company's clinical sales specialists.

Non-refundable payments to the Company under these agreements may include (i) up-front license fees, (ii) payments for research and development activities, (iii) payments for the manufacture of finished drug product, API, or development materials, (iv) payments based upon the achievement of certain milestones, (v) payments for sales detailing, promotional support services and medical education initiatives, and (vi) royalties on product sales. The Company receives its share of the net profits or bears its share of the net losses from the sale of linaclotide in the U.S. through its collaboration agreement with AbbVie for North America. The Company has adopted a policy to recognize revenue net of tax withholdings, as applicable.

Collaboration, License, and Other Commercial Agreements

Upon licensing intellectual property to a customer, the Company determines if the license is distinct from the other performance obligations identified in the arrangement. The Company recognizes revenues from the transaction price, including non-refundable, up-front fees allocated to the license when the license is transferred to the customer if the license has distinct benefit to the customer. For licenses that are combined with other promises, the Company assesses the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time. For performance obligations that are satisfied over time, the Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

The Company's license and collaboration agreements include milestone payments, such as development and other milestones. The Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method at the inception of the agreement. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation on a relative standalone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. The Company re-evaluates the probability of achievement of such milestones and any related constraint at each reporting period, and any adjustments are recorded on a cumulative catch-up basis.

Agreements that include the supply of API or drug product for either clinical development or commercial supply at the customer's discretion are generally considered as options. The Company assesses if these options provide a material right to its partner, and if so, they are accounted for as separate performance obligations. If the Company is entitled to additional payments when the customer exercises these options, any additional payments are recorded as revenue when the customer obtains control of the goods, which is typically upon shipment for sales of API and finished drug product.

For agreements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue when the related sales occur.

Net Profit or Net Loss Sharing

In accordance with ASC Topic 808, *Collaborative Arrangements* ("ASC 808"), the Company considers the nature and contractual terms of the arrangement and the nature of the Company's business operations to determine the classification of payments under the Company's collaboration agreements. While ASC 808 provides guidance on classification, the standard is silent on matters of separation, initial measurement, and recognition. Therefore, the Company applies the separation, initial measurement, and recognition principles of ASC Topic 606, *Revenue from Contracts with Customers* ("ASC 606"), as applicable.

The Company's collaborative arrangements revenues generated from sales of LINZESS in the U.S. are considered akin to sales-based royalties. In accordance with the sales-based royalty exception, the Company recognizes its share of the pre-tax commercial net profit or net loss generated from the sales of LINZESS in the U.S. in the period the product sales are earned, as reported by AbbVie, and related cost of goods sold and selling, general and administrative expenses as incurred by the Company and AbbVie. These amounts are partially determined based on amounts provided by AbbVie and involve the use of estimates and judgments, such as product sales allowances and accruals related to prompt payment discounts, chargebacks, governmental and contractual rebates, wholesaler fees,

product returns, and co-payment assistance costs, which could be adjusted based on actual results in the future. The Company is highly dependent on AbbVie for timely and accurate information regarding net revenues from sales of LINZESS in the U.S. in accordance with both ASC 808 and ASC 606, and the related costs, in order to accurately report its results of operations. If the Company does not receive timely and accurate information or incorrectly estimates activity levels associated with the collaboration at a given point in time, the Company could be required to record adjustments in future periods.

In accordance with ASC 606-10-55, *Principal Agent Considerations*, the Company records revenue transactions as net product revenue in its consolidated statements of income if it is deemed the principal in the transaction, which includes being the primary obligor, retaining inventory risk, and control over pricing. Given that the Company is not the primary obligor and does not have the inventory risks in the collaboration agreement with AbbVie for North America, it records its share of the net profits or net losses from the sales of LINZESS in the U.S. on a net basis and presents the settlement payments to and from AbbVie as collaboration expense or collaborative arrangements revenue, as applicable. The Company and AbbVie settle the cost sharing quarterly such that the Company's statements of income reflect 50% of the pre-tax net profit or loss generated from sales of LINZESS in the U.S.

Sale of Active Pharmaceutical Ingredient

During the year ended December 31, 2020 the Company produced linaclotide API, finished drug product, finished goods, and/or development materials for certain of its partners. As of December 31, 2020, the Company was no longer responsible for the supply of linaclotide API, finished drug product, finished goods or development materials to its partners, though the Company may provide development materials to certain of its partners on a periodic basis. Sales of such development materials have been and are expected to continue to be immaterial.

The Company recognizes revenue on linaclotide API, finished drug product, finished goods, and development materials when control has transferred to the partner, which generally occurs upon shipment after the material passed all quality testing required for acceptance by the partner.

Other

The Company's deferred revenue balance consists of advance billings and payments received from customers in excess of revenue recognized.

Cost of Revenues

Cost of revenues includes cost related to the sales of linaclotide API, finished drug product, and finished goods and are generally recognized upon shipment to certain of the Company's partners outside of the U.S. The Company's cost of revenues for linaclotide consists of the internal and external costs of producing such API, finished drug product, and finished goods.

Research and Development Costs

The Company generally expenses research and development costs to operations as incurred. The Company capitalizes nonrefundable advance payments made by the Company for research and development activities and defers expense recognition until the related goods are received or the related services are performed.

Research and development expenses are comprised of costs incurred in performing research and development activities, including salary, benefits, share-based compensation, and other employee-related expenses; laboratory supplies and other direct expenses; facilities expenses; overhead expenses; third-party contractual costs relating to nonclinical studies and clinical trial activities and related contract manufacturing expenses, development of manufacturing processes and regulatory registration of third-party manufacturing facilities; licensing fees for the Company's product candidates; and other outside expenses.

The Company has certain collaboration agreements pursuant to which it shares or has shared research and development expenses related to linaclotide. The Company records expenses incurred under such linaclotide collaboration arrangements as research and development expense. Under the Company's collaboration agreement with

AbbVie for North America, the Company is reimbursed for certain research and development expenses and nets these reimbursements against its research and development expenses as incurred.

Research and development expense includes up-front payment, non-contingent payment, and milestone payment obligations under the COUR Collaboration Agreement (Note 4). Expense is recognized when the obligation is determined to be probable.

Restructuring Expenses

Restructuring expenses are comprised primarily of costs associated with exit and disposal activities in accordance with ASC Topic 420, *Exit or Disposal Cost Obligations*, and include one-time termination benefits and contract-related costs. Such costs are based on estimates of fair value in the period liabilities are incurred. The Company evaluates and adjusts these costs for changes in circumstances as additional information becomes available.

Selling, General and Administrative Expenses

The Company expenses selling, general and administrative costs to operations as incurred. Selling, general and administrative expenses consist primarily of compensation, benefits and other employee-related expenses for personnel in the Company's administrative, finance, legal, information technology, business development, commercial, sales, marketing, communications and human resources functions. Other costs include the legal costs of pursuing patent protection of the Company's intellectual property, general and administrative related facility costs, insurance costs and professional fees for accounting, tax, consulting, legal and other services.

The Company includes AbbVie's selling, general and administrative cost-sharing payments in the calculation of the net profits and net losses from the sale of LINZESS in the U.S. and presents the net payment to or from AbbVie as collaboration expense or collaborative arrangements revenue, respectively.

Share-Based Compensation Expense

The Company grants awards under its share-based compensation programs, including stock awards, restricted stock awards ("RSAs"), restricted stock units ("RSUs") (including both time-based and performance-based RSUs), stock options, and shares issued under the Company's employee stock purchase plan ("ESPP"). Share-based compensation is recognized as expense in the consolidated statements of income based on the grant date fair value over the requisite service period, net of estimated forfeitures. The Company estimates forfeitures over the requisite service period using historical forfeiture activity and records share-based compensation expense only for those awards that are expected to vest.

The Company estimates the fair value of stock options using the Black-Scholes option-pricing model, which requires the use of subjective assumptions including volatility and expected term, among others. The fair value of stock awards, RSAs, and RSUs is based on the market value of the Company's Class A Common Stock on the date of grant, with the exception of performance-based RSUs with market conditions, which are measured using the Monte Carlo simulation method on the date of grant (Note 12). Discounted stock purchases under the Company's ESPP are valued on the first date of the offering period using the Black-Scholes option-pricing model to compute the fair value of the lookback provision plus the purchase discount.

For awards that vest based on service conditions and market conditions, the Company uses a straight-line method to recognize compensation expense over the respective service period. For awards that contain performance conditions, the Company determines the appropriate amount to expense at each reporting date based on the anticipated achievement of performance targets, which requires judgement, including forecasting the achievement of future specified targets. At the date performance conditions are determined to be probable of achievement, the Company records a cumulative expense catch-up, with remaining expense amortized over the remaining service period. Throughout the performance period, the Company re-assesses the estimated performance and updates the number of performance-based awards that it believes will ultimately vest. Discounted stock purchases under the Company's ESPP are recognized over the offering period.

Compensation expense related to modified awards is measured based on the fair value for the awards as of the modification date. Any incremental compensation expense arising from the excess of the fair value of the awards on the

modification date compared to the fair value of the awards immediately before the modification date is recognized at the modification date or ratably over the requisite remaining service period, as appropriate.

While the assumptions used to calculate and account for share-based compensation awards represent management's best estimates, these estimates involve inherent uncertainties and the application of management's judgment. As a result, if revisions are made to the Company's underlying assumptions and estimates, the Company's share-based compensation expense could vary significantly from period to period.

Patent Costs

The Company incurred and recorded as operating expense legal and other fees related to patents of $1.3 million, $1.7 million, and $2.3 million for the years ended December 31, 2022, 2021 and 2020, respectively. These costs were charged to selling, general and administrative expenses as incurred.

Net Income Per Share

Basic net income per common share is computed by dividing the net income by the weighted average number of common shares outstanding during the period. Diluted net income per share reflects the potential dilution beyond common shares for basic net income per share that could occur if securities or other contracts to issue common shares were exercised, converted into common shares, or resulted in the issuance of common shares that would have shared in the Company's earnings.

Subsequent Events

The Company considers events or transactions that have occurred after the balance sheet date of December 31, 2022, but prior to the filing of the financial statements with the Securities and Exchange Commission ("SEC") to provide additional evidence relative to certain estimates or to identify matters that require additional recognition or disclosure. Subsequent events have been evaluated through the filing of the financial statements accompanying this Annual Report on Form 10-K.

New Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board (the "FASB") or other standard setting bodies that are adopted by the Company as of the specified effective date. Except as set forth below, the Company did not adopt any new accounting pronouncements during the year ended December 31, 2022 that had a material effect on its consolidated financial statements.

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"). The amendments in ASU 2020-06 simplify the accounting for certain financial instruments with characteristics of liabilities and equity, including convertible instruments and contracts on an entity's own equity. Under ASU 2020-06, embedded conversion features are no longer separately reported in equity and convertible debt instruments are now accounted for as a single liability measured at amortized cost, as long as no other features require bifurcation and recognition as derivatives. These changes will reduce reported interest expense and increase reported net income for entities with convertible instruments that were bifurcated between liabilities and equity under previously existing guidance. Additionally, temporary differences between the book and tax bases resulting from the bifurcation of the embedded conversion feature under previously existing guidance have been eliminated and deferred tax assets and liabilities arising from such temporary differences will no longer be reported. The new guidance also requires the if-converted method to be used in diluted earnings per share computations for all convertible instruments and revised the if-converted method to preclude the addback of interest expense to the numerator if the principal portions of the convertible instruments are required to be settled in cash. The standard is effective for public companies for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2021. Upon adoption, entities may apply the new standard on a modified retrospective or full retrospective basis.

The Company adopted ASU 2020-06 on January 1, 2022 using the modified retrospective approach, which resulted in a cumulative-effect adjustment recorded on the date of adoption as follows (in thousands):

Consolidated Balance Sheet	**December 31, 2021 As Reported**	**Effect of the Adoption of ASU 2020-06**	**January 1, 2022 As Adjusted**
Deferred tax assets	$ 333,294	$ 16,855	$ 350,149
Current portion of convertible senior notes	116,858	3,581	120,439
Long-term portion of convertible senior notes	337,333	57,324	394,657
Additional paid-in-capital	1,543,357	(110,217)	1,433,140
Retained earnings	(937,608)	66,167	(871,441)

Interest expense recognized in subsequent periods is reduced as a result of accounting for convertible debt instruments as a single liability measured at amortized cost, with a decrease of $22.1 million of non-cash interest expense during the year ended December 31, 2022 compared to the year ended December 31, 2021 related to convertible debt instruments outstanding on the adoption date.

The adoption of ASU 2020-06 does not impact the Company's liquidity or cash flows.

In May 2021, the FASB issued ASU No. 2021-04, *Earnings Per Share (Topic 260), Debt—Modifications and Extinguishments (Subtopic 470-50), Compensation—Stock Compensation (Topic 718), and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Issuer's Accounting for Certain Modifications or Exchanges of Freestanding Equity-Classified Written Call Options* ("ASU 2021-04"). The guidance in ASU 2021-04 clarifies and reduces diversity in an issuer's accounting for modifications or exchanges of freestanding equity-classified written call options that remain equity classified after modification or exchange. The standard is effective for public companies for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2021.The Company adopted ASU 2021-04 as of January 1, 2022. The adoption of ASU 2021-04 did not have a material impact on the Company's financial position and results of operations.

Other recent accounting pronouncements issued, but not yet effective, are not expected to be applicable to the Company or have a material effect on the consolidated financial statements upon future adoption.

3. Net Income Per Share

The following table sets forth the computation of basic and diluted net income per common share (in thousands, except per share amounts):

	Year Ended December 31,		
	2022	2021	2020
Numerator:			
Net income	$ 175,065	$ 528,448	$ 106,176
Add back interest expense, net of tax benefit, on assumed conversion of 2024 Convertible Notes	1,781	—	—
Add back interest expense, net of tax benefit, on assumed conversion of 2026 Convertible Notes	2,668	—	—
Numerator used in computing net income per share — diluted	$ 179,514	$ 528,448	$ 106,176
Denominator:			
Weighted average number of common shares outstanding used in computing net income per share — basic	154,366	162,245	159,427
Effect of dilutive securities:			
Stock options	306	488	367
Time-based restricted stock units	1,375	1,422	766
Performance-based restricted stock units	282	146	1
Restricted stock	115	117	94
2024 Convertible Notes assumed conversion	14,934	—	—
2026 Convertible Notes assumed conversion	14,934	—	—
Dilutive potential common shares			
Weighted average number of common shares outstanding used in computing net income per share — diluted	186,312	164,418	160,655
Net income per share — basic	$ 1.13	$ 3.26	$ 0.67
Net income per share — diluted	$ 0.96	$ 3.21	$ 0.66

The outstanding securities have been excluded from the computation of diluted weighted average shares outstanding, as applicable, as their effect would be anti-dilutive (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Stock options	6,152	7,701	11,746
Restricted stock awards	—	—	2
Time-based restricted stock units	10	102	209
Performance-based restricted stock units	1,182	121	93
Note Hedge Warrants	8,318	8,318	8,318
2022 Convertible Notes	—	8,318	8,318
2024 Convertible Notes	—	14,934	14,934
2026 Convertible Notes	—	14,934	14,934
Total	15,662	54,428	58,554

Prior to the adoption of ASU 2020-06, the potentially dilutive impact of the Convertible Senior Notes (Note 9) was determined using the treasury stock method. Under this method, no numerator or denominator adjustments arose from the principal and interest components of the Convertible Senior Notes because the Company had the intent and ability to settle the Convertible Senior Notes' principal and interest in cash. Instead, the Company was required to increase the diluted net income per share denominator by the variable number of shares that would be issued upon conversion if it settled the conversion spread obligation with shares. For diluted net income per share purposes, the conversion spread obligation was calculated based on whether the average market price of the Company's Class A Common Stock during the reporting period was in excess of the conversion price of the Convertible Senior Notes. There was no calculated spread added to the denominator for the years ended December 31, 2021 or 2020.

Following the adoption of ASU 2020-06 on January 1, 2022, the dilutive impact of the Convertible Senior Notes is determined using the if-converted method. Under the if-converted method, the Convertible Senior Notes are assumed to be converted into common stock at the beginning of the period (or at the time of issuance, if later). Interest

charges are deducted from the numerator, unless the principal amount of the convertible instruments is required to be paid in cash.

There was no dilutive impact of the 2022 Convertible Notes for the year ended December 31, 2022 because the Company had elected prior to the beginning of the period to settle the conversion of 2022 Convertible Notes, if any, with a combination settlement of a cash payment equal to the principal value of converted notes and shares of Class A Common Stock equal to the conversion value in excess of the principal value, if any. Accordingly, interest expense was not removed from the numerator and there was no calculated spread added to the denominator because the average market price of the Company's Class A common stock during the portion of each period in which the 2022 Convertible Notes were outstanding was not in excess of the conversion price.

4. Collaboration, License, and Other Agreements

For the year ended December 31, 2022, the Company had linaclotide collaboration agreements with AbbVie for North America and AstraZeneca for China (including Hong Kong and Macau), as well as linaclotide license agreements with Astellas for Japan and with AbbVie for the AbbVie License Territory. The Company also had an agreement with Alnylam Pharmaceuticals, Inc ("Alnylam") to perform disease awareness activities for acute hepatic porphyria ("AHP") and sales detailing activities for GIVLAARI® (givosiran). The following table provides amounts included in the Company's consolidated statements of income as collaborative arrangements revenue and sale of API primarily attributable to transactions from these arrangements (in thousands):

	Year Ended December 31,		
Collaborative Arrangements Revenue	**2022**	**2021**	**2020**
Linaclotide Collaboration and License Agreements:			
AbbVie (North America)	$ 401,498	$ 403,085	$ 370,902
AbbVie (Europe and other)	2,444	2,558	2,196
AstraZeneca (China, including Hong Kong and Macau)	635	743	682
Astellas (Japan)	2,001	2,232	2,128
Other Agreements:			
Alnylam (GIVLAARI)	2,194	2,411	4,302
Other	1,824	1,755	1,335
Total collaborative arrangements revenue	$ 410,596	$ 412,784	$ 381,545
Sale of API			
Linaclotide Agreements:			
Astellas (Japan)	$ —	$ 149	$ 2,017
AstraZeneca (China, including Hong Kong and Macau)	—	597	5,540
Other	—	223	421
Total sale of API	$ —	$ 969	$ 7,978

Accounts receivable, net, included $130.0 million and $138.0 primarily related to collaborative arrangements revenue and sale of API, collectively, as of December 31, 2022 and 2021, respectively. Accounts receivable, net, included $104.4 million and $112.2 million due from the Company's partner, AbbVie, net of $4.0 million and $5.0 million of accounts payable at December 31, 2022 and 2021, respectively.

The Company routinely assesses the creditworthiness of its license and collaboration partners. The Company has not experienced any material losses related to receivables from its license or collaboration partners during the years ended December 31, 2022, 2021, or 2020.

Linaclotide Agreements

Collaboration Agreement for North America with AbbVie

In September 2007, the Company entered into a collaboration agreement with AbbVie to develop and commercialize linaclotide for the treatment of IBS-C, CIC, and other GI conditions in North America. Under the terms of this collaboration agreement, the Company received an upfront licensing fee, equity investment, and development and regulatory milestones, and shares equally with AbbVie all development costs as well as net profits or losses from the

development and sale of linaclotide in the U.S. In addition, the Company receives royalties in the mid-teens percent based on net sales in Canada and Mexico. AbbVie is solely responsible for the further development, regulatory approval and commercialization of linaclotide in those countries and funding any costs.

During the years ended December 31, 2022, 2021 and 2020, the Company incurred $8.0 million, $8.2 million, and $20.1 million in total research and development expenses under the linaclotide collaboration for North America. As a result of the research and development cost-sharing provisions of the linaclotide collaboration for North America, the Company incurred $8.9 million, $11.5 million, and $5.6 million in incremental research and development costs during the years ended December 31, 2022, 2021, and 2020, respectively, to reflect the obligations of each party under the collaboration to bear 50% of the development costs incurred.

The Company and AbbVie began commercializing LINZESS in the U.S. in December 2012. The Company receives 50% of the net profits and bears 50% of the net losses from the commercial sale of LINZESS in the U.S. Net profits or net losses consist of net sales of LINZESS to third-party customers and sublicense income in the U.S. less the cost of goods sold as well as selling, general and administrative expenses. LINZESS net sales are calculated and recorded by AbbVie and may include gross sales net of discounts, rebates, allowances, sales taxes, freight and insurance charges, and other applicable deductions.

The Company evaluated its collaboration arrangement for North America with AbbVie and concluded that all development-period performance obligations had been satisfied as of September 2012. The Company has determined that there are three remaining commercial-period performance obligations, which include the sales detailing of LINZESS, participation in the joint commercialization committee, and approved additional trials. The consideration remaining includes cost reimbursements in the U.S. and net profit and loss sharing payments based on net sales in the U.S. Additionally, the Company receives royalties in the mid-teens percent based on net sales in Canada and Mexico. Royalties and net profit and loss sharing payments will be recorded as collaborative arrangements revenue or expense in the period earned, as these payments relate predominately to the license granted to AbbVie. The Company records royalty revenue in the period earned based on royalty reports from its partner, if available, or based on the projected sales and historical trends. The cost reimbursements received from AbbVie during the commercialization period will be recognized as earned in accordance with the right-to-invoice practical expedient, as the Company's right to consideration corresponds directly with the value of the services transferred during the commercialization period.

Under the Company's collaboration agreement with AbbVie for North America, LINZESS net sales are calculated and recorded by AbbVie and include gross sales net of discounts, rebates, allowances, sales taxes, freight and insurance charges, and other applicable deductions, as noted above. These amounts include the use of estimates and judgments, which could be adjusted based on actual results in the future. The Company records its share of the net profits or net losses from the sales of LINZESS in the U.S. less commercial expenses on a net basis, and presents the settlement payments to and from AbbVie as collaboration expense or collaborative arrangements revenue, as applicable. This treatment is in accordance with the Company's revenue recognition policy, given that the Company is not the primary obligor and does not have the inventory risks in the collaboration agreement with AbbVie for North America. The Company relies on AbbVie to provide accurate and complete information related to net sales of LINZESS in accordance with U.S. generally accepted accounting principles in order to calculate its settlement payments to and from AbbVie and record collaboration expense or collaborative arrangements revenue, as applicable.

The Company recognized collaborative arrangements revenue from the AbbVie collaboration agreement for North America during the years ended December 31, 2022, 2021, and 2020 as follows (in thousands):

	Year Ended December 31,		
	2022	**2021**	**2020**
Collaborative arrangements revenue related to sales of LINZESS in the U.S.	$ 398,767	$ 400,371	$ 368,603
Royalty revenue	2,731	2,714	2,299
Total collaborative arrangements revenue	$ 401,498	$ 403,085	$ 370,902

The Company incurred $34.3 million, $30.3 million, and $39.9 million in total selling, general and administrative costs related to the sale of LINZESS in the U.S. in accordance with the cost-sharing arrangement with AbbVie for the years ended December 31, 2022, 2021, and 2020, respectively.

In May 2014, CONSTELLA® became commercially available in Canada and, in June 2014, LINZESS became commercially available in Mexico. The Company records royalties on sales of CONSTELLA in Canada and LINZESS in Mexico in the period earned. The Company recognized $2.7 million, $2.7 million, and $2.3 million of combined royalty revenues from Canada and Mexico during the years ended December 31, 2022, 2021, and 2020, respectively.

License Agreement with AbbVie (All countries other than the countries and territories of North America, China (including Hong Kong and Macau), and Japan)

The Company has a license agreement with AbbVie to develop, manufacture and commercialize linaclotide in (i) Europe, and (ii) all countries other than China (including Hong Kong and Macau), Japan, and the countries and territories of North America, or collectively the "Expanded Territory," for the treatment of IBS-C, CIC and other GI conditions.

Under the license agreement, as amended, AbbVie is obligated to pay the Company, (i) royalties based on sales volume in Europe in the upper-teens percent, and (ii) on a country-by-country and product-by-product basis in the Expanded Territory, a royalty as a percentage of net sales of products containing linaclotide as an active ingredient in the upper-single digits for five years following the first commercial sale of a linaclotide product in a country, and in the low-double digits thereafter. The royalty rate for products in Europe and the Expanded Territory will decrease, on a country-by-country basis, to the lower-single digits, or cease entirely, following the occurrence of certain events. The license agreement also contains certain sales-based milestones and commercial launch milestones, which could total up to $42.5 million.

The Company recognized $2.4 million, $2.6 million and $2.2 million of royalty revenue from the Amended European License Agreement during the years ended December 31, 2022, 2021, and 2020, respectively.

License Agreement for Japan with Astellas

The Company has a license agreement with Astellas to develop, manufacture, and commercialize linaclotide for the treatment of IBS-C, CIC and other GI conditions in Japan.

Under the license agreement, as amended, Astellas is required to pay royalties to the Company at rates beginning in the mid-single digit percent and escalating to low-double-digit percent, based on aggregate annual net sales in Japan of products containing linaclotide as an active ingredient. These royalty payments are subject to reduction following the expiration of certain licensed patents and the occurrence of generic competition in Japan.

During the year ended December 31, 2022, the Company recognized $2.0 million in collaborative arrangements revenue related to royalties.

During the year ended December 31, 2021, the Company recognized $2.2 million in collaborative arrangements revenue related to royalties, and $0.2 million from the sale of API to Astellas under the Amended Astellas License Agreement.

During the year ended December 31, 2020, the Company recognized $2.1 million in collaborative arrangements revenue related to royalties, an insignificant amount of collaborative arrangements revenue related to adverse event reporting services, and $2.0 million from the sale of API to Astellas under the Amended Astellas License Agreement.

Collaboration Agreement for China (including Hong Kong and Macau) with AstraZeneca

The Company has a collaboration agreement with AstraZeneca under which AstraZeneca has the exclusive right to develop, manufacture and commercialize products containing linaclotide in the AstraZeneca License Territory.

Under the collaboration agreement, AstraZeneca is required to pay tiered royalties to the Company at rates beginning in the mid-single-digit percent and increasing up to twenty percent based on the aggregate annual net sales of products containing linaclotide in the AstraZeneca License Territory.

During the year ended December 31, 2022, the Company recognized $0.6 million in collaborative arrangements revenue related to the Amended AstraZeneca Agreement related to royalties.

During the year ended December 31, 2021, the Company recognized $0.7 million in collaborative arrangements revenue related to the Amended AstraZeneca Agreement, of which $0.5 million related to royalties and $0.2 million related to services provided under a transition services agreement, and recognized $0.6 million in sales of API relating to the supply of development material.

During the year ended December 31, 2020, the Company recognized $0.7 million in collaborative arrangements revenue related to the Amended AstraZeneca License, of which $0.6 million related to services provided under a transition services agreement and $0.1 million related to royalties, and recognized $5.5 million of sales of API relating to the supply of linaclotide finished drug product and finished goods under a commercial supply agreement.

The Company is entitled to receive non-contingent payments totaling $35.0 million in three installments through 2024, of which $25.0 million remained outstanding at December 31, 2022. In addition, AstraZeneca may be required to make milestone payments totaling up to $90.0 million contingent on the achievement of certain sales targets. The significant financing component of the transaction was $2.6 million and is recognized as interest income through 2024 using the effective interest method. At December 31, 2022, the current portion and non-current portion of the non-contingent receivable due from AstraZeneca was $10.0 million and $14.6 million, respectively. At December 31, 2021, the non-contingent receivable due from AstraZeneca was $24.0 million and was classified as non-current.

Other Collaboration and License Agreements

Collaboration and License Option Agreement with Cour

In November 2021, the Company entered into the COUR Collaboration Agreement, pursuant to which the Company has been granted an option (the "Option") to acquire an exclusive license to research, develop, manufacture and commercialize, in the U.S., products containing CNP-104, a tolerizing immune modifying nanoparticle ("CNP-104") for the treatment of primary biliary cholangitis. COUR has initiated a clinical study to evaluate the safety, tolerability, and pharmacodynamic effects and efficacy of CNP-104 in PBC patients, with early data assessing T-cell response from patients enrolled in the clinical study expected in the second half of 2023. We expect that such early data will inform timing of topline data readout.

Pursuant to the terms of the COUR Collaboration Agreement, the Company made an upfront, non-refundable payment of $6.0 million to COUR during the year ended December 31, 2021, and agreed to pay $13.5 million in non-contingent payments and milestone payments in connection with certain development activities and regulatory milestones. After reviewing the data from the clinical study for CNP-104, if the Company exercises the Option, the Company will pay COUR $35.0 million in exchange for the license. Upon commercialization, COUR will be eligible to receive commercial milestone payments of up to $440.0 million over the term of the agreement and royalties in the high-single digits to low-double digits percentage of the aggregated annual net sales in the U.S. of products containing CNP-104.

During the year ended December 31, 2021, the Company recognized research and development expense totaling $19.5 million related to the up-front payment, non-contingent payment, and milestone payments for which payment is probable to occur. At December 31, 2022 and 2021, payment obligations of $3.8 million and $13.5 million, respectively, were included in accrued research and development costs related to the COUR Collaboration Agreement.

Other Agreements

Disease Education and Promotional Agreement with Alnylam

In August 2019, the Company and Alnylam entered into a disease education and promotional agreement (the "Alnylam Agreement") for Alnylam's GIVLAARI for the treatment of AHP. The Alnylam Agreement, as amended, was terminated in June 2021 with an effective termination date of September 30, 2021. Under the terms of the Alnylam Agreement, the Company's sales force performed disease awareness activities and sales detailing activities for GIVLAARI. The Company remained eligible to receive royalties based on a percentage of net sales of GIVLAARI that are directly attributable to the Company's promotional efforts through September 30, 2022, which was one year following the termination of the agreement.

During the years ended December 31, 2022, 2021 and 2020, the Company recognized $2.2 million, $2.4 million and $0.8 million, respectively, in collaborative arrangements revenue related to royalties. During the year ended December 31, 2020, the Company recognized $3.5 million in collaborative arrangements revenue related to the service fees.

5. Fair Value of Financial Instruments

The tables below present information about the Company's assets that are measured at fair value on a recurring basis as of December 31, 2022 and 2021 and indicate the fair value hierarchy of the valuation techniques the Company utilized to determine such fair value. In general, fair values determined by Level 1 inputs utilize observable inputs such as quoted prices in active markets for identical assets or liabilities. Fair values determined by Level 2 inputs utilize data points that are either directly or indirectly observable, such as quoted prices for similar instruments in active markets, interest rates and yield curves. Fair values determined by Level 3 inputs utilize unobservable data points in which there is little or no market data, which require the Company to develop its own assumptions for the asset or liability.

The Company's investment portfolio may include fixed income securities that do not always trade on a daily basis. As a result, the pricing services used by the Company apply other available information as applicable through processes such as benchmark yields, benchmarking of like securities, sector groupings and matrix pricing to prepare valuations. In addition, model processes are used to assess interest rate impact and develop prepayment scenarios. These models take into consideration relevant credit information, perceived market movements, sector news and economic events. The inputs into these models may include benchmark yields, reported trades, broker-dealer quotes, issuer spreads and other relevant data. The Company validates the prices provided by its third party pricing services by obtaining market values from other pricing sources and analyzing pricing data in certain instances. The Company periodically invests in certain reverse repurchase agreements, which are collateralized by Government Securities and Obligations for an amount not less than 102% of their principal amount. The Company does not record an asset or liability for the collateral as the Company is not permitted to sell or re-pledge the collateral. The collateral has at least the prevailing credit rating of U.S. Government Treasuries and Agencies. The Company utilizes a third party custodian to manage the exchange of funds and ensure the collateral received is maintained at 102% of the reverse repurchase agreements principal amount on a daily basis.

The following tables present the assets and liabilities the Company has measured at fair value on a recurring basis (in thousands):

		Fair Value Measurements at Reporting Date Using		
	December 31, 2022	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Assets:				
Cash and cash equivalents:				
Money market funds	$ 250,313	$ 250,313	$ —	$ —
Repurchase agreements	261,075	—	261,075	—
Commercial paper	138,809	—	138,809	—
Restricted cash:				
Money market funds	1,735	1,735	—	—
Total assets measured at fair value	$ 651,932	$ 252,048	$ 399,884	$ —
Liabilities:				
Note hedge warrants	$ 19	$ —	$ —	$ 19
Total liabilities measured at fair value	$ 19	$ —	$ —	$ 19

	December 31, 2021	Fair Value Measurements at Reporting Date Using Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Assets:				
Cash and cash equivalents:				
Money market funds	$ 595,233	$ 595,233	$ —	$ —
Restricted cash:				
Money market funds	1,735	1,735	—	—
Convertible note hedges	1,115	—	—	1,115
Total assets measured at fair value	$ 598,083	$ 596,968	$ —	$ 1,115
Liabilities:				
Note hedge warrants	$ 1,316	$ —	$ —	$ 1,316
Total liabilities measured at fair value	$ 1,316	$ —	$ —	$ 1,316

Cash equivalents, accounts receivable, prepaid expenses and other current assets, accounts payable, accrued research and development costs, accrued expenses and other current liabilities and current portion of operating lease obligations at December 31, 2022 and 2021 are carried at amounts that approximate fair value due to their short-term maturities.

Convertible Note Hedges and Note Hedge Warrants with Respect to 2022 Convertible Notes

The Company's Convertible Note Hedges and the Note Hedge Warrants are recorded as derivative assets and liabilities, respectively, and are classified as Level 3 measurements under the fair value hierarchy. These derivatives are not actively traded and are valued using the Black-Scholes option-pricing model, which requires the use of subjective assumptions.

The following inputs were used in the fair market valuation of the Convertible Note Hedges as of December 31, 2021 and the Note Hedge Warrants as of December 31, 2022 and 2021:

	December 31, 2022	December 31, 2021	
	Note Hedge Warrants	Convertible Note Hedges	Note Hedge Warrants
Risk-free interest rate [1]	4.5 %	0.2 %	0.4 %
Expected term	0.3	0.5	1.0
Stock price [2]	$ 12.39	$ 11.66	$ 11.66
Strike price [3]	$ 18.82	$ 14.51	$ 18.82
Common stock volatility [4]	27.1 %	27.0 %	32.2 %
Dividend yield [5]	— %	— %	— %

(1) Based on U.S. Treasury yield curve, with terms commensurate with the expected terms of the Convertible Note Hedges and the Note Hedge Warrants.
(2) The closing price of the Company's Class A Common Stock on the last trading days of the years ended December 31, 2022 and 2021, respectively.
(3) As per the respective agreements for the Convertible Note Hedges and Note Hedge Warrants.
(4) Expected volatility based on historical volatility of the Company's Class A Common Stock.
(5) The Company has not paid and does not anticipate paying cash dividends on its shares of common stock in the foreseeable future; therefore, the expected dividend yield is assumed to be zero.

The Convertible Note Hedges and the Note Hedge Warrants are recorded at fair value at each reporting date and changes in fair value are recorded in other (expense) income, net within the Company's consolidated statements of income.

The following table reflects the change in the Company's Level 3 Convertible Note Hedges and Note Hedge Warrants from December 31, 2020 through December 31, 2022 (in thousands):

	Convertible Note Hedges	Note Hedge Warrants
Balance at December 31, 2020	$ 13,065	$ (12,088)
Change in fair value, recorded as a component of gain (loss) on derivatives	(11,950)	10,772
Balance at December 31, 2021	$ 1,115	$ (1,316)
Change in fair value, recorded as a component of gain (loss) on derivatives	(1,115)	1,297
Balance at December 31, 2022	$ —	$ (19)

Convertible Senior Notes

In June 2015, the Company issued $335.7 million aggregate principal amount of its 2022 Convertible Notes. In August 2019, the Company issued $200.0 million aggregate principal amount of its 2024 Convertible Notes and $200.0 million aggregate principal amount of its 2026 Convertible Notes, and used a portion of the proceeds from such issuances to repurchase $215.0 million aggregate principal amount of its 2022 Convertible Notes. In June 2022, the Company repaid the $120.7 million remaining aggregate principal amount of its 2022 Convertible Notes. Prior to the adoption of ASU 2020-06, the Company separately accounted for the liability and equity components of each of the 2022 Convertible Notes, 2024 Convertible Notes, and 2026 Convertible Notes by allocating the proceeds between the liability component and equity component (Note 9). Following the adoption of ASU 2020-06 on January 1, 2022, the equity component was eliminated and each of the 2022 Convertible Notes, 2024 Convertible Notes, and 2026 Convertible Notes are measured as a single liability. The fair value of the respective convertible senior notes, which differs from their carrying value, is influenced by interest rates, the price of the Company’s Class A Common Stock and the volatility thereof, and the prices for the respective convertible senior notes observed in market trading, which are Level 2 inputs.

The estimated fair value of the 2022 Convertible Notes was $125.2 million as of December 31, 2021. The estimated fair value of the 2024 Convertible Notes was $215.9 million and $221.9 million as of December 31, 2022 and 2021, respectively. The estimated fair value of the 2026 Convertible Notes was $219.0 million and $227.2 million as of December 31, 2022 and 2021, respectively.

Capped Calls with Respect to 2024 Convertible Notes and 2026 Convertible Notes

In connection with the issuance of the 2024 Convertible Notes and the 2026 Convertible Notes, the Company entered into the Capped Calls with certain financial institutions. The Capped Calls cover 29,867,480 shares of Class A Common Stock (subject to anti-dilution and certain other adjustments), which is the same number of shares of Class A Common Stock that initially underlie the 2024 Convertible Notes and the 2026 Convertible Notes. The Capped Calls have an initial strike price of approximately $13.39 per share, which corresponds to the initial conversion price of the 2024 Convertible Notes and the 2026 Convertible Notes, and have a cap price of approximately $17.05 per share (Note 9). The strike price and cap price are subject to anti-dilution adjustments generally similar to those applicable to the 2024 Convertible Notes and the 2026 Convertible Notes. These instruments meet the conditions outlined in ASC 815 to be classified in stockholders’ equity (deficit) and are not subsequently remeasured as long as the conditions for equity classification continue to be met (Note 9).

6. Leases

The Company’s lease portfolio for the year ended December 31, 2022 includes: an office lease for its current headquarters location, vehicle leases for its salesforce representatives, and leases for computer and office equipment.

The Company’s office lease and vehicle lease require letters of credit to secure the Company’s obligations under the lease agreements totaling $1.7 million and are collateralized by money market accounts recorded as restricted cash on the Company’s consolidated balance sheets as of December 31, 2022 and 2021.

Lease cost is recognized on a straight-line basis over the lease term. The components of lease cost for the years ended December 31, 2022, 2021 and 2020 are as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Operating lease cost	$ 2,509	$ 2,520	$ 2,530
Short-term lease cost	1,070	960	1,420
Total lease cost	$ 3,579	$ 3,480	$ 3,950

Supplemental information related to leases for the periods reported is as follows:

	Year Ended December 31,		
	2022	2021	2020
Cash paid for amounts included in the measurement of lease liabilities (in thousands)	$ 3,114	$ 3,128	$ 1,146
Weighted-average remaining lease term of operating leases (in years)	7.3	8.3	9.3
Weighted-average discount rate of operating leases	5.8 %	5.8 %	5.8 %

Summer Street Lease

In June 2019, the Company entered into a non-cancelable operating lease (the "Summer Street Lease") for approximately 39,000 square feet of office space on the 23rd floor of 100 Summer Street, Boston, Massachusetts, which began serving as the Company's headquarters in October 2019. The Summer Street Lease terminates on June 11, 2030 and includes a 2% annual rent escalation, free rent periods, a tenant improvement allowance, and an option to extend the term of the lease for an additional five years at a market base rental rate. The extension option is not included in the lease term used for the measurement of the lease, as it is not reasonably certain to be exercised. The lease expense, inclusive of the escalating rent payments and lease incentives, is recognized on a straight-line basis over the lease term.

At lease commencement, the Company recorded a right-of-use asset and a lease liability using an incremental borrowing rate of 5.8%. At December 31, 2022, the balances of the right-of-use asset and operating lease liability were $14.0 million and $19.7 million, respectively. At December 31, 2021, the balances of the right-of-use asset and operating lease liability were $15.3 million and $21.5 million, respectively.

Lease costs related to the Summer Street Lease recorded during each of the years ended December 31, 2022, 2021 and 2020 were $2.5 million.

Future minimum lease payments under the Summer Street Lease as of December 31, 2022 are as follows (in thousands):

2023	$ 3,066
2024	3,126
2025	3,189
2026	3,252
2027	3,317
2028 and thereafter	8,285
Total future minimum lease payments	24,235
Less: present value adjustment	(4,571)
Operating lease liabilities	19,664
Less: current portion of operating lease liabilities	(3,065)
Operating lease liabilities, net of current portion	$ 16,599

7. Property and Equipment

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2022	2021
Software	$ 5,414	$ 5,667
Leasehold improvements	7,407	7,407
Laboratory equipment	1,327	1,327
Furniture and fixtures	1,542	1,517
Computer and office equipment	1,362	1,285
	17,052	17,203
Less accumulated depreciation and amortization	(10,764)	(9,628)
	$ 6,288	$ 7,575

Depreciation expense of property and equipment was $1.4 million, $1.5 million and $2.3 million for the years ended December 31, 2022, 2021 and 2020, respectively.

During the year ended December 31, 2020, the Company recorded $1.2 million, in restructuring expenses in its consolidated statement of income related to the impairment of certain fixed assets as a result of its decision to discontinue IW-3718 development.

8. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31,	
	2022	2021
Accrued compensation and benefits	$ 12,268	$ 16,653
Restructuring liabilities	—	462
Stock repurchase	—	3,009
Other	4,432	3,442
Total accrued expenses and other current liabilities	$ 16,700	$ 23,566

As of December 31, 2022 and 2021, other accrued expenses of $4.4 million and $3.4 million were comprised primarily of $3.6 million and $2.7 million of uninvoiced vendor liabilities, respectively.

9. Notes Payable

2.25% Convertible Senior Notes due 2022

In June 2015, the Company issued $335.7 million aggregate principal amount of the 2022 Convertible Notes. The Company received net proceeds of $324.0 million from the sale of the 2022 Convertible Notes, after deducting fees and expenses of $11.7 million. The Company used $21.1 million of the net proceeds from the sale of the 2022 Convertible Notes to pay the net cost of the Convertible Note Hedges (after such cost was partially offset by the proceeds to the Company from the sale of the Note Hedge Warrants), as described below.

In connection with the issuance of the 2024 Convertible Notes and the 2026 Convertible Notes in August 2019, the Company repurchased $215.0 million aggregate principal amount of the 2022 Convertible Notes. Such portion of the 2022 Convertible Notes were repurchased at a premium totaling $227.3 million.

In June 2022, the Company repaid the remaining $120.7 million aggregate principal amount of the 2022 Convertible Notes upon maturity.

The 2022 Convertible Notes were governed by an indenture (the "2022 Indenture") between the Company and U.S. Bank National Association, as trustee (the "Trustee"). The 2022 Convertible Notes were senior unsecured obligations and bore cash interest at the annual rate of 2.25%, payable on June 15 and December 15 of each year. The

2022 Convertible Notes matured on June 15, 2022. No conversions were exercised by holders of the 2022 Convertible Notes.

Upon issuance, the Company separately accounted for the liability and equity components of the 2022 Convertible Notes by allocating the proceeds between the liability component and the embedded conversion option, or equity component, due to the Company's ability to settle the 2022 Convertible Notes in cash, its Class A Common Stock, or a combination of cash and Class A Common Stock at the option of the Company. The carrying amount of the liability component was calculated by measuring the fair value of a similar liability that does not have an associated conversion feature. The equity component of the 2022 Convertible Notes was recognized as a debt discount and represents the difference between the gross proceeds from the issuance of the 2022 Convertible Notes and the fair value of the liability component of the 2022 Convertible Notes on the date of issuance. The debt discount was amortized to interest expense using the effective interest method over seven years, or the expected life of the 2022 Convertible Notes. The equity component was not remeasured as long as it continued to meet the conditions for equity classification.

Upon the adoption of ASU 2020-06 on January 1, 2022, the equity component is no longer bifurcated from the liability component and each debt instrument is accounted for as a single liability measured at amortized cost. Accordingly, the unamortized debt discount as of the adoption date in the amount of $3.5 million was derecognized, resulting in an increase to the current portion of convertible senior notes and a decrease to stockholders' equity. Additionally, there is no longer non-cash interest expense associated with the amortization of the original issue discount. During the years ended December 31, 2021 and 2020, the Company recognized $7.2 million and $6.6 million in non-cash interest expense, respectively, related to the debt discount.

0.75% Convertible Senior Notes due 2024 and 1.50% Convertible Senior Notes due 2026

In August 2019, the Company issued $200.0 million aggregate principal amount of the 2024 Convertible Notes and $200.0 million aggregate principal amount of the 2026 Convertible Notes. The Company received net proceeds of $391.0 million from the sale of the 2024 Convertible Notes and 2026 Convertible Notes, after deducting fees and expenses of $9.0 million. The Company used $25.2 million of the net proceeds from the sale of the 2024 Convertible Notes and 2026 Convertible Notes to pay the cost of the Capped Calls, as described below. For purposes of this section, "Notes" refer to the 2024 Convertible Notes and the 2026 Convertible Notes, collectively.

The 2024 Convertible Notes and 2026 Convertible Notes were issued by the Company on August 12, 2019, pursuant to separate Indentures, each dated as of such date (each an "Indenture" and together the "Indentures"), between the Company and the Trustee. The 2024 Convertible Notes bear cash interest at the annual rate of 0.75% and the 2026 Convertible Notes bear cash interest at the annual rate of 1.50%, each payable on June 15 and December 15 of each year. The 2024 Convertible Notes will mature on June 15, 2024 and the 2026 Convertible Notes will mature on June 15, 2026, unless earlier converted or repurchased. The Company will settle conversions of the 2024 Convertible Notes and 2026 Convertible Notes through payment or delivery, as the case may be, of cash, shares of the Company's Class A Common Stock or a combination of cash and shares of Class A Common Stock, at the Company's option (subject to, and in accordance with, the settlement provisions of the applicable Indenture). The initial conversion rate for each of the 2024 Convertible Notes and the 2026 Convertible Notes is 74.6687 shares of Class A Common Stock (subject to adjustment as provided for in the applicable Indenture) per $1,000 principal amount of the 2024 Convertible Notes and 2026 Convertible Notes, which is equal to an initial conversion price of approximately $13.39 per share.

Holders of the 2024 Convertible Notes and 2026 Convertible Notes may convert their Notes at their option at any time prior to the close of business on the business day immediately preceding December 15, 2023, with respect to the 2024 Convertible Notes, and December 15, 2025, with respect to the 2026 Convertible Notes, in multiples of $1,000 principal amount, only under the following circumstances:

- during any calendar quarter commencing after the calendar quarter ending on December 31, 2019 (and only during such calendar quarter), if the last reported sale price of Class A Common Stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price for the Notes on each applicable trading day;

- during the five business day period after any five consecutive trading day period (the "measurement period") in which the "trading price" (as defined in each Indenture) per $1,000 principal amount of Notes

for each trading day of the measurement period was less than 98% of the product of the last reported sale price of Class A Common Stock and the conversion rate for the Notes on each such trading day; or

- upon the occurrence of specified corporate events described in each Indenture.

On or after December 15, 2023, with respect to the 2024 Convertible Notes, and December 15, 2025, with respect to the 2026 Convertible Notes, until the close of business on the second scheduled trading day immediately preceding the applicable maturity date, the holders of the Notes may convert their Notes, in multiples of $1,000 principal amount, regardless of the foregoing conditions.

Upon the occurrence of fundamental changes, as described in the Indentures, prior to the maturity date of the respective Notes, holders of such Notes may require the Company to repurchase for cash all or a portion of their Notes at a repurchase price equal to 100% of the principal amount of the Notes to be repurchased, plus accrued and unpaid interest. If a make-whole fundamental change, as described in the Indentures, occurs and a holder elects to convert its Notes in connection with such make-whole fundamental change, such holder may be entitled to an increase in the conversion rate as described in the Indentures.

The Indentures do not contain any financial covenants or restrict the Company's ability to repurchase the Company's securities, pay dividends or make restricted payments in the event of a transaction that substantially increases the Company's level of indebtedness. The Indentures provide for customary events of default. In the case of an event of default with respect to a series of Notes arising from specified events of bankruptcy or insolvency, all outstanding Notes of such series will become due and payable immediately without further action or notice. If any other event of default with respect to a series of Notes under the relevant Indenture occurs or is continuing, the Trustee or holders of at least 25% in aggregate principal amount of the then outstanding Notes of such series may declare the principal amount of such Notes to be immediately due and payable.

Upon issuance, the Company separately accounted for the liability and equity components of the 2024 Convertible Notes and the 2026 Convertible Notes by allocating the proceeds between the liability components and the embedded conversion options, or equity components, due to the Company's ability to settle the 2024 Convertible Notes and the 2026 Convertible Notes in cash, its Class A Common Stock, or a combination of cash and Class A Common Stock at the option of the Company. The carrying amount of the respective liability components were calculated by measuring the fair value of a similar liability that does not have an associated conversion feature. The respective equity components of the 2024 Convertible Notes and the 2026 Convertible Notes were recognized as a debt discount and represent the difference between the gross proceeds from the issuance of the 2024 Convertible Notes and 2026 Convertible Notes and the fair value of the liability of the 2024 Convertible Notes and 2026 Convertible Notes on their respective dates of issuance. The debt discount was amortized to interest expense using the effective interest method over approximately five and seven years, or the expected life of the 2024 Convertible Notes and the 2026 Convertible Notes, respectively. The respective equity components were not remeasured as long as they continued to meet the conditions for equity classification.

Upon the adoption of ASU 2020-06 on January 1, 2022, the equity component is no longer bifurcated from the liability component and each debt instrument is accounted for as a single liability measured at amortized cost. Accordingly, the unamortized debt discount as of the adoption date in the amount of $22.3 million and $35.8 million for the 2024 Convertible Notes and 2026 Convertible Notes, respectively, was derecognized, resulting in an increase to the non-current portion of convertible senior notes and a decrease to stockholders' equity. Additionally, there is no longer non-cash interest expense associated with the amortization of the original issue discount. During the years ended December 31, 2021 and 2020, the Company recognized $8.2 million and $7.8 million in non-cash interest expense, respectively, related to the debt discount for the 2024 Convertible Notes and $6.8 million and $6.4 million in non-cash interest expense, respectively, related to the debt discount for the 2026 Convertible Notes.

The Company's outstanding balances for the convertible senior notes as of December 31, 2022 and 2021 consisted of the following (in thousands):

	December 31,	
	2022	2021
Liability component:		
Principal:		
2022 Convertible Notes	$ —	$ 120,699
2024 Convertible Notes	200,000	200,000
2026 Convertible Notes	200,000	200,000
Less: unamortized debt discount	—	(61,641)
Less: unamortized debt issuance costs	(3,749)	(4,867)
Net carrying amount	$ 396,251	$ 454,191
Equity component:		
2022 Convertible Notes	—	19,807
2024 Convertible Notes	—	41,152
2026 Convertible Notes	—	51,350
Total equity component	$ —	$ 112,309

In connection with the issuance of the 2022 Convertible Notes, the Company incurred $11.7 million of debt issuance costs, which primarily consisted of initial purchasers' discounts and legal and other professional fees. The Company allocated these costs to the liability and equity components based on the allocation of the proceeds. The portion of these costs allocated to the equity components totaling $4.0 million were recorded as a reduction to additional paid-in capital upon issuance. The portion of these costs allocated to the liability components totaling $7.7 million were recorded as a reduction in the carrying value of the debt on the consolidated balance sheet and are amortized to interest expense using the effective interest method over the expected life of the 2022 Convertible Notes. In connection with the partial repurchase of the 2022 Convertible Notes, the Company recorded a loss on extinguishment of debt of $23.4 million, of which $2.8 million related to the initial debt issuance costs, during the year ended December 31, 2019. Upon the adoption of ASU 2020-06, the costs originally allocated to the equity component are reflected within the current portion of convertible senior notes and recorded as interest expense over the life of the 2022 Convertible Notes.

The Company determined the expected life of the 2022 Convertible Notes was equal to their seven-year term. From the date of the partial repurchase of the 2022 Convertible Notes in August 2019 through maturity in June 2022, the effective annual interest rate on the 2022 Convertible Notes was 2.7%. The effective annual interest rate is computed using the contractual interest and the amortization of debt issuance costs. Prior to the adoption of ASU 2020-06, the effective annual interest rate calculation also included the amortization of the original issue discount.

In connection with the issuance of the 2024 Convertible Notes and the 2026 Convertible Notes, the Company incurred $9.0 million of debt issuance costs, which primarily consisted of initial purchaser's discounts and legal and other professional fees. The Company allocated these costs to the liability and equity components based on the allocation of the proceeds. The portion of these costs allocated to the equity components totaling $2.1 million were recorded as a reduction to additional paid-in capital. The portion of these costs allocated to the liability components totaling $6.9 million were recorded as a reduction in the carrying value of the debt on the consolidated balance sheet and are amortized to interest expense using the effective interest method over the expected lives of the 2024 Convertible Notes and the 2026 Convertible Notes. Upon the adoption of ASU 2020-06 on January 1, 2022, the costs originally allocated to the equity component are reflected within the current portion of convertible senior notes and recorded as interest expense over the life of the 2024 Convertible Notes and the 2026 Convertible Notes.

The Company determined the expected life of the 2024 Convertible Notes and the 2026 Convertible Notes was equal to their approximately five and seven-year terms, respectively. The effective annual interest rates of the 2024 Convertible Notes and the 2026 Convertible Notes for the period from the date of issuance through December 31, 2022 was 1.2% and 1.9%, respectively. The effective annual interest rate is computed using the contractual interest and the amortization of debt issuance costs. Prior to the adoption of ASU 2020-06, the effective annual interest rate calculation also included the amortization of the original issue discount.

The following table sets forth total interest expense recognized related to convertible senior notes during the years ended December 31, 2022, 2021, and 2020 (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Contractual interest expense	$ 5,745	$ 7,216	$ 7,216
Amortization of debt issuance costs	1,853	1,678	1,462
Amortization of debt discount	—	22,256	20,800
Total interest expense	$ 7,598	$ 31,150	$ 29,478

Future minimum payments under the convertible senior notes as of December 31, 2022, are as follows (in thousands):

2023	$ 4,500
2024	203,750
2025	3,000
2026	201,500
Total future minimum payments under the convertible senior notes	412,750
Less: amounts representing interest	(12,750)
Less: unamortized debt issuance costs	(3,749)
Convertible senior notes balance	$ 396,251

Convertible Note Hedge and Note Hedge Warrant Transactions with Respect to 2022 Convertible Notes

To minimize the impact of potential dilution to the Company's Class A common stockholders upon conversion of the 2022 Convertible Notes, the Company entered into the Convertible Note Hedges. The Convertible Note Hedges had an exercise price of $14.51 per share and covered 23,135,435 shares. If the 2022 Convertible Notes had been converted and the price of the Company's Class A Common Stock was above the exercise price of the Convertible Note Hedges, the counterparties were obligated to deliver shares of the Company's Class A Common Stock and/or cash with an aggregate value approximately equal to the difference between the price of the Company's Class A Common Stock at the conversion date and the exercise price, multiplied by the number of shares of the Company's Class A Common Stock related to the Convertible Note Hedge being exercised.

Concurrently with entering into the Convertible Note Hedges, the Company sold Note Hedge Warrants to the Convertible Note Hedge counterparties to acquire shares of the Company's Class A Common Stock. An aggregate of 23,135,435 shares underlie the Note Hedge Warrants and each warrant has a strike price of $18.82 per share, subject to customary anti-dilution adjustments. The Note Hedge Warrants are exercisable over the 150 trading day period beginning on September 15, 2022. The Note Hedge Warrants could have a dilutive effect on the Class A Common Stock to the extent that the market price per share of the Company's Class A Common Stock exceeds the applicable strike price of such warrants.

The Convertible Note Hedges and the Note Hedge Warrants are separate transactions entered into by the Company and are not part of the terms of the 2022 Convertible Notes. Holders of the Convertible Note Hedges and the Note Hedge Warrants do not have any rights with respect to the 2022 Convertible Notes. The Company paid $91.9 million for the Convertible Note Hedges and received $70.8 million for the Note Hedge Warrants, resulting in a net cost to the Company of $21.1 million.

In August 2019, concurrently with the repurchase of $215.0 million aggregate principal amount of the 2022 Convertible Notes, the Company terminated the respective portion of the Convertible Note Hedges and Note Hedge Warrants. The Company received $3.2 million of termination payments from the counterparties of the Convertible Note Hedges and Note Hedge Warrants.

In June 2022, the Convertible Note Hedges terminated unexercised upon expiry. The Note Hedge Warrants remain outstanding as of December 31, 2022.

The Convertible Note Hedges and Note Hedge Warrants are accounted for as derivative assets and liabilities, respectively, in accordance with ASC 815, and are remeasured to fair value at each reporting date (Note 5).

As of December 31, 2022, the Note Hedge Warrants were classified as current liabilities on the Company's consolidated balance sheet. As of December 31, 2021, the Convertible Note Hedges and Note Hedge Warrants were classified as current assets and current liabilities, respectively, on the Company's consolidated balance sheet.

Capped Calls with Respect to 2024 Convertible Notes and 2026 Convertible Notes

To minimize the impact of potential dilution to the Company's Class A common stockholders upon conversion of the 2024 Convertible Notes and the 2026 Convertible Notes, the Company entered into separate Capped Calls in connection with the issuance of the 2024 Convertible Notes and the 2026 Convertible Notes. The Company paid the counterparties $25.2 million to enter into the Capped Calls.

The Capped Calls have an initial strike price of approximately $13.39 per share, which corresponds to the initial conversion price of the 2024 Convertible Notes and the 2026 Convertible Notes and is subject to anti-dilution adjustments generally similar to those applicable to the 2024 Convertible Notes and the 2026 Convertible Notes. The Capped Calls have a cap price of approximately $17.05 per share, subject to certain adjustments. The Capped Calls cover 29,867,480 shares of Class A Common Stock (subject to anti-dilution and certain other adjustments), which is the same number of shares of Class A Common Stock that initially underlie the 2024 Convertible Notes and the 2026 Convertible Notes.

The Capped Calls are expected generally to reduce the potential dilution to the Class A Common Stock upon conversion of the 2024 Convertible Notes and the 2026 Convertible Notes in the event that the market price per share of Class A Common Stock is greater than the strike price of the Capped Calls as adjusted pursuant to the anti-dilution adjustments. If, however, the market price per share of Class A Common Stock exceeds the cap price of the Capped Calls, there would nevertheless be dilution upon conversion of the 2024 Convertible Notes and the 2026 Convertible Notes to the extent that such market price exceeds the cap price of the Capped Calls.

The Capped Calls are separate transactions entered into by and between the Company and the Capped Calls counterparties and are not part of the terms of the 2024 Convertible Notes or the 2026 Convertible Notes. Holders of the 2024 Convertible Notes and the 2026 Convertible Notes do not have any rights with respect to the Capped Calls. The Company recorded a reduction to additional paid-in capital of $25.0 million during the year ended December 31, 2019 related to the premium payments for the Capped Calls. Additionally, the Company recorded a $0.2 million reduction to equity related to transaction costs incurred in connection with the Capped Calls during the year ended December 31, 2019. These instruments meet the conditions outlined in ASC 815 to be classified in stockholders' equity and are not subsequently remeasured as long as the conditions for equity classification continue to be met.

10. Commitments and Contingencies

Commitments with AbbVie

The Company and AbbVie are jointly obligated to make minimum purchases of linaclotide API for the territories covered by the Company's collaboration with AbbVie for North America. Currently, AbbVie fulfills all such minimum purchase commitments.

Under the collaboration agreement with AbbVie for North America, the Company shares all development and commercialization costs related to linaclotide in the U.S. with AbbVie. The actual amounts that the Company pays to AbbVie or that AbbVie pays to the Company will depend on numerous factors outside of the Company's control, including the success of certain clinical development efforts with respect to linaclotide, the content and timing of decisions made by the regulators, the reimbursement and competitive landscape around linaclotide and the Company's other product candidates, and other factors.

Other Funding Commitments

As of December 31, 2022, the Company has ongoing studies in various pre-clinical and clinical trial stages. The Company's most significant clinical trial expenditures are to contract research organizations. These contracts are generally cancellable, with notice, at the Company's option and do not have any significant cancellation penalties.

Guarantees

As permitted under Delaware law, the Company indemnifies its directors and certain of its officers for certain events or occurrences while such director or officer is, or was, serving at the Company's request in such capacity. The maximum potential amount of future payments the Company could be required to make is unlimited; however, the Company has directors' and officers' insurance coverage that is intended to limit its exposure and enable it to recover a portion of any future amounts paid.

The Company enters into certain agreements with other parties in the ordinary course of business that contain indemnification provisions. These typically include agreements with business partners, contractors, landlords, clinical sites and customers. Under these provisions, the Company generally indemnifies and holds harmless the indemnified party for losses suffered or incurred by the indemnified party as a result of the Company's activities. These indemnification provisions generally survive termination of the underlying agreements. The maximum potential amount of future payments the Company could be required to make under these indemnification provisions is unlimited. However, to date the Company has not incurred material costs to defend lawsuits or settle claims related to these indemnification provisions. As a result, the estimated fair value of these obligations is minimal. Accordingly, the Company did not have any liabilities recorded for these obligations as of December 31, 2022 and 2021.

Litigation

From time to time, the Company is involved in various legal proceedings and claims, either asserted or unasserted, which arise in the ordinary course of business. While the outcome of these other claims cannot be predicted with certainty, management does not believe that the outcome of any of these ongoing legal matters, individually and in aggregate, will have a material adverse effect on the Company's consolidated financial statements.

In January 2020, the Company and AbbVie entered into settlement agreements with Sandoz Inc. and Teva Pharmaceuticals, USA, Inc., ("Teva"), resolving patent litigation brought in response to the last outstanding abbreviated new drug applications seeking approval to market generic versions of LINZESS prior to the expiration of the Company's and AbbVie's applicable patents.

In May 2021, the Company and AbbVie entered into a settlement agreement with Teva, under which the Company and AbbVie will grant Teva a license to market a generic version of 72 mcg LINZESS beginning March 31, 2029 (subject to FDA approval), unless certain limited circumstances, customary for settlement agreements of this nature, occur. With this settlement agreement, the Company and AbbVie have settled with the filers of all known ANDAs to date seeking approval to market generic versions of LINZESS.

11. Stockholders' Equity

Preferred Stock

The Company's preferred stock may be issued from time to time in one or more series, with each such series to consist of such number of shares and to have such terms as adopted by the board of directors. Authority is given to the board of directors to determine and fix such voting powers, full or limited, or no voting powers, and such designations, preferences and relative participating, optional or other special rights, and qualifications, limitation or restrictions thereof, including without limitation, dividend rights, conversion rights, redemption privileges and liquidation preferences.

Common Stock

The Company has one class of common stock ("Class A Common Stock"). Class A Common Stock is entitled to one vote per share. The Company has reserved, out of its authorized but unissued shares of Class A Common Stock,

sufficient shares to effect the conversion of the convertible senior notes and the Note Hedge Warrants pursuant to the terms thereof (Note 9).

The Company's stockholders are entitled to dividends if and when declared by the board of directors.

Share Repurchase Program

In May 2021, the Company's Board of Directors authorized a program to repurchase up to $150.0 million of the Company's Class A Common Stock. The Company completed the share repurchase program in May 2022 and retired the repurchased shares.

During the year ended December 31, 2022, the Company repurchased 10.8 million shares of Class A Common Stock at an aggregate purchase price of $123.4 million. For the overall program, under which repurchases commenced in December 2021, the Company repurchased 13.1 million shares of Class A Common Stock at an average price per share of $11.47.

12. Employee Stock Benefit Plans

The Company has several share-based compensation plans under which stock options, RSAs, RSUs, and other share-based awards are available for grant to employees, officers, directors and consultants of the Company.

The following table summarizes share-based compensation expense by award type (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Stock options	$ 1,471	$ 3,154	$ 7,680
Time-based restricted stock units	17,643	14,539	18,624
Performance-based restricted stock units	5,008	1,295	2,190
Restricted stock awards	2,439	2,684	1,886
Employee stock purchase plan	412	419	722
Stock awards	75	190	73
Total share-based compensation expense	$ 27,048	$ 22,281	$ 31,175

The following table summarizes the share-based compensation expense reflected in the consolidated statements of income (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Share-based compensation expense:			
Research and development	$ 4,936	$ 4,849	$ 5,569
Selling, general and administrative	22,112	17,323	23,825
Restructuring expenses	—	109	1,781
Total share-based compensation expense included in operating expenses	27,048	22,281	31,175
Income tax benefit	1,644	—	—
Total share-based compensation expense, net of tax	$ 28,692	$ 22,281	$ 31,175

Restructuring expenses include modifications to share-based awards held by employees impacted by various workforce reductions (Note 16).

Stock Benefit Plans

As of December 31, 2022, the Company has the following active stock benefit plans pursuant to which awards are currently outstanding: the 2019 Equity Incentive Plan (the "2019 Equity Plan"), the Amended and Restated 2010 Employee Stock Purchase Plan (the "2010 Purchase Plan") and the Amended and Restated 2010 Employee, Director, and Consultant Equity Incentive Plan (the "2010 Equity Plan"). At December 31, 2022, there were 11,790,625 shares available for future grant under the 2019 Equity Plan and the 2010 Purchase Plan.

2019 Equity Plan

During 2019, the Company's stockholders approved the 2019 Equity Plan under which stock options, RSAs, RSUs, and other stock-based awards may be granted to employees, officers, directors, or consultants of the Company. Under the 2019 Equity Plan, 10,000,000 shares of Class A Common Stock were initially reserved for issuance. Awards that are returned to the 2010 Equity Plan as a result of their expiration, cancellation, termination or repurchase are automatically made available for issuance under the 2019 Equity Plan. Awards that expire, cancel, terminate, or are repurchased under the 2019 Equity Plan will no longer be available for future grant. As of December 31, 2022, 7,366,153 shares were available for future grant under the 2019 Equity Plan.

2010 Purchase Plan

During 2010, the Company's stockholders approved the 2010 Purchase Plan, which gives eligible employees the right to purchase shares of common stock at the lower of 85% of the fair market value on the first or last day of an offering period. Each offering period is six months. There were 400,000 shares of common stock initially reserved for issuance pursuant to the 2010 Purchase Plan. The number of shares available for future grant under the 2010 Purchase Plan may be increased on the first day of each fiscal year by an amount equal to the lesser of: (i) 1,000,000 shares, (ii) 1% of the Class A shares of common stock outstanding on the last day of the immediately preceding fiscal year, or (iii) such lesser number of shares as is determined by the board of directors. As of December 31, 2022, there were 4,424,472 shares available for future grant under the 2010 Purchase Plan.

2010 Equity Plan

The 2010 Equity Plan provided for the granting of stock options, RSAs, RSUs, and other share-based awards to employees, officers, directors, consultants, or advisors of the Company. At December 31, 2022, there were no shares available for future grant under the 2010 Equity Plan.

Restricted Stock Awards

RSAs are granted to non-employee members of the board of directors under restricted stock agreements in accordance with the terms of the 2019 Equity Plan and the Company's non-employee director compensation policy, effective May 2019. Annual restricted stock grants to each non-employee member of the board of directors vest in full on the date immediately preceding the next annual meeting of stockholders, provided the individual continues to serve on the Company's board of directors through each vest date. Initial restricted stock grants to new non-employee members of the board of directors vest annually over a three-year period from the date of grant provided the individual continues to serve on the Company's board of directors through each vest date.

A summary of restricted stock activity for the year ended December 31, 2022 is presented below:

	Number of Shares	Weighted-Average Grant Date Fair Value
Unvested as of December 31, 2021	263,260	$ 11.61
Granted	172,568	11.22
Vested	(246,710)	11.64
Forfeited	—	—
Unvested as of December 31, 2022	189,118	$ 11.22

The weighted-average grant date fair value per share of RSAs granted during the years ended December 31, 2022, 2021, and 2020 was $11.22, $11.67, and $10.16, respectively. The total fair value of RSAs that vested during the years ended December 31, 2022, 2021, and 2020 was $2.8 million, $2.5 million, and $1.9 million, respectively.

Restricted Stock Units

RSUs granted under the Company's equity plans represent the right to receive one share of the Company's Class A Common Stock pursuant to the terms of the applicable award agreement. Shares of the Company's Class A Common Stock are delivered to the employee upon vesting, subject to payment of applicable withholding taxes.

Time-based RSUs

Time-based RSUs generally vest over a two-to-four-year period on the approximate anniversary of the date of grant until fully vested, provided the individual remains in continuous service with the Company through each vesting date. The fair value of all time-based RSUs is based on the market value of the Company's Class A Common Stock on the date of grant. Compensation expense, including the effect of estimated forfeitures, is recognized over the applicable service period.

A summary of time-based RSU activity for the year ended December 31, 2022 is as follows:

	Number of RSUs	Weighted-Average Grant Date Fair Value
Outstanding as of December 31, 2021	3,864,108	$ 10.89
Granted	2,265,661	11.08
Vested and released	(1,327,573)	11.15
Forfeited	(512,051)	10.95
Outstanding as of December 31, 2022	4,290,145	$ 10.91

Amounts relating to time-based RSUs granted prior to the Separation of the Company's soluble guanylate cycle business, and certain other assets and liabilities, into Cyclerion Therapeutics, Inc. (the "Separation) have not been adjusted to reflect the effect of the Separation on the Company's stock price. For additional information related to the Separation, refer to Note 15, *Related Parties*, to these consolidated financial statements.

The weighted-average grant date fair value per share of time-based RSUs granted during the years ended December 31, 2022, 2021, and 2020 was $11.08, $10.40, and $11.59, respectively. The total fair value of time-based RSUs that vested during the years ended December 31, 2022, 2021, and 2020 was $14.8 million, $17.8 million, and $11.1 million, respectively.

Performance-based RSUs

Performance-based RSUs ("PSUs") were granted to certain executives. PSUs vest upon the achievement of specified performance criteria over a two to three-year performance period, generally subject to the executive remaining in continuous service with the Company through the applicable vesting dates. The performance criteria applicable to the PSUs granted in 2020 were (i) gaining the U.S. FDA's acceptance of one or more additional New Drug Applications through internal development or acquisition of development-stage or commercial-stage programs ("Pipeline PSUs"), (ii) achieving certain profitability metrics ("Profitability PSUs") and (iii) realizing relative total shareholder return goals (the "Relative TSR PSUs"). PSUs granted in 2022 and 2021 consisted entirely of Relative TSR PSUs.

The fair value of Pipeline PSUs and Profitability PSUs is based on the market value of the Company's Class A Common Stock on the date of grant. The Relative TSR PSUs are valued using the Monte Carlo simulation method on the date of grant. The weighted average assumptions used to estimate the fair value of Relative TSR PSUs were as follows for the years ended December 31, 2022, 2021, and 2020:

	Year Ended December 31,		
	2022	2021	2020
Fair value of common stock	$ 11.13	$ 11.39	$ 11.78
Expected volatility	41.7 %	47.9 %	53.3 %
Expected term (in years)	2.8	2.6	2.8
Risk-free interest rate	1.6 %	0.3 %	1.0 %
Expected dividend yield	— %	— %	— %

A summary of PSU activity for the year ended December 31, 2022 is as follows:

	Number of PSUs	Weighted-Average Grant Date Fair Value
Outstanding as of December 31, 2021	833,286	$ 14.06
Granted [(1)]	598,814	14.30
Vested and released	(151,859)	11.68
Forfeited	(111,470)	11.65
Outstanding as of December 31, 2022	1,168,771	$ 14.72

(1) Includes an adjustment of 70,759 PSUs related to PSUs granted in prior years which vested during the year ended December 31, 2022 in excess of the target number of PSUs.

The weighted-average grant date fair value per share of PSUs granted during the years ended December 31, 2022, 2021, and 2020 was $14.30, $14.65, and $12.48, respectively. The total fair value of PSUs that vested during the year ended December 31, 2022 was $1.7 million. No PSUs vested during the years ended December 31, 2021 and 2020.

Stock Options

Stock options granted under the Company's equity plans represent the right to purchase one share of the Company's Class A Common Stock pursuant to the terms of the applicable award agreement. Shares of the Company's Class A Common Stock are delivered to the employee upon exercise, subject to payment of applicable withholding taxes.

As of April 2020, the Company no longer grants stock options. Stock options previously granted under the Company's equity plans generally have a ten-year term and vest over a period of four years, provided the individual continues to serve at the Company through the vesting dates. Options granted under all equity plans are exercisable at a price per share not less than the fair market value of the underlying common stock on the date of grant. The estimated fair value of options, including the effect of estimated forfeitures, is recognized over the requisite service period, which is typically the vesting period of each option.

The weighted average assumptions used to estimate the fair value of the stock options using the Black-Scholes option-pricing model were as follows for the year ended December 31, 2020:

	Year Ended December 31, 2020
Expected volatility	46.6 %
Expected term (in years)	6.1
Risk-free interest rate	1.5 %
Expected dividend yield	— %

Expected volatility is based on the historical volatility of the Company's Class A Common Stock. The Company estimates the expected term using historical data. The risk-free interest rate used for each grant is based on a zero-coupon U.S. Treasury instrument with a remaining term similar to the expected term of the share-based award. The Company has not paid and does not anticipate paying cash dividends on its shares of common stock in the foreseeable future; therefore, the expected dividend yield is assumed to be zero.

The weighted-average grant date fair value per share of options granted during the year ended December 31, 2020 was $5.89.

The following table summarizes stock option activity under the Company's share-based compensation plans:

	Number of Stock Options	Weighted-Average Exercise Price[(1)]	Weighted-Average Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2021	9,372,794	$ 12.30	3.51	$ 4,528
Granted	—	—	—	—
Exercised	(951,355)	10.88	—	—
Cancelled	(1,490,067)	13.04	—	—
Outstanding at December 31, 2022	6,931,372	12.34	3.32	5,786
Vested or expected to vest at December 31, 2022	6,929,248	12.34	3.32	5,782
Exercisable at December 31, 2022	6,877,104	12.35	3.30	5,709

(1) Amounts relating to stock options granted prior to the Separation have not been adjusted to reflect the effect of the Separation on the Company's stock price.

The total intrinsic value of options exercised during the years ended December 31, 2022, 2021, and 2020 was $0.9 million, $2.7 million, and $3.5 million, respectively. The intrinsic value was calculated as the difference between the fair value of the Company's Class A Common Stock at the date of exercise and the exercise price of the option issued.

The following table sets forth the Company's unrecognized share-based compensation expense, net of estimated forfeitures, as of December 31, 2022, by type of award and the weighted-average period over which that expense is expected to be recognized:

	Unrecognized Expense, Net of Estimated Forfeitures (in thousands)	Weighted-Average Remaining Recognition Period (in years)
Type of award:		
Stock options with time-based vesting	$ 183	0.54
Restricted stock awards	968	0.45
Time-based restricted stock units	24,436	2.41
Performance-based restricted stock units	6,387	1.49

The total unrecognized share-based compensation cost will be adjusted for future changes in estimated forfeitures.

13. Income Taxes

The components of the provision for (benefit from) income taxes during the years ended December 31, 2022, 2021, and 2020 consisted of the following (in thousands):

	Year Ended December 31, 2022	2021	2020
Current taxes:			
Federal	$ —	$ —	$ —
State	11,618	5,503	2,685
Total current taxes	11,618	5,503	2,685
Deferred taxes:			
Federal	52,191	(251,367)	—
State	13,548	(81,927)	—
Total deferred taxes	65,739	(333,294)	—

Income tax expense (benefit)	$ 77,357	$ (327,791)	$ 2,685

During the year ended December 31, 2022, the Company recorded income tax expense of $77.4 million, comprised of non-cash tax expense of $73.4 million and cash tax expense of $4.0 million for state income taxes in certain states in which state taxable income exceeded available net operating losses. Due to the Company's ability to utilize its net operating losses to offset federal taxable income and taxable income in many states, the majority of the Company's tax provision is a non-cash tax expense until the Company's net operating losses have been fully utilized. During the year ended December 31, 2021, the Company recorded income tax benefit of $327.8 million, which primarily pertains to the income tax benefit of $333.3 million related to the release of the valuation allowance on the majority of the Company's tax attributes and other deferred tax assets, partially offset by $5.5 million of state income taxes in certain states in which the Company is unable to utilize net operating losses to fully offset taxable income. During the year ended December 31, 2020, the Company recorded $2.7 million in income tax expense related to state income taxes in certain states which had temporarily disallowed or only partially allow the use of net operating losses to offset taxable income. The Company did not record a provision for federal income taxes for the period ended December 31, 2020, as it offset taxable income with federal net operating losses and recorded a full valuation allowance against net deferred tax assets. The Company has not recorded a foreign tax provision as it has had cumulative net operating losses outside of the United States since inception.

On March 27, 2020. the Coronavirus Aid, Relief, and Economic Security ("CARES") Act was enacted and signed into law. The Company benefitted from certain provisions of the CARES Act, specifically, the increase in allowable business interest deduction from 30% of adjusted taxable income to 50% of adjusted taxable income, which allowed the Company to take additional interest deductions for the period ended December 31, 2020. Additionally, the Company was able to claim 100% bonus depreciation on leasehold improvements incurred in the period ended December 31, 2020 and 2019.

A reconciliation of income taxes computed using the U.S. federal statutory rate of 21% to that reflected in the consolidated statements of income are as follows (in thousands):

	Year Ended December 31,		
	2022	**2021**	**2020**
Income tax expense using U.S. federal statutory rate	$ 53,009	$ 42,138	$ 22,861
Permanent differences	(290)	426	325
State income taxes, net of federal benefit	16,160	12,554	7,565
Executive compensation - Section 162(m)	2,654	695	1,718
Excess tax benefits	3,613	6,270	5,132
Fair market valuation of Note Hedge Warrants and Convertible Note Hedges	(50)	325	1,680
Tax credits	(252)	(9)	(3,149)
Expiring net operating losses and tax credits	1,087	491	1,991
Effect of change in state tax rate on deferred tax assets and deferred tax liabilities	2,581	123	(208)
Change in the valuation allowance	(1,155)	(390,804)	(35,230)
Income tax expense (benefit)	$ 77,357	$ (327,791)	$ 2,685

The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the financial reporting and tax bases of assets and liabilities. These differences are measured using the enacted statutory tax rates that are expected to be in effect for the years in which differences are expected to reverse. Deferred tax assets and liabilities were determined based on the difference between financial statement and tax bases using enacted tax rates in effect for the year in which the differences are expected to reverse.

	December 31,	
	2022	2021
Deferred tax assets:		
Net operating loss carryforwards	$ 88,769	$ 165,022
Tax credit carryforwards	59,290	60,125
Capitalized research and development	12,683	4,981
Share-based compensation	13,666	16,857
Basis difference on collaboration agreement for North America with AbbVie	95,460	78,194
Accruals and reserves	5,935	5,003
Basis difference on Convertible Notes	2,845	8,166
Intangible assets	5,299	5,396
Operating lease liability	5,337	5,971
Other	1,242	3,997
Total deferred tax assets	290,526	353,712
Deferred tax liabilities:		
Basis difference on Convertible Notes	—	(11,960)
Operating lease right-of-use assets	(3,810)	(4,248)
Total deferred tax liabilities	(3,810)	(16,208)
Net deferred tax asset	286,716	337,504
Valuation allowance	(3,055)	(4,210)
Net deferred tax asset	$ 283,661	$ 333,294

On a periodic basis, the Company reassesses the valuation allowance on its deferred income tax assets weighing positive and negative evidence to assess the recoverability of the deferred tax assets. During the year ended December 31, 2021, the Company reassessed the valuation allowance noting the shift of positive evidence outweighing negative evidence, including: continued strong prescription demand growth of LINZESS, continued profitability of a GI-focused business since completing the tax-free spin-off of Cyclerion, and expectations regarding future profitability. After assessing both the positive evidence and negative evidence, management determined it was more likely than not that the Company will realize the majority of its deferred tax assets and during the year ended December 31, 2021, released the majority of its valuation allowance for the deferred tax assets that are expected to be utilized in future years. As of December 31, 2022, the Company maintained a valuation allowance of $3.1 million on deferred tax assets not expected to be realized, related primarily to certain tax credits that are expected to expire prior to utilization.

The valuation allowance decreased by $1.2 million during the year ended December 31, 2022 primarily for certain tax credits that expired unused during 2022.

The valuation allowance decreased by $390.8 million during the year ended December 31, 2021 primarily due to the Company's release of the majority of its valuation allowance, as described above, as well as the use of net operating losses to offset taxable income.

The valuation allowance decreased $35.2 million during the year ended December 31, 2020 primarily due to the Company's offsetting taxable income with previously disallowed interest expense and net operating losses, partially offset by an increase in deferred tax asset for the basis difference of the collaboration agreement for North America with AbbVie.

Subject to the limitations described below, at December 31, 2022, the Company had federal net operating loss carryforwards of $689.4 million, of which $559.8 million is subject to expiration between 2033 and 2038 and $129.6 million may be carried forward indefinitely. As of December 31, 2022, the Company had state net operating loss carryforwards of $509.5 million to offset future state taxable income, which is subject to expiration between 2032 and 2039. The Company also had tax credit carryforwards of $63.9 million as of December 31, 2022 to offset future federal and state income taxes, which is subject to expiration at various times through 2040.

Utilization of net operating loss carryforwards and research and development credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that could occur in the future in accordance with Section 382 of the Internal Revenue Code of 1986 ("IRC Section 382") and with Section 383 of the Internal Revenue Code of 1986, as well as similar state provisions. These ownership changes may limit the amount of net

operating loss carryforwards and research and development credit carryforwards that can be utilized annually to offset future taxable income and taxes, respectively. In general, an ownership change, as defined by IRC Section 382, results from transactions increasing the ownership of certain stockholders or public groups in the stock of a corporation by more than 50 percentage points over a three-year period.

The following table summarizes the changes in the Company's unrecognized income tax benefits for the years ended December 31, 2022, 2021, and 2020 (in thousands):

	December 31,		
	2022	2021	2020
Balance at the beginning of the period	$ 84,606	$ 68,087	$ 53,099
Increases based on tax positions related to the current period	101,225	83,206	66,687
Decreases for tax positions in prior periods	(83,206)	(66,687)	(51,699)
Balance at the end of the period	$ 102,625	$ 84,606	$ 68,087

The Company had gross unrecognized tax benefits of $102.6 million, $84.6 million, and $68.1 million as of December 31, 2022, 2021 and 2020, respectively. Of the $102.6 million of total unrecognized tax benefits at December 31, 2022, $1.4 million would, if recognized, affect the Company's effective tax rate, and the remaining amount would not affect the Company's effective tax rate, as it relates to a temporary timing difference. Reserves for uncertain tax positions of $9.2 million and $2.9 million are recorded in other liabilities on the Company's consolidated balance sheets as of December 31, 2022 and 2021, respectively.

The Company will recognize interest and penalties, if any, related to uncertain tax positions in income tax expense. As of December 31, 2022 and 2021, an insignificant amount of penalties have been accrued.

The statute of limitations for assessment by the Internal Revenue Service ("IRS") and state tax authorities is open for tax years ended December 31, 2019 through the present, although net operating losses generated from years prior to 2019 could be subject to examination and adjustments to the extent utilized in future years. There are currently no federal or state income tax audits in progress.

14. Defined Contribution Plan

The Ironwood Pharmaceuticals, Inc. 401(k) Savings Plan is a defined contribution plan in the form of a qualified 401(k) plan in which substantially all employees are eligible to participate upon employment. Subject to certain IRS limits, eligible employees may elect to contribute from 1% to 100% of their compensation. Company contributions to the plan are at the sole discretion of the Company. During the years ended December 31, 2022 and 2021, the Company provided a matching contribution equal to the greater of: (a) 100% of employee contributions on the first 3% of eligible compensation and 50% of employee contributions on the next 3% of eligible compensation; or (b) 75% of the first $10,000 of employee contributions. During the year ended December 31, 2020, the Company provided a matching contribution of 75% of the employee's contributions, up to $6,000 annually. During the years ended December 31, 2022, 2021, and 2020, the Company recorded $2.2 million, $2.2 million, and $1.8 million of expense related to its 401(k) company match, respectively.

15. Related Party Transactions

The Company previously reflected amounts due from and due to Allergan prior to its acquisition by AbbVie in May 2020 as related party receivables and payables, as appropriate. Following the acquisition of Allergan by AbbVie, the Company determined that AbbVie is not a related party to the Company.

On April 1, 2019, the Company completed the Separation of its soluble guanylate cyclase business, and certain other assets and liabilities, into Cyclerion. The Separation was effected by means of a distribution of all of the outstanding shares of common stock, with no par value, of Cyclerion through a dividend of Cyclerion's common stock, to the Company's stockholders of record as of the close of business on March 19, 2019. Prior to the Separation on April 1, 2019, Cyclerion was a wholly owned subsidiary of the Company. In connection with the Separation, the Company executed certain contracts with Cyclerion, whose President and Chief Scientific Officer at the time of the Separation became a member of the Company's Board of Directors in April 2019. Pursuant to a development agreement with Cyclerion, Cyclerion provided the Company with certain research and development services with respect to certain of

the Company's products and product candidates. Services received were paid at a mutually agreed upon rate and development activities were governed by a joint steering committee comprised of representatives from both Cyclerion and the Company. The Company recorded $2.3 million in research and development expenses under the development agreement during the year ended December 31, 2020. As of December 31, 2020, the Company determined that Cyclerion was no longer considered a related party.

16. Workforce Reductions and Restructuring

In September 2020, the Company announced that one of its two identical Phase III trials evaluating IW-3718 in refractory GERD did not meet certain criteria, including the study's primary endpoint of achieving a statistically significant improvement in heartburn severity. Based on these findings, the Company discontinued development of IW-3718. In connection with this decision, the Company reduced its workforce by approximately 100 full-time employees. This workforce reduction affected both field-based and home-office employees, including the relevant general and administrative support functions. The Company substantially completed the reduction in its workforce in the year ended December 31, 2020. The Company incurred $15.5 million for the year ended December 31, 2020, in restructuring expenses, primarily for severance, benefits and related costs related to this reduction in its workforce. Restructuring expenses during the year ended December 31, 2020 also included $1.2 million related to the impairment of certain fixed assets as a result of the Company's decision to discontinue IW-3718 development. The Company incurred no restructuring expenses and an insignificant amount of restructuring expenses during the years ended December 31, 2022 and 2021, respectively.

The following table summarizes the accrued liabilities activity recorded in connection with the reduction in workforce in September 2020 and related restructuring activities during the year ended December 31, 2022 (in thousands):

	Amounts Accrued at December 31, 2021	Charges	Amount Paid	Adjustments	Amounts Accrued at December 31, 2022
Employee severance, benefits and related costs	$ 462	$ —	$ (462)	$ —	$ —

The following table summarizes the accrued liabilities activity recorded in connection with the reductions in workforce and related restructuring activities during the year ended December 31, 2021 (in thousands):

	Amounts Accrued at December 31, 2020	Charges	Amount Paid	Adjustments	Amounts Accrued at December 31, 2021
Employee severance, benefits and related costs	$ 10,902	$ 1,025	$ (10,611)	$ (854)	$ 462
Contract related costs	5	48	(53)	—	—
Total	$ 10,907	$ 1,073	$ (10,664)	$ (854)	$ 462

17. Selected Quarterly Financial Data (Unaudited)

The following table contains quarterly financial information for the years ended December 31, 2022 and 2021. The Company believes that the following information reflects all normal recurring adjustments necessary for a fair presentation of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total Year
	(in thousands, except per share data)				
2022					
Total revenues	$ 97,529	$ 97,231	$ 108,637	$ 107,199	$ 410,596
Total cost and expenses	39,683	41,576	40,164	38,836	160,259
Other expense, net	(1,381)	(1,870)	1,434	3,902	2,085
Net income and comprehensive income	38,801	37,080	50,317	48,867	175,065
Net income per share—basic [1]	0.25	0.24	0.33	0.32	1.13
Net income per share—diluted [1]	0.21	0.21	0.28	0.27	0.96

(1) Quarterly basic and diluted net income per share do not add to full fiscal year total due to rounding.

	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total Year
	(in thousands, except per share data)				
2021					
Total revenues	$ 88,845	$ 104,031	$ 103,747	$ 117,130	$ 413,753
Total cost and expenses	43,447	38,933	38,576	60,538	181,494
Other expense, net	(5,040)	(10,726)	(5,499)	(10,337)	(31,602)
Net income and comprehensive income	39,926	391,303	55,845	41,374	528,448
Net income per share—basic	0.25	2.42	0.34	0.25	3.26
Net income per share—diluted	0.25	2.39	0.34	0.25	3.21

Exhibit 10.8

Ironwood Pharmaceuticals, Inc.
Amended and restated 2019 Non-Employee Director Compensation Policy

Effective as of January 1, 2023 (the "Effective Date"), each individual who provides services to Ironwood Pharmaceuticals, Inc. (the "Company) as a member of its Board of Directors (the "Board"), other than a director who is employed by the Company or a subsidiary of the Company (a "Non-Employee Director"), will be entitled to receive the following compensation:

Type of Compensation	Amount and Form of Payment
Annual retainer	$50,000 ($80,000 for the chair of the Board)
Additional annual retainer for members of the Audit Committee	$10,000 ($20,000 for the chair)
Additional annual retainer for members of the Compensation and HR Committee	$10,000 ($20,000 for the chair)
Additional annual retainer for members of the Governance and Nominating Committee	$5,000 ($10,000 for the chair)
Initial equity award	Each Non-Employee Director who is first elected to the Board following the Effective Date will, upon his or her initial election to the Board, be granted restricted shares of the Company's Class A common stock ("Restricted Stock") having a grant date fair value of $250,000, determined based on the average closing price of the Company's Class A common stock on the Nasdaq Global Select Market (or the stock exchange on which the Company's Class A common stock is being actively traded) for the six months preceding the month in which the award is granted, as may be adjusted by the Board (the "Average Stock Price"), rounded down to the nearest whole share. For example, if the award is being granted on May 29, 2023, the Average Stock Price is the average closing price of the Company's Class A common stock on the Nasdaq Global Select Market (or the stock exchange on which the Company's Class A common stock is being actively traded) from November 1, 2022 – April 30, 2023. Such award will vest in three equal annual installments on the first three anniversaries of the date of grant, subject to the Non-Employee Director's continued service on the Board through each applicable vesting date. For clarity, if a Non-Employee Director ceases serving as a member of the Board at any time prior to the date on which the award of Restricted Stock is fully vested, any shares of Restricted Stock that remain unvested on the date of such Non-Employee Director's termination of service will be forfeited on the date of such termination of service.

Annual equity award	Beginning with the 2019 annual meeting of stockholders of the Company (the "2019 Annual Meeting"), on the date of each annual meeting of stockholders of the Company, each Non-Employee Director shall be granted Restricted Stock having a grant date fair value of $250,000, determined based on the Average Stock Price, rounded down to the nearest whole share, provided, however, that such awards made in connection with the 2019 Annual Meeting shall be granted on the date immediately preceding the 2019 Annual Meeting. If a Non-Employee Director is initially elected to the Board other than at an annual meeting of the stockholders of the Company, upon his or her initial election to the Board (the "Start Date"), such Non-Employee Director shall be granted an award of Restricted Stock equal to the number of shares of Restricted Stock granted to the Non-Employee Directors in connection with the last annual meeting of the stockholders of the Company preceding the Start Date multiplied by a ratio equal to (i) 365 minus the number of days between the last annual meeting of the stockholders of the Company preceding the Start Date and the Start Date (ii) divided by 365. Such awards will vest in full on the date immediately preceding the date of the next annual meeting of stockholders, subject to the Non-Employee Director's continued service on the Board through such vesting date. For clarity, if a Non-Employee Director ceases serving as a member of the Board at any time prior to the award's vesting date, the award will be forfeited on the date of such Non-Employee Director's termination of service.

Cash Fees. All cash fees will be payable in arrears on a quarterly basis on March 15, June 15, September 15, and December 15 of each year (or if such date is not a trading day, the last trading day preceding such date) (each, a "Grant Date") and will be prorated for any calendar quarter of partial service, based on the number of calendar days during the quarter the Non-Employee Director was a member of the Board, served on a committee, or served as Board or committee chair, as applicable.

Annual Election to Receive Cash or Stock. Each Non-Employee Director may elect to receive fully vested shares of the Company's Class A common stock (each, a "Stock Grant"), at no cash cost to the Non-Employee Director, in lieu of his or her annual cash retainer and any additional cash retainers for Board chair, committee or committee chair service set forth above. If a Stock Grant is so elected, the shares shall automatically be issued to the Non-Employee Director as of the applicable Grant Date without further action by the Board. The number of shares of the Company's Class A common stock to be issued will be determined by dividing the applicable cash retainer(s) the Non-Employee Director would be eligible to receive on such Grant Date, by the Fair Market Value (as defined in the Equity Incentive Plan) of a share of the Company's Class A common stock on the Grant Date, rounded down to the nearest whole share.

Any election to receive Company Class A common stock in lieu of a cash retainer must be received by the Company prior to January 1 of the year with respect to which the election is effective, except as otherwise permitted by the Company. In the event that a Non-Employee Director has not submitted his or her election for the applicable year by December 31 of the preceding year, then the election of such Non-Employee Director shall be deemed the same as the election made by such Non-Employee Director for the prior year. If a Non-Employee Director has never made an election, all such retainer amounts shall be paid in cash.

Equity Grants. Each award of Restricted Stock and Stock Grants, other than those awards of Restricted Stock granted in connection with the 2019 Annual Meeting, will be subject to the terms and conditions of the Company's 2019 Equity Incentive Plan (or any successor plan) (the "Equity Incentive Plan"), including any individual limits contained therein, with respect to Non-Employee Directors and otherwise, and transfer restrictions, and, in the case of a Restricted Stock Award, a Restricted Stock agreement thereunder. Each award of Restricted Stock granted in connection with the 2019 Annual Meeting will be subject to the terms and conditions of the Company's Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan (the "2010 Plan"), including any individual limits contained therein, with respect to Non-Employee Directors and otherwise, and transfer restrictions, and a Restricted Stock agreement thereunder. Each award of Restricted Stock that is then outstanding will vest in full upon the Non-Employee Director's death or (i) if the award of Restricted Stock was granted under the Equity Incentive Plan, upon a Covered Transaction (as defined in the Equity Incentive Plan) following which the Non-Employee Director is not appointed to the board of directors of the surviving entity, and (ii) if the award of Restricted Stock was granted under the 2010 Plan, upon a Corporate Transaction (as defined in the 2010 Plan), following which the Non-Employee Director is not appointed to the board of directors of the surviving entity. Directors will be responsible for the satisfaction of any state or federal income taxation liabilities resulting from each award of Restricted Stock and Stock Grants. Each award of Restricted Stock or Stock Grants shall be rounded down to the nearest whole number of shares so that no fractional shares shall be issued, and no cash shall be paid in lieu of fractional shares.

Stock Ownership Requirements. Each Non-Employee Director must accumulate and continuously hold shares of the Company's Class A common stock with a value equal to or greater than three (3) times the amount of the then-current annual retainer paid to the Non-Employee Director for service on the Board (excluding additional Board chair, committee, or committee chair retainers, if any). Non-Employee Directors are required to achieve the applicable level of ownership by the later of (a) two years from the Effective Date and (b) two years from the date the individual first became a Non-Employee Director (the "Ownership Date").

Interests that count towards satisfaction of these stock ownership requirements include shares of the Company's Class A common stock owned by the Non-Employee Director under the definition of "beneficial ownership" under the Securities Exchange Act of 1934 or the Treasury Regulations and guidance thereunder. Notwithstanding the foregoing, unexercised stock options and/or unvested equity awards do not count towards satisfaction of the stock ownership requirements.

Compliance with the stock ownership requirements will be measured on the date of the annual meeting of stockholders of the Company each year (each, a "Measurement Date"), based on the annual retainer then in effect for Non-Employee Directors. The value of shares of the Company's Class A common stock will be based on the average closing price of the Company's Class A common stock on the Nasdaq Global Select Market (or the stock exchange on which the Company's Class A common stock is being actively traded) for the six months preceding the month in which the Measurement Date occurs.

Following the Ownership Date, until a Non-Employee Director holds the required ownership level and if such Non-Employee Director does not hold the number of shares of the Company's Class A common stock to meet this requirement at any time thereafter, such Non-Employee Director shall be required to retain 100% of any shares of Company Class A common stock, net of shares sold to cover applicable taxes and the payment of any exercise or purchase price (if applicable), held or received upon the vesting or settlement of equity awards or the exercise of stock options, in each case, in accordance with the applicable award agreement. Further, following the Ownership Date, to the extent a Non-Employee Director does not a hold the number of shares of the Company's Class A common stock that meets this threshold, the Non-Employee Director will be automatically deemed to have elected to receive his or her annual cash retainer and any additional cash retainer for service as Board chair, committee service, or service as a committee chair in the form of shares of the Company's Class A common stock in an amount that satisfies the threshold shortfall.

Expense Reimbursement. In addition, Non-Employee Directors will be reimbursed by the Company for reasonable travel and other expenses incurred in connection with the Non-Employee Director's attendance Board and committee meetings, in accordance with the Company's policies as in effect from time to time.

Employee Directors. For the avoidance of doubt, directors who are employees of the Company or one of its subsidiaries will not receive compensation for their service as a director.

Administration. This Non-Employee Director Compensation Policy shall be administered by the Compensation and HR Committee of the Board.

Amendment and Termination. The Board (or the Compensation and HR Committee thereof if so delegated authority) may terminate or amend this Non-Employee Director Compensation Policy at any time, including any amendments in the type and amount of compensation provided herein.

EXHIBIT 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statements (Form S-3 Nos. 333-179430, 333-199885, 333-221294, and 333-249896) of Ironwood Pharmaceuticals, Inc.;

(2) Registration Statement (Form S-8 No. 333-231887) pertaining to the 2019 Equity Incentive Plan of Ironwood Pharmaceuticals, Inc.;

(3) Registration Statements (Form S-8 Nos. 333-189340, 333-197875, 333-206228, 333-213001, 333-219670, 333-226613, and 333-231890) pertaining to the Amended and Restated 2010 Employee Stock Purchase Plan of Ironwood Pharmaceuticals, Inc.;

(4) Registration Statements (Form S-8 Nos. 333-184396, 333-189339, 333-197874, 333-206227, 333-213002, 333-219669, and 333-226612) pertaining to the Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan of Ironwood Pharmaceuticals, Inc.;

(5) Registration Statement (Form S-8 No. 333-165230) pertaining to the 2010 Employee Stock Purchase Plan of Ironwood Pharmaceuticals, Inc.;

(6) Registration Statement (Form S-8 No. 333-165231) pertaining to the 2010 Employee, Director and Consultant Equity Incentive Plan of Ironwood Pharmaceuticals, Inc.;

(7) Registration Statement (Form S-8 No. 333-165228) pertaining to the Amended and Restated 2005 Stock Incentive Plan of Ironwood Pharmaceuticals, Inc.;

(8) Registration Statement (Form S-8 No. 333-165229) pertaining to the Amended and Restated 2002 Stock Incentive Plan of Ironwood Pharmaceuticals, Inc.; and

(9) Registration Statement (Form S-8 No. 333-165227) pertaining to the 1998 Amended and Restated Stock Option Plan of Ironwood Pharmaceuticals, Inc.;

of our reports dated February 16, 2023, with respect to the consolidated financial statements of Ironwood Pharmaceuticals, Inc. and the effectiveness of internal control over financial reporting of Ironwood Pharmaceuticals, Inc. included in this Annual Report (Form 10-K) of Ironwood Pharmaceuticals, Inc. for the year ended December 31, 2022.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 16, 2023

EXHIBIT 31.1

**CERTIFICATION PURSUANT
TO RULE 13a-14(a) UNDER
THE SECURITIES EXCHANGE ACT OF 1934**

I, Thomas McCourt, certify that:

1. I have reviewed this Annual Report on Form 10-K of Ironwood Pharmaceuticals, Inc. (the "registrant");

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 16, 2023

/s/ THOMAS MCCOURT

Thomas McCourt
Chief Executive Officer

EXHIBIT 31.2

**CERTIFICATION PURSUANT
TO RULE 13a-14(a) UNDER
THE SECURITIES EXCHANGE ACT OF 1934**

I, Sravan K. Emany, certify that:

1. I have reviewed this Annual Report on Form 10-K of Ironwood Pharmaceuticals, Inc. (the “registrant”);

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant’s other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

    a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    c. Evaluated the effectiveness of the registrant’s disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d. Disclosed in this report any change in the registrant’s internal control over financial reporting that occurred during the registrant’s most recent fiscal quarter (the registrant’s fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant’s internal control over financial reporting; and

5. The registrant’s other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant’s auditors and the audit committee of the registrant’s board of directors (or persons performing the equivalent functions):

    a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant’s ability to record, process, summarize and report financial information; and

    b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant’s internal control over financial reporting.

Date: February 16, 2023

/s/ Sravan K. Emany

Sravan Emany
Chief Financial Officer

EXHIBIT 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Ironwood Pharmaceuticals, Inc. (the "Company") on Form 10-K for the period ended December 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Thomas McCourt, Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, to my knowledge that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ THOMAS MCCOURT

Thomas McCourt
Chief Executive Officer
February 16, 2023

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

EXHIBIT 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Ironwood Pharmaceuticals, Inc. (the “Company”) on Form 10-K for the period ended December 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the “Report”), I, Sravan K. Emany, Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, to my knowledge that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ SRAVAN K. EMANY

Sravan K. Emany
Chief Financial Officer
February 16, 2023

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.