2025 Annual Report

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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2025

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: 001-33277

MADRIGAL PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**04-3508648**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
Four Tower Bridge 200 Barr Harbor Drive, Suite 200 West Conshohocken, Pennsylvania	**19428**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's telephone number, including area code: (267) 824-2827

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 Par Value Per Share	**MDGL**	**The Nasdaq Stock Market LLC**

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

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

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

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

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

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

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

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

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

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

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

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

The aggregate market value of the voting stock held by non-affiliates of the registrant based upon the closing sale price of the registrant's common stock on June 30, 2025 (the last business day of the registrant's most recently completed second fiscal quarter), as reported on the Nasdaq Global Market, was approximately $5.6 billion. For purposes of this calculation, the registrant has assumed that all of its directors, executive officers, persons beneficially owning 10% or more of the registrant's outstanding common stock and certain other stockholders of the registrant may be considered to be affiliates. This assumption shall not be deemed conclusive as to affiliate status for this or any other purpose.

As of February 12, 2026, the registrant had 22,939,969 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Certain information required by Part III, Items 10-14 of this Annual Report on Form 10-K is incorporated by reference to the registrant's definitive Proxy Statement for the 2026 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, provided that if such Proxy Statement is not filed within such period, such information will be included in an amendment to this Annual Report on Form 10-K to be filed within such 120-day period.

Table of Contents

		Page
PART I		
Item 1.	Business	5
Item 1A.	Risk Factors	31
Item 1B.	Unresolved Staff Comments	70
Item 1C.	Cybersecurity	70
Item 2.	Properties	72
Item 3.	Legal Proceedings	72
Item 4.	Mine Safety Disclosures	72
PART II		
Item 5.	Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	73
Item 6.	[Reserved]	74
Item 7.	Management's Discussion and Analysis of Financial Condition and Results of Operations	75
Item 7A.	Quantitative and Qualitative Disclosures About Market Risk	84
Item 8.	Financial Statements and Supplementary Data	84
Item 9.	Changes in and Disagreements With Accountants on Accounting and Financial Disclosure	85
Item 9A.	Controls and Procedures	85
Item 9B.	Other Information	86
Item 9C.	Disclosure Regarding Foreign Jurisdictions that Prevent Inspections	86
PART III		
Item 10.	Directors, Executive Officers and Corporate Governance	87
Item 11.	Executive Compensation	87
Item 12.	Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	87
Item 13.	Certain Relationships and Related Transactions and Director Independence	87
Item 14.	Principal Accountant Fees and Services	87
PART IV		
Item 15.	Exhibits and Financial Statement Schedules	88
Item 16.	Form 10-K Summary	91
	Signatures	92

Unless otherwise stated, all references to "us," "our," "we," "Madrigal," the "Company" and similar designations in this Annual Report on Form 10-K refer to Madrigal Pharmaceuticals, Inc. and its consolidated subsidiaries. Madrigal Pharmaceuticals, Rezdiffra™ and associated logos are trademarks of Madrigal Pharmaceuticals, Inc. Other brands, names and trademarks contained in this Annual Report on Form 10-K are the property of their respective owners.

Solely for convenience, the trademarks and trade names in this Annual Report on Form 10-K may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (this "Annual Report") for the fiscal year ended December 31, 2025 includes "forward-looking statements" made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 that are based on our beliefs and assumptions and on information currently available to us, but are subject to factors beyond our control. Forward-looking statements reflect management's current knowledge, assumptions, judgment and expectations regarding future performance or events; include all statements that are not historical facts and can be identified by terms such as "accelerate," "achieve," "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "goal," "believes," "estimates," "positions," "predictive," "projects," "predicts," "intends," "potential," "continue," "seeks" and similar expressions and the negatives of those terms. In particular, forward-looking statements contained in or incorporated by reference to this Annual Report include statements related to, among other things, the following:

- our ability to successfully commercialize Rezdiffra, our only approved product, in the United States and the European Union for the treatment of metabolic dysfunction-associated steatohepatitis ("MASH") with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis);
- our ability to obtain and maintain full approval for Rezdiffra from the U.S. Food and Drug Administration (the "FDA") and the European Medicines Agency ("EMA"), including our ability to successfully, or in a timely manner, report positive results from either of our outcomes trials, which is required for full approval of Rezdiffra;
- our ability to obtain and maintain regulatory approval to expand Rezdiffra's indication to a broader MASH patient population;
- the degree of market acceptance of Rezdiffra by physicians, patients, third-party payors and others in the healthcare community;
- our ability to obtain and maintain adequate reimbursement from government and third-party payors for Rezdiffra or acceptable prices for Rezdiffra;
- our ability to effectively scale our operations in Europe to successfully commercialize Rezdiffra;
- our possible or assumed future business strategies and plans (including potential ex-U.S. commercial or partnering opportunities) and potential growth opportunities;
- competition in the market and our ability to adapt to our highly competitive environment;
- our ability to acquire or in-license new product candidates and technologies, or the potential clinical or commercial success of such product candidates or technologies;
- safety or efficacy matters related to Rezdiffra or any other product candidate;
- our ability to successfully advance our clinical pipeline and achieve positive results from our clinical trials;
- anticipated timing of receipt of data from our clinical trials and the public disclosure of such data;
- our potential achievement of primary and key secondary endpoints in our clinical trials;
- estimates of the number of potential patients with MASH or physicians identified;
- our ability to maintain and extend our leadership position in the MASH sector;
- our ability to establish and maintain an effective commercial organization, including sales and marketing representatives;
- our ability to attract and retain qualified personnel or to effectively manage our growth;
- our ability to successfully conduct our current or any future clinical trials necessary for regulatory approval and our ability to enroll or retain sufficient patients to conduct and complete the trials or generate data necessary for regulatory approval;
- the ability of third parties on which we rely to manufacture sufficient quantities of Rezdiffra or any other future product candidate for our commercial or clinical needs and their ability to comply with our agreements or applicable regulations;
- the timely distribution of our product;
- the regulation of the healthcare industry, including pricing reform, and our ability to comply with an evolving regulatory landscape;

- anticipated or estimated future results, including our future operating performance and financial position;
- estimates of our expenses and liquidity and our ability to raise additional capital as needed;
- our ability to achieve or maintain profitability;
- our ability to comply with the covenants included in our loan facility;
- our ability to delay certain research activities and related clinical expenses as necessary;
- general economic conditions in the United States, Europe and globally, affecting us, our suppliers, third-party service providers and potential partners;
- our ability to adequately protect our intellectual property rights or prevent disclosure of our trade secrets and other proprietary information and costs associated with litigation or other proceedings related to such matters;
- our ability to comply with our obligations under our license agreements, including our license agreement with Hoffman-La Roche ("Roche"); and
- the potential impact of cyber-attacks and other security incidents on our operations or business.

We caution you that the foregoing list may not include all of the forward-looking statements made in this Annual Report. Although management presently believes that the expectations reflected in such forward-looking statements are reasonable, management cannot assure that such expectations will prove to be correct and you should be aware that actual results could differ materially from those contained in such forward-looking statements.

You should not place undue reliance on any such forward-looking statements. Any forward-looking statement is based on information current as of the date of this Annual Report and speaks only as of the date on which such statement is made. Actual events or results may differ materially from the results, plans, intentions or expectations expressed or implied in these forward-looking statements as a result of a variety of factors, many of which are beyond our control. More information on factors that could cause actual results to differ materially from those anticipated is included from time to time in our reports filed with the U.S. Securities and Exchange Commission ("SEC"), including, but not limited to, those described in the section titled "Risk Factors" included in this Annual Report. Moreover, we operate in an evolving environment. New risks and uncertainties emerge from time to time and it is not possible for our management to predict all risks and uncertainties, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual future results to be materially different from those expressed or implied by any forward-looking statements. We disclaim any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in such forward-looking statements.

RISK FACTORS SUMMARY

Our business is subject to numerous risks and uncertainties that could affect our ability to successfully implement our business strategy and affect our financial results. You should carefully consider all of the information in this report and, in particular, the following principal risks and all of the other specific factors described in Item 1A. of this report, "Risk Factors," before deciding whether to invest in our company.

- We are highly dependent on the success of our only approved product, Rezdiffra. If we are unable to successfully commercialize or maintain approval for Rezdiffra, our business, financial condition, results of operations, prospects and the value of our common stock will be materially adversely affected.
- We obtained accelerated approval in the United States and conditional marketing authorization in the European Union ("EU") for Rezdiffra, and we are subject to certain post-marketing commitments.
- The commercial success of Rezdiffra will depend on market acceptance by physicians, patients, third-party payors and others in the healthcare community.
- If we are unable to successfully further develop and maintain internal commercialization capabilities, future sales of Rezdiffra may be negatively impacted.
- If we are unable to obtain or maintain adequate coverage and reimbursement from government or third-party payors for Rezdiffra or, if approved, any other product candidates, our prospects for generating revenue may be adversely affected.
- Changes in healthcare law and policy, including changes to Medicare, could have a material adverse effect on our business and financial condition.
- Federal legislative and regulatory efforts to implement reference pricing or most-favored-nation pricing models could impact our product revenues and materially harm our business.
- Rezdiffra remains subject to ongoing regulatory review, and if we fail to comply with regulations or satisfy our post-approval commitments, we could lose our approval and the sale of Rezdiffra could be suspended.
- Rezdiffra could develop unexpected safety or efficacy concerns, which would likely have a material adverse effect on us.
- We operate in a highly competitive and changing environment, and if we are unable to adapt to our environment, we may be unable to compete successfully.
- Rezdiffra was approved for treatment in a limited population of patients with MASH with moderate to advance liver fibrosis, and additional clinical trials and regulatory applications are required to expand its indication. We may not be successful in obtaining such regulatory approval to expand Rezdiffra's indication.
- EU pricing and reimbursement regulations may materially affect our ability to market and receive coverage for Rezdiffra in the EU Member States.
- If the FDA or other applicable regulatory authorities approve generic products that compete with Rezdiffra, the sales of Rezdiffra would be adversely affected.
- We currently rely on a limited number of specialty pharmacies for distribution of Rezdiffra in the United States, and the loss of one or more of these specialty pharmacies or their failure to effectively distribute Rezdiffra could materially harm our business.
- If estimates of the size of the potential market for Rezdiffra is overstated or data we have used to identify physicians is inaccurate, our ability to earn revenue could be materially adversely affected.
- Product liability lawsuits brought against us could cause us to incur substantial liabilities and could limit commercialization of Rezdiffra or any future product candidates that we may develop.
- Pharmaceutical research and development is very expensive, time-consuming and difficult to design and implement and involves uncertain outcomes. Furthermore, the results of preclinical studies and earlier clinical trials are not always predictive of future results. Any product candidate that we advance into clinical trials may not have favorable results in later clinical trials or receive regulatory approval.
- If we fail to successfully develop and commercialize our other product candidates, we may be unable to grow our business.
- Interim, topline and preliminary data from our clinical trials that we announce or publish from time to time may change as more data become available, may be interpreted differently if additional data are disclosed and are subject to audit and verification procedures that could result in material changes in the final data.

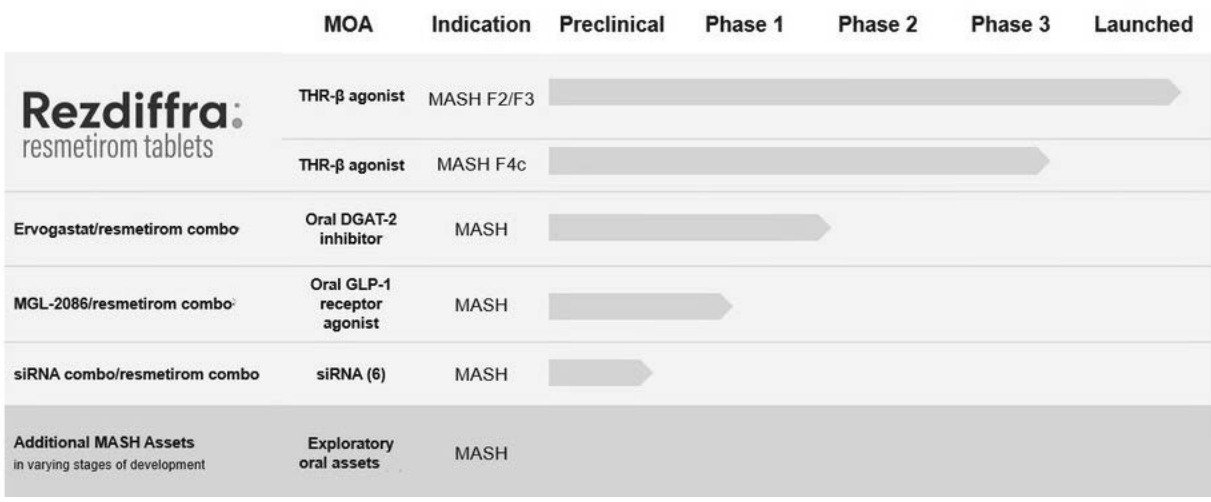
- If clinical trials or regulatory approval processes are prolonged, delayed or suspended, we may be unable to advance the development of or commercialize our product candidates on a timely basis, which would require us to incur additional costs and delay our receipt of any revenue from potential product sales.
- If we fail to comply with foreign regulatory requirements governing human clinical trials and marketing approval for drugs, we could be prevented from selling our drug candidates in such foreign markets.
- We depend on enrollment of patients in our clinical trials. If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.
- We are dependent on retaining and attracting key personnel, the loss of whose services could materially adversely affect our business, financial condition and results of operations.
- We expect to continue to expand our development and commercialization capabilities, and as a result, we may encounter challenges in managing our growth, which could disrupt our operations.
- Any strategic transactions we enter into may not be clinically or commercially successful and may require financing or a significant amount of cash, which could adversely affect our business.
- A failure of our information technology infrastructure and cybersecurity threats may adversely affect our business and operations.
- If the third parties on which we rely for the conduct of our clinical trials and results do not perform our clinical trial activities in accordance with our agreements, good clinical practices ("GCP") and related regulatory requirements, we may be unable to obtain regulatory approval for our product candidates.
- Adverse consequences to our business could result if our manufacturing partners fail to comply with applicable regulations or our agreements or fail to maintain required approvals.
- We have a history of operating losses, expect to incur operating losses in the future and may never achieve or maintain profitability.
- We may need to raise additional capital to fund our operations, but we may not be able to access capital.
- The agreement governing our senior secured debt contains restrictive and financial covenants that may limit our operating flexibility.
- Government healthcare reform could materially increase our costs, which could materially adversely affect our business, financial condition, results of operations, prospects and the value of our common stock.
- If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional rebate requirements, penalties or other sanctions.
- If we are found to be in violation of federal or state "fraud and abuse" laws, we may be required to pay a penalty or may be suspended from participation in federal or state healthcare programs.
- Our rights to develop and commercialize resmetirom are subject in part to the terms and conditions of the Roche Agreement.
- We may fail to comply with any of our obligations under agreements pursuant to which we license rights or technology, which could result in the loss of rights or technology that may be material to our business.
- Risks associated with operations outside of the United States could adversely affect our business.
- Our success depends on our ability to protect our intellectual property and our proprietary technologies.
- The price of our common stock has been, and may continue to be, volatile.

Item 1. Business

Overview

We are a biopharmaceutical company focused on delivering novel therapeutics for metabolic dysfunction-associated steatohepatitis ("MASH"), a serious liver disease with high unmet medical need that can lead to cirrhosis, liver failure, liver cancer, need for liver transplantation and premature mortality. MASH was previously known as nonalcoholic steatohepatitis ("NASH"). MASH is the leading cause of liver transplantation in women, the second leading cause of all liver transplantation in the United States and the fastest-growing indication for liver transplantation in Europe. Our medication, Rezdiffra (resmetirom), is a once-daily, oral, liver-directed thyroid hormone receptor beta ("THR-β") agonist designed to target key underlying causes of MASH. In March 2024, Rezdiffra became the first therapy approved by the FDA for patients with MASH and was commercially available in the United States beginning in April 2024. Following receipt of conditional marketing authorization ("CMA") from the European Commission ("EC"), we launched Rezdiffra in Germany in September 2025. Rezdiffra was the first medication approved by both the FDA and EC for the treatment of adults with noncirrhotic MASH with moderate to advanced liver fibrosis (F2 to F3 fibrosis). We are also evaluating Rezdiffra in patients with compensated MASH cirrhosis (consistent with F4c fibrosis) in our MAESTRO-NASH OUTCOMES trial, that, if successful, could expand the eligible patient population for Rezdiffra.

In addition, we are advancing a focused pipeline to lead the evolution of MASH treatment for patients for decades to come. Through our business development efforts, we have acquired rights to MGL-2086, an oral glucagon-like peptide-1 ("GLP-1") receptor agonist, ervogastat, an oral diacylglycerol O-acyltransferase 2 ("DGAT2") inhibitor, six small interfering RNA ("siRNA") programs and additional preclinical MASH candidates. We plan to evaluate these candidates with the goal of delivering best-in-disease therapies for the treatment of MASH. As we continue to build our pipeline, we will evaluate mechanisms that fit scientifically, strategically and commercially to enhance our leading position in MASH care.



Key 2025 and Recent Highlights

We experienced tremendous growth in 2025, highlighted by our strong commercial execution. For the year ended December 31, 2025, we generated $958.4 million in product revenue from sales of Rezdiffra. In addition, 2025 featured the following key achievements:

- In May 2025, we announced positive two-year results from the open-label compensated MASH cirrhosis (F4c) arm of the Phase 3 MAESTRO-NAFLD-1 trial of Rezdiffra. Patients (n=122) achieved significant improvements from baseline in liver stiffness, liver fat, fibrosis biomarkers, liver volume and risk scores for clinically significant portal hypertension ("CSPH"). The results were presented in a late-breaking oral abstract at the European Association for the Study of the Liver ("EASL") Congress. In addition, in November 2025, we announced additional data showing Rezdiffra's impact in patients with more advanced compensated MASH cirrhosis (those with a platelet count of <100,000/μL at baseline). In this patient population, Rezdiffra demonstrated improvements from baseline across multiple imaging tests and biomarkers including liver stiffness, liver enzymes and lipids, as well as Baveno risk scores for CSPH.
- In July 2025, we announced that we received a Notice of Allowance from the U.S. Patent and Trademark Office for a new U.S. patent covering the FDA-approved use of Rezdiffra. The patent, which was issued on August 5, 2025, includes claims directed to Rezdiffra's commercial weight-threshold dosing regimen as prescribed in the FDA-approved label. The U.S. patent provides protection to February 2045 and was listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book, in August 2025.
- In July 2025, we entered into a Financing Agreement (as amended, the "Financing Agreement") with certain funds managed by Blue Owl Capital Corporation as the lenders (the "Lenders") and LSI Financing LLC as the administrative agent for the Lenders (the "Administrative Agent"). Under the Financing Agreement, the Lenders committed up to $500.0 million in senior secured credit facilities, consisting of (a) an initial term loan in an aggregate principal amount equal to $350.0 million (the "Initial Term Loan") and (b) delayed draw term loans in an aggregate principal amount not to exceed $150.0 million (the loans thereunder, if any, the "Delayed Draw Term Loans"). In addition, the Financing Agreement includes an uncommitted incremental facility in an aggregate principal amount not to exceed $250.0 million (the loans thereunder, if any, the "Incremental Term Loans," and together with the Initial Term Loan and any Delayed Draw Term Loans, collectively, the "Term Loans"), subject to the satisfaction of certain terms and conditions set forth in the Financing Agreement. The Initial Term Loan was funded on July 17, 2025. Delayed Draw Term Loans are available at our election from time to time until December 31, 2027. Incremental Term Loans are available at our and the Lenders' mutual consent from time to time.
- In July 2025, we entered into an exclusive global license agreement (the "CSPC License Agreement") with CSPC Pharmaceutical Group Limited ("CSPC") for MGL-2086 (formerly SYH2086), an oral GLP-1 receptor agonist. Pursuant to the CSPC License Agreement, CSPC granted us an exclusive global license to develop, manufacture and commercialize MGL-2086. We expect to initiate a single ascending dose study of MGL-2086 in the second quarter of 2026.
- In August 2025, we announced that the EC granted a CMA for Rezdiffra for the treatment of MASH with moderate to advanced liver fibrosis. We launched Rezdiffra in Germany in September 2025. Rezdiffra was the first medication approved for patients with MASH in the European Union and is included in the European MASH treatment guidelines.
- In January 2026, we announced the expansion of our pipeline with an exclusive global license for ervogastat, a Phase 2 oral DGAT-2 inhibitor. DGAT-2 inhibitors work by blocking the final step in triglyceride assembly and storage, resulting in lower hepatic triglycerides, reduced lipotoxic fat and decreased inflammation. In 2026, we plan to conduct a drug-to-drug interaction study with resmetirom and consult with the FDA on the design of a Phase 2 combination trial.
- In February 2026, we announced an exclusive global license agreement (the "Ribocure License Agreement") with Suzhou Ribo Life Science Co. Ltd. and Ribocure Pharmaceuticals AB (together, "Ribocure") for six novel siRNA programs designed to silence certain genes implicated in MASH disease progression. By pairing the precision of gene-silencing with Rezdiffra, we are exploring

whether reducing drivers of disease at the genetic level can complement Rezdiffra's therapeutic effects. IND-enabling activities in initial candidates are expected to begin in 2026.

Our Strategy

The critical components of our business strategy include the following:

Maximize the value of Rezdiffra. We generated $958.4 million in net product revenue from sales of Rezdiffra in 2025. With quarterly sales now annualizing at greater than $1.0 billion as of December 31, 2025 and a low market penetration rate, we believe we are well positioned to continue to deliver on this strategic priority. We have secured broad first-line access across commercial payers through our payer contracting efforts and believe that we will continue to steadily add patients through 2026. In the United States, we continue to educate healthcare providers and patients on the risks of MASH and the potential clinical benefits and appropriate use of Rezdiffra and believe that the MASH market will continue to grow significantly over time given low MASH diagnosis rates today. We also launched Rezdiffra in Germany in September 2025 and expect to launch Rezdiffra in other international markets over time. We continue to believe that Rezdiffra's product profile as a liver-directed, once-daily, generally well-tolerated oral therapy, as well as its first-to-market position, provide meaningful points of differentiation in the MASH competitive landscape.

Deliver transformational outcomes data in F4c. A key component of our strategy is to expand Rezdiffra's label to treat patients with compensated MASH cirrhosis (F4c), which currently has no approved treatments available. We have fully enrolled our Phase 3 MAESTRO-NASH OUTCOMES trial evaluating Rezdiffra in patients with compensated MASH cirrhosis, and we expect a data readout from this trial in 2027. A positive outcome from this trial is expected to support the full approval of Rezdiffra in the United States for moderate to advanced liver fibrosis (F2 to F3 fibrosis) and an additional indication for Rezdiffra in patients with F4c, which we believe could double Rezdiffra's commercial opportunity. In 2025, we announced positive two-year data from a 122-patient open label cohort from our MAESTRO-NAFLD-1 trial evaluating Rezdiffra in the F4c patient population, reinforcing our confidence in receiving positive results from our OUTCOMES trial. We plan to continue to evaluate opportunities to expand Rezdiffra's label and generate new data to maintain our leadership position in the MASH treatment landscape.

Build an industry-leading MASH pipeline. MASH is a complex and heterogeneous disease, and we expect future treatment will include multiple therapies, combinations and personalized regimens. Through our business development efforts, we have added several product candidates to our pipeline, including MGL-2086, ervogastat and multiple siRNA programs, and we plan to continue to invest in new mechanisms with complementary biology and combination potential with resmetirom. We expect to initiate clinical testing of our product candidates with the goal of delivering enhanced efficacy across the MASH spectrum. By leveraging our research and development capabilities that pioneered MASH treatment, we believe we will be able to design and advance more informative clinical trials and progress the most promising programs to later stage testing in a capital efficient manner. With patent protection for Rezdiffra expected into 2045, we believe we have a long runway to invest in innovative therapies and build a pipeline that will define the future of MASH care.

Rezdiffra for Patients with MASH

Rezdiffra is our first and only approved product. Rezdiffra received accelerated approval from the FDA in March 2024 in conjunction with diet and exercise for the treatment of adults with noncirrhotic MASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis). In August 2025, the EC granted a CMA for Rezdiffra, making it the first medication approved by both the FDA and EC for the treatment of adults with noncirrhotic MASH with moderate to advanced liver fibrosis. Rezdiffra is a once-daily, oral, liver-directed THR-β agonist designed to target key underlying causes of MASH.

Approval of Rezdiffra

In March 2024, the FDA granted accelerated approval for Rezdiffra for the treatment of adults with noncirrhotic MASH with moderate to advanced liver fibrosis (F2 to F3 fibrosis) pursuant to section 506(c) of the Federal Food, Drug and Cosmetic Act and 21 C.F.R. Part 314 Subpart H (Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses) (Subpart H). In addition, in June 2025, we received a positive opinion from the Committee for Medicinal Products for Human Use ("CHMP") of the EMA recommending the granting of a CMA of resmetirom for the treatment of adults with noncirrhotic MASH with moderate to advanced liver fibrosis (F2 to F3 fibrosis). The EC issued a decision to grant the CMA for Rezdiffra in August 2025. The EC decision is valid in all 27 member states of the European Union, as well as in Iceland, Liechtenstein and Norway. The FDA's accelerated approval and the EC's CMA, as well as Rezdiffra's approved prescribing information, were supported by results from our Phase 3 MAESTRO-NASH trial and additional safety data from the Phase 3 MAESTRO-NAFLD-1 and MAESTRO-NAFLD-OLE extensions trials, each of which was 52 weeks in duration. Following 52 weeks of treatment in the MAESTRO-NASH trial, both 100 mg and 80 mg doses of

Rezdiffra demonstrated statistically significant improvement compared to placebo on two primary endpoints: MASH resolution (including a reduction in the non-alcoholic fatty liver disease ("NAFLD") activity score by ≥ 2 points) with no worsening of fibrosis, and an improvement in fibrosis by at least one stage with no worsening of the NAFLD activity score. See the section titled "—Clinical Trial Overview" in this Annual Report for additional information on our clinical trials for resmetirom.

In connection with Rezdiffra's approvals, we have agreed to certain post-marketing commitments, including completing our MAESTRO-NASH trial to demonstrate a clinical benefit of Rezdiffra on composite endpoints. Patients enrolled in the MAESTRO-NASH trial have continued on therapy after the initial 52-week treatment period for up to 54 months to accrue and measure hepatic clinical outcome events, including progression to cirrhosis on biopsy and hepatic decompensation events, as well as all-cause mortality. We expect outcomes data from this trial in 2028. Positive confirmatory outcomes data from this trial is expected to verify a clinical benefit and support the full approval of Rezdiffra in noncirrhotic MASH in the United States. Separate from our commitment to complete the MAESTRO-NASH trial, we have fully enrolled our Phase 3 MAESTRO-NASH OUTCOMES trial, which is a double-blind, randomized, placebo-controlled trial that noninvasively measures progression to liver decompensation events in patients with compensated MASH cirrhosis. The primary endpoint of MAESTRO-NASH OUTCOMES is the incidence of composite liver-related outcome events. Key inclusion criteria are well-compensated MASH cirrhosis (Child-Pugh A) and presence of three metabolic risk factors (metabolic syndrome). Patients are randomized 3:1 in a blinded manner to receive 80 mg resmetirom or matching placebo, given orally once daily. We expect results from the OUTCOMES trial in 2027. Positive data from our MAESTRO-NASH OUTCOMES trial is expected to support the full approval of Rezdiffra in noncirrhotic MASH (F2 to F3 fibrosis) in the United States and support approval for patients with compensated cirrhosis (F4c), expanding the eligible patient population for Rezdiffra. We have agreed to submit results from these trials to the EMA in support of transitioning the Rezdiffra CMA into a standard marketing authorization in the European Union.

Market Opportunity for Rezdiffra in MASH

Disease Overview

MASH is a more advanced form of metabolic dysfunction-associated steatotic liver disease ("MASLD"). MASLD has become the most common liver disease in the United States and other developed countries and is characterized by an accumulation of fat in the liver with no other apparent causes. MASH can progress to cirrhosis or liver failure, can require liver transplantation and can also result in liver cancer. Patients with MASH, especially those with more advanced metabolic risk factors (hypertension, concomitant type 2 diabetes), are at increased risk for adverse cardiovascular events and increased morbidity and mortality. In addition, MASH patients with moderate to advanced fibrosis (consistent with fibrosis stages F2 and F3) have a 10- to 17-times higher risk of liver-related mortality. MASH is also an independent driver of cardiovascular disease, which is the leading cause of mortality for patients.

In addition to the accumulation of fat in the liver, MASH is characterized by inflammation and cellular damage with or without fibrosis, which may ultimately progress to cirrhosis. Within MASH cirrhosis, patients can be categorized as being compensated or decompensated. MASH with compensated cirrhosis (consistent with F4c fibrosis) is characterized by liver scarring or damage that reduces the ability to process blood supplied to the liver, though patients generally remain asymptomatic with normal liver function. MASH patients with compensated cirrhosis are on the cusp of negative consequences associated with end-stage liver disease including decompensation, esophageal varices, ascites, hepatic encephalopathy, liver cancer and liver failure. Patients with compensated MASH cirrhosis have a 42-times higher risk of liver-related mortality, underscoring the need to treat MASH before complications of cirrhosis develop.

Progression to cirrhosis generally occurs in approximately 20% of MASH patients with moderate-to-advanced fibrosis and can occur within ten to fifteen years from initial diagnosis. Further, approximately 20% of patients with advanced fibrosis (stage F3) will progress to cirrhosis in approximately two years. MASH patients with type-2 diabetes have a heightened risk of MASH disease progression, with an estimated two-to-three times faster rate of progression of fibrosis. Once the disease advances beyond MASH to such life-threatening conditions as liver cancer or liver failure, liver transplantation is the only treatment alternative. MASH is the leading cause of liver transplants for women, the second leading cause of all liver transplantation in the United States, and the fastest-growing indication for liver transplantation in Europe. With more advanced liver disease as a result of unaddressed MASH with fibrosis, the burden to the healthcare system in terms of healthcare resource utilization and cost increases, driven by hospitalization due to decompensated disease, treatment of hepatocellular carcinoma and liver transplants. Importantly, due to the limited availability of donor organs and the comorbidities associated with MASH, patients with MASH who are put on the transplant list are at much lower odds of actually getting transplanted relative to those with liver disease driven by other causes. As such, Rezdiffra addresses a significant unmet medical need for patients with MASH.

Commercial Strategy

We launched Rezdiffra in the United States in April 2024 and in Germany in September 2025. Prior to receiving approval, we conducted quantitative and qualitative market research studies and secondary data analytics to inform the

commercial strategy for Rezdiffra. These studies and analytics evaluated the size of the market opportunity for Rezdiffra as well as physician, patient and payer perspectives on unmet needs in MASH patient care and the Rezdiffra product profile.

Based on published epidemiology data and an analysis of medical claims using ICD-10 disease diagnosis codes as of 2023, we estimate that 315,000 patients diagnosed with MASH with moderate to advanced fibrosis (stages F2 to F3) are under the care of specialist prescribers which we are targeting during the launch of Rezdiffra in the U.S. In addition, we estimate that approximately 370,000 patients with MASH with moderate to advanced fibrosis are currently diagnosed and under the care of specialists across Europe. We believe the number of patients under specialist care in the U.S. has grown nearly 50% through 2025, and as disease awareness improves and disease prevalence increases, we expect the number of identified MASH patients with moderate to advanced fibrosis eligible for treatment to grow significantly going forward.

With a growing body of real-world supportive data, we continue to educate healthcare providers and patients on the risks of MASH and the potential clinical benefits and appropriate use of Rezdiffra. During our first six quarters of launch in the United States, we focused our efforts on hepatologists and gastroenterologists. Beginning in the fourth quarter of 2025, we expanded our field team to further target select endocrinologists that provide care to MASH patients. We are also supporting the creation of care pathways for patients at physician offices, driving breadth and depth of Rezdiffra prescribers and engaging with payers to support patient access to therapy.

Beyond Germany, we expect to launch Rezdiffra on a country-by-country basis in Europe dependent on multiple factors, including the completion of reimbursement procedures and regulatory approval where required. In addition, we may enter into distribution agreements with third parties to distribute Rezdiffra in smaller European countries and in other jurisdictions globally.

Clinical Trial Overview

Set forth below is a summary of our clinical trial programs for Rezdiffra:

- The pivotal MAESTRO-NASH (moderate to advanced fibrosis) trial evaluated daily oral doses of resmetirom at 80 mg and 100 mg doses. The primary 52-week results of the MAESTRO-NASH trial supported the grant of accelerated approval by the FDA and were published in the *New England Journal of Medicine* in February 2024. This trial remains ongoing as part of our post-marketing commitments to the FDA. The 54-month outcomes portion of the trial is designed to generate confirmatory data that, if positive, is expected to verify a clinical benefit and support the full approval of Rezdiffra in noncirrhotic MASH in the United States. We expect outcomes data from this trial in 2028.
- The MAESTRO-NAFLD-1 (Safety) trial was a 52-week trial that noninvasively evaluated the safety and tolerability of resmetirom and provided a larger safety database to support regulatory benefit-risk assessment. The primary results from the MAESTRO-NAFLD-1 trial were published in *Nature Medicine* in October 2023. MAESTRO-NAFLD-OLE, an open-label active treatment extension of MAESTRO-NAFLD-1, is ongoing to collect additional data in patients with noncirrhotic MASH and patients with compensated MASH cirrhosis. In 2025, we announced positive two-year data from the open-label compensated MASH cirrhosis (F4c) arm of this trial.
- MAESTRO-NASH OUTCOMES (Compensated Cirrhosis) is ongoing to evaluate progression to liver decompensation events in patients with compensated MASH cirrhosis treated with resmetirom versus placebo. A positive outcome is expected to support the full approval of Rezdiffra for noncirrhotic MASH in the United States and expand the eligible patient population for Rezdiffra with an additional indication in patients with compensated MASH cirrhosis. This event-driven trial is expected to deliver results in 2027.

MAESTRO-NASH Trial

In December 2022, we announced topline results from the pivotal Phase 3 MAESTRO-NASH biopsy trial of resmetirom and the primary results were published in the *New England Journal of Medicine* in February 2024. Resmetirom achieved both primary endpoints with both daily oral doses, 80 mg and 100 mg, relative to placebo.

Patients meeting eligibility requirements for MAESTRO-NASH were randomized 1:1:1 to receive resmetirom 80 mg, resmetirom 100 mg or placebo taken orally once daily. Baseline liver biopsy fibrosis scores included F3 (~60%), F2 (~35%), F1B (~5%) (primary analysis population) with 84% with nonalcoholic fatty liver disease activity score ("NAS") of ≥5. A second biopsy was conducted after 52 weeks of treatment for assessment of the dual primary endpoints. The primary efficacy analysis assessed histological response at 52 weeks in 955 patients with biopsy-confirmed MASH with significant fibrosis (modified intent-to-treat (mITT) population) that excluded 11 intent-to-treat patients who had their Week 52 biopsy after Week 60 due to COVID-related reasons per regulatory guidelines. Patients without a second biopsy due to early trial discontinuation or missing liver biopsy (approximately 17% across treatment arms) were included and considered as non-

responders in the primary efficacy analyses (mITT). The compliance to treatment was high and minimally impacted by COVID-19 pandemic restrictions.

Dual Primary Endpoints (52 Weeks) and Key Secondary Endpoint (24 Weeks)

Primary Endpoint	**Resmetirom 80 mg (n=316)**	**p-value**	**Resmetirom 100 mg (n=321)**	**p-value**	**Placebo (n=318)**
MASH resolution (ballooning 0, inflammation 0,1 with ≥2-point reduction in NAS) and no worsening of fibrosis	25.9	<0.001	29.9	<0.001	9.7
≥1-stage improvement in fibrosis with no worsening of NAS	24.2	<0.001	25.9	<0.001	14.2
Key Secondary Endpoint					
LDL-C lowering (24 weeks)	-13.6	<0.001	-16.3	<0.001	0.1

Biopsy endpoints were achieved independent of baseline fibrosis stage or diabetes status, including similar statistical significance and magnitude of effect at both doses in subgroups of F2, F3 and F2/F3 patients. Other secondary liver biopsy endpoints that were achieved at both doses include ≥2 point reduction in NAS with no worsening of fibrosis, ≥2 point reduction in NAS with ≥1-stage improvement in fibrosis, MASH resolution (with ≥2 point reduction in NAS) with ≥1-stage improvement in fibrosis and a 2-stage reduction in fibrosis without worsening of NAS. Multiple secondary endpoints were achieved, including statistically significant reduction from baseline in liver enzymes. Reductions in atherogenic lipids and lipoproteins, fibrosis biomarkers and imaging tests were also observed in resmetirom treatment arms as compared with placebo.

Safety

The frequency of serious adverse events (SAEs) was similar across treatment arms in the MAESTRO-NASH trial. SAEs occurred at expected rates based on the patient population. The rate of trial discontinuation for adverse events ("AEs") over the entire treatment period was low.

Consistent with previous Phase 2 and Phase 3 data, the most common AEs reported with greater frequency in the resmetirom groups versus placebo were an excess of generally mild and transient diarrhea at the beginning of therapy and generally mild nausea. Trial data indicated resmetirom treatment had no effect on heart rate or body weight and was not associated with arrhythmias. Blood pressure appeared slightly reduced among resmetirom-treated patients. Sex hormones were unchanged from baseline. Independent of thyroxine replacement status, resmetirom treatment reduced prohormone T4, as reflected by free thyroxine (FT4), with no effect on thyroid-stimulating hormone (TSH) or the active thyroid hormone, free triiodothyronine (FT3). Relative to placebo, resmetirom-treated patients did not show increases in fractures or fracture risk scores.

MAESTRO-NAFLD-1 Trial

In January 2022, we announced topline results from the Phase 3 MAESTRO-NAFLD-1 safety trial of resmetirom. The MAESTRO-NAFLD-1 trial was published in *Nature Medicine* in November 2023. We reported that resmetirom demonstrated statistical significance for primary and key secondary endpoints summarized below from the double-blind placebo-controlled 969-patient portion of the trial. These endpoints indicated that resmetirom (i) was well-tolerated at 80 and 100 mg in patients treated for 52 weeks, (ii) provided significant and clinically relevant reductions in liver fat as measured by magnetic resonance imaging proton density fat fraction (MRI-PDFF) and (iii) significantly reduced atherogenic lipids, including low-density lipoprotein cholesterol ("LDLc"), apolipoprotein B and triglycerides.

A total of 972 patients were randomized in the double-blind arms of the MAESTRO-NAFLD-1 trial: 969 patients were included in the safety population and 943 patients were included in a modified ITT population for evaluation of key secondary and other endpoints. Important inclusion criteria included the presence of three risk factors of metabolic syndrome, a level of liver fibrosis (measured by FibroScan) consistent with a range of stages of liver fibrosis and ≥8% liver fat (measured by MRI-PDFF).

AEs observed in the MAESTRO-NAFLD-1 trial were generally mild to moderate in severity. The frequency of SAEs was similar across treatment arms and discontinuation for AEs was low. Consistent with published data, the most common AE reported with greater frequency in the resmetirom groups as compared to the placebo was generally mild diarrhea or increased stool frequency at the beginning of therapy.

Compensated MASH Cirrhosis

The MAESTRO-NAFLD-1 trial also included an open label active treatment arm with 180 patients with compensated MASH cirrhosis. Data following 52 weeks of treatment with 80 or 100 mg of resmetirom daily showed improved liver chemistry tests, a reduction in vibration-controlled transient elastography ("VCTE") in a responder analysis and a statistically significant reduction in liver volume by an average of approximately 20%. In May 2025, we reported two-year data showing that 122 patients in the study achieved significant improvements from baseline in liver stiffness, liver fat, fibrosis biomarkers, liver volume and risk scores for CSPH. In November 2025, we announced additional positive data from this cohort examining patients with more advanced compensated MASH cirrhosis (those with a platelet count of <100,000/μL at baseline). In this population, Rezdiffra demonstrated improvements from baseline across multiple imaging tests and biomarkers including liver stiffness, liver enzymes and lipids, as well as Baveno risk scores for CSPH.

These data from this open label active treatment arm continue to support the rationale for our MAESTRO-NASH OUTCOMES trial evaluating Rezdiffra in patients with compensated MASH cirrhosis.

MAESTRO-NASH OUTCOMES Trial

In October 2024, we announced that we completed enrollment of MAESTRO-NASH OUTCOMES, a Phase 3, double-blind, randomized, placebo-controlled trial that is designed to noninvasively measure progression to liver decompensation events in 845 patients with compensated MASH cirrhosis, exceeding our initial enrollment target.

The primary endpoint of MAESTRO-NASH OUTCOMES is the incidence of composite liver-related outcome events, including all-cause mortality, liver transplant, hepatic decompensation (ascites, hepatic encephalopathy, gastroesophageal variceal hemorrhage) and confirmed increase of Model for End-Stage Liver Disease (MELD) score from <12 to ≥15 due to progression of MASH cirrhosis. Key inclusion criteria are well-compensated MASH cirrhosis (Child-Pugh A) and presence of three metabolic risk factors (metabolic syndrome). Patients were randomized 3:1 in a blinded manner to receive 80 mg resmetirom or matching placebo, given orally once daily. We expect results from this event-driven trial in 2027.

A positive outcome is expected to support the full approval of Rezdiffra for noncirrhotic MASH in the United States, potentially accelerating the timeline to full approval. In addition, this trial has the potential to support approval of an additional indication for Rezdiffra in patients with compensated MASH cirrhosis.

Pipeline

Our research and development objective is to build the leading pipeline in MASH. Through our business development efforts, we have added several mechanisms with biology that we believe is complimentary to resmetirom to potentially enhance efficacy across the spectrum of MASH. Given Rezdiffra's profile as a liver-directed therapy, we believe it is the best foundation on which to build the future of MASH treatment. In addition to the following programs, we are evaluating several other candidates that may have the potential to treat MASH either as a monotherapy or as part of a combination.

MGL-2086 (oral GLP-1)

In September 2025, we acquired from CSPC an exclusive global license for MGL-2086 (formerly SYH2086), an oral small molecule GLP-1 receptor agonist. GLP-1 receptor agonists improve systemic metabolism, insulin sensitivity and weight loss. Rezdiffra reverses hypothyroidism in the liver, restoring mitochondrial function and increasing fat processing through beta-oxidation. Based on data from our MAESTRO-NASH trial, Rezdiffra's efficacy is enhanced by even modest amounts of weight loss. By combining these complementary mechanisms in an oral combination therapy, we expect to see greater reductions in both liver fat and fibrosis. An Investigational New Drug application ("IND") has been accepted and we plan to start a Phase 1 single ascending dose trial of MGL-2086 in the second quarter of 2026.

Ervogastat (oral DGAT-2 inhibitor)

In December 2025, we acquired an exclusive global license for ervogastat, a liver-directed, oral DGAT-2 inhibitor, from Pfizer. DGAT-2 inhibitors work by blocking the final step in triglyceride assembly and storage, resulting in lower hepatic triglycerides, reduced lipotoxic fat and decreased inflammation. In a Phase 2b trial conducted by Pfizer, ervogastat demonstrated impressive liver fat reduction as measured by MRI-PDFF, a noninvasive technique to precisely measure the percentage of fat in the liver. 72% of patients treated with ervogastat (150 mg) achieved at least a 30% reduction in liver fat, with 61% experiencing at least a 50% reduction. Improvements in liver enzymes and liver stiffness as measured by VCTE were also observed, and all active doses studied were well tolerated. By inhibiting DGAT-2, we believe we can decrease lipid accumulation in the liver and lower inflammation and fibrosis by keeping stellate cells in their inactive state. Rezdiffra restores mitochondrial function and increases fat processing via beta-oxidation which leads to lower inflammation and a reduction in downstream fibrosis. In combination, we believe these two mechanisms can be

complementary by addressing both the production and clearance of hepatic fat. In 2026, we expect to conduct a Phase 1 drug-to-drug interaction study with ervogastat and resmetirom. In addition, we expect to initiate a Phase 2 combination trial with ervogastat and resmetirom in 2027 following discussions with the FDA.

siRNA programs

In February 2026, we entered into the Ribocure License Agreement pursuant to which we obtained an exclusive global license to six preclinical siRNA programs. These siRNAs target clinically validated genes implicated in MASH disease progression. siRNAs may offer a precision approach to gene silencing in MASH by potentially reducing the production of disease-driving proteins. The siRNAs are N-acetylgalactosamine ("GalNac") conjugated. When linked to a GalNac ligand, siRNA molecules are delivered directly into hepatocytes, where they silence genes that have been identified as key risk factors for MASH by breaking down targeted mRNA. By pairing this precise gene-silencing approach with Rezdiffra, we aim to explore whether reducing drivers of disease at the genetic level can complement Rezdiffra's therapeutic effects. IND-enabling activities in initial candidates are expected to begin in 2026.

Collaborations

Roche Agreement

VIA Pharmaceuticals, Inc. ("VIA") entered into a research, development and commercialization agreement (as amended from time to time, the "Roche Agreement") with Hoffmann-La Roche ("Roche"), in December 2008. We subsequently assumed all of VIA's rights in, to and under, and all of VIA's obligations under, the Roche Agreement pursuant to an asset purchase agreement in September 2011. Pursuant to the terms of the Roche Agreement, we, as successor-in-interest to VIA, assumed control of all development and commercialization of resmetirom and hold exclusive worldwide rights for all potential indications. Under the Roche Agreement, Roche exclusively licensed certain patent rights and know-how relating to resmetirom in exchange for consideration consisting of an upfront payment, milestone payments and tiered single-digit royalty payments based on net sales of Rezdiffra and any derivative products of resmetirom, subject to certain reductions. In 2011, we commenced Phase 1 clinical trials and subsequently paid Roche a related milestone payment. In October 2016, we commenced a Phase 2 clinical trial in MASH and subsequently paid Roche a related milestone payment. In 2019, we commenced a Phase 3 clinical trial in MASH and subsequently paid Roche a $2.0 million related milestone payment. In March 2024, we received FDA approval of Rezdiffra and subsequently paid Roche a $5.0 million related milestone payment. In August 2025, upon receiving a CMA from the EC, a milestone was achieved and we paid $3.0 million to Roche.

Pursuant to the Roche Agreement, we agreed to use commercially reasonable efforts to conduct clinical and commercial development programs for products containing resmetirom. If we determine not to pursue the development or commercialization of resmetirom in certain jurisdictions, Roche may terminate the license for such territories. Our obligation to pay royalties based on net sales of resmetirom in a given country will expire, unless earlier terminated pursuant to other provisions of the Roche Agreement, on the last to occur of (i) the expiration of the last valid claim of a licensed patent covering the manufacture, use or sale of products containing resmetirom in a given country, or (ii) ten years after the first sale of a product containing resmetirom in such country. In January 2026, we entered into an amendment to the Roche Agreement to provide us the full and exclusive right and discretion to control all patent term adjustments and patent term extensions applicable to Rezdiffra, including patents owned by Roche and jointly owned between the parties. In consideration of the foregoing, the royalty payable to Roche based on net sales of Rezdiffra will not be reduced until the expiration of certain patent term extensions that have been, or could have been, filed.

CSPC License (MGL-2086)

In July 2025, we entered into the CSPC License Agreement with CSPC for MGL-2086 (formerly known as SYH2086), an oral small molecule GLP-1 receptor agonist. Pursuant to the CSPC License Agreement, CSPC has granted us an exclusive global license to develop, manufacture, and commercialize MGL-2086. The transaction closed in September 2025. We paid CSPC an upfront payment of $120.0 million in October 2025. CSPC is eligible to receive up to $2.0 billion in development, regulatory and commercial milestone payments, as well as royalties on net sales ranging from mid-single digits to low-double digits.

Pfizer License (ervogastat)

In December 2025, we entered into an exclusive global license agreement with Pfizer (the "Pfizer License Agreement") to develop, manufacture and commercialize ervogastat, a Phase 2 oral DGAT-2 inhibitor, and two additional early-stage MASH assets. We paid Pfizer an upfront payment of $50.0 million in December 2025. In addition, Pfizer is eligible to receive up to $70.0 million in development and regulatory milestone payments related to ervogastat and low-

double digit royalties on net sales of ervogastat. Pfizer is eligible to receive additional development, regulatory and commercial milestone payments and royalty payments on net sales of the two licensed early stage assets.

Ribocure License (siRNA programs)

In February 2026, we entered into the Ribocure License Agreement granting us exclusive global rights to develop, manufacture and commercialize six siRNA programs. Pursuant to the Ribocure License Agreement, we will pay Ribocure an upfront payment of $60.0 million. In addition, Ribocure is eligible to receive up to $4.4 billion in development, regulatory and commercial milestone payments across all programs, as well as royalties on net sales ranging from mid-single digits to low-double digits.

Competition

The development and commercialization of drugs in MASH is highly competitive. We will face competition with respect to Rezdiffra and all product candidates we may develop or commercialize in the future from pharmaceutical and biotechnology companies worldwide. The key factors affecting the success of an approved product will generally be such product's efficacy, safety profile, drug interactions, method of administration, pricing, reimbursement and level of promotional activity relative to those of competing drugs.

Our potential competitors include companies with substantially greater financial, technical and personnel resources than us. In addition, our competitors may have significantly greater research, development, manufacturing and commercial infrastructures. Our ability to compete successfully will depend largely on our ability to leverage our collective experience in drug development and commercialization to:

- develop medicines that are differentiated from other products in the market;
- obtain patent or proprietary protection for our products and technologies;
- obtain required regulatory approvals;
- commercialize our drugs, if approved; and
- attract and retain high-quality research, development and commercial personnel.

Rezdiffra was the first medication approved by both the FDA and EC for the treatment of MASH with moderate to advanced fibrosis. Since then, semaglutide, a GLP-1 agonist developed and commercialized by Novo Nordisk A/S ("Novo"), was approved for the treatment of MASH by the FDA and is pending approval in the EU. In addition, there are more than 140 drugs in development for MASH by companies ranging in size from small biotechnology companies to large pharmaceutical organizations. Investigational candidates include, among others, THR-β agonists, peroxisome proliferator-activated receptor agonists (PPAR), GLP-1 agonists, dual GLP-1/glucose-dependent insulinotropic polypeptide (GIP) agonists, fatty acid synthase (FASN) inhibitors, fibroblast growth factor 21 (FGF-21) stimulators, farnesoid X receptor (FXR) agonists and dual GLP-1/glucagon receptor agonists. Other companies are conducting Phase 3 trials, including Novo, Inventiva S.A., Roche, Eli Lilly and Boehringer Ingelheim International GmbH. In addition, there are 51 investigational therapies being evaluated in Phase 2 clinical trials in MASH.

We believe that Rezdiffra's product profile and first-to-market advantage provide meaningful points of differentiation in the MASH competitive landscape. In addition, we believe positive results from the Phase 3 MAESTRO-NASH OUTCOMES trial could position Rezdiffra as the first medication to receive approval in both MASH with moderate to advanced fibrosis (consistent with stages F2 to F3 fibrosis) and MASH with compensated cirrhosis (consistent with stage F4c fibrosis). See the section titled "Risk Factors—Risks Related to the Commercialization and Continued Approval of Rezdiffra—We operate in a highly competitive and changing environment, and if we are unable to adapt to our environment, we may be unable to compete successfully." in this Annual Report for additional discussion of the competitive risks we face.

Manufacturing, Supply and Distribution

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We currently rely, and expect to continue to rely, on third-party contract manufacturers ("CMOs") for all required starting materials, active pharmaceutical ingredients ("API") and finished product for the manufacture of any product candidates that we may develop for larger-scale preclinical and clinical testing, as well as for commercial quantities of Rezdiffra and any future drug candidates that may be approved.

In December 2024, we entered into a Resmetirom Commercial Supply Agreement (the "Evonik Agreement") with Evonik Corporation ("Evonik"). Pursuant to the Evonik Agreement, Evonik has agreed to manufacture and supply resmetirom, the API in Rezdiffra, in commercial quantities. We have agreed to provide Evonik with a forecast of our

purchases on a rolling basis. Under the Evonik Agreement, our purchase price for supply of resmetirom is based on the volume of material subject to a purchase order. The initial term of the Evonik Agreement will expire on December 31, 2029 and will be automatically renewed for successive two-year periods, unless terminated in accordance with the terms of the Evonik Agreement. In addition, in August 2023, we entered into a Commercial Supply Agreement (the "UPM Agreement") with UPM Pharmaceuticals, Inc. ("UPM") for the primary commercial supply of Rezdiffra tablets in the United States. Pursuant to the UPM Agreement, we must purchase a specified percentage of our annual requirements for Rezdiffra from UPM at volume-driven prices. The initial term of the UPM Agreement will expire in April 2032 and will be automatically renewed for two-year periods unless terminated in accordance with the terms of the UPM Agreement. We have also entered into a supply agreement (the "Corden Supply Agreement") with Corden Pharma GmbH ("Corden"), a German-based manufacturer, for the primary commercial supply of Rezdiffra tablets in Europe and to serve as a secondary commercial supplier for the U.S. market. Pursuant to the Corden Supply Agreement, we must submit to Corden binding forecasts for our expected delivery of Rezdiffra. The initial term of the Corden Supply Agreement will expire in 2029 and is expected to renew for successive two-year terms. All of our CMO partners have extensive technical expertise, GMP experience and experience manufacturing our specific technology. We believe our supply arrangements are satisfactory for our current operations.

Rezdiffra is distributed in the United States through a network of specialty pharmacy providers that deliver Rezdiffra to patients. We may expand our distribution network in the future.

Intellectual Property

Our success will depend in part on our ability to obtain and maintain patent and other proprietary protection for Rezdiffra and any current or future product candidates, technology and know-how, our ability to freely operate without infringing on the proprietary rights of others and our ability to establish proprietary rights and prevent others from infringing our proprietary rights. We seek to protect our proprietary position by, among other methods, filing United States and foreign patent applications related to our proprietary technology, and maintaining the confidentiality of inventions and improvements that are material to the development of our business. We also rely on trade secrets, know-how, continuing technological innovation and licensing opportunities to develop and maintain our competitive position.

We will be able to protect our technology and products from unauthorized use by third parties only to the extent we are covered by valid and enforceable patents or such knowledge is effectively maintained as trade secrets. Patents and other proprietary rights are thus an essential element of our business. We monitor for activities that may infringe our proprietary rights, as well as the progression of third-party patent applications that may have the potential to interfere with the development of our business.

As of December 31, 2025, we owned or co-owned nine United States issued patents and 107 foreign issued patents, 24 United States pending patent applications and 97 foreign pending patent applications and three international patent application filed under the Patent Cooperation Treaty. Issued patents directed to resmetirom have statutory expiration dates between 2026 and 2045, excluding any patent term extensions or equivalents thereof that might be available following the grant of marketing authorizations. Each of these patents and patent applications is directed to resmetirom, including composition-of-matter, certain polymorph forms, Rezdiffra's commercial weight-threshold dosing regimen as prescribed in the FDA-approved label, methods of making resmetirom, the use of resmetirom in the treatment of key disease indications or other THR-β analogs and uses thereof. Our current patent portfolio covers the United States and certain other jurisdictions worldwide. The international patent application can be used as the basis for multiple additional patent applications worldwide. In addition, pursuant to the Roche Agreement, Roche granted us an exclusive license to certain United States and foreign patents and patent applications owned by Roche and Roche know-how relating to resmetirom. The Roche Agreement imposes various diligence, milestone payment, royalty payment, insurance, indemnification, and other obligations on us. In addition, pursuant to the Roche Agreement, we have the exclusive right to control all patent term adjustments and patent term extensions applicable to Rezdiffra patents, including patents owned by Roche and jointly owned between the parties.

Of the patents and applications related to Rezdiffra, there are six U.S.-issued patents listed in the FDA Orange Book. These patents and their expiration dates, excluding any patent term extensions, are as follows:

- U.S. Patent No. 7,452,882 (expires September 12, 2026)
- U.S. Patent No. 9,266,861 (expires September 17, 2033)
- U.S. Patent No. 10,376,517 (expires September 17, 2033)
- U.S. Patent No. 11,564,926 (expires September 17, 2033)
- U.S. Patent No. 11,986,481 (expires September 17, 2033)
- U.S. Patent No. 12,377,104 (expires February 4, 2045)

In addition, we have licensed several patents and patent applications related to our pipeline candidates, and have filed several patent applications directed toward our product candidates in combination with resmetirom.

Our trademarks are protected under the common law or by registration in the United States and other countries. We seek to protect our proprietary processes, in part, by confidentiality agreements and invention assignment agreements with our personnel, including consultants and commercial partners. These agreements are designed to protect our proprietary information.

See the section titled "Risk Factors—Risks Related to our Intellectual Property" in this Annual Report for a discussion of the risks associated with our intellectual property.

Government Regulation

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, monitoring and reporting, promotion, advertising, distribution, marketing and export and import of drug products such as those we are developing. A new drug must be approved by the FDA through the new drug application ("NDA") process before it may be legally marketed in the United States and must be approved by foreign regulatory authorities via various analogous procedures before it can be marketed in the applicable country. The animal and other non-clinical data and the results of human clinical trials performed under an IND and under similar foreign applications will become part of the NDA. Even after obtaining initial marketing approval, a product and its manufacturer remain subject to extensive, continuing regulatory requirements, including with respect to manufacturing, quality control, adverse event reporting, advertising and promotion and periodic inspections by regulatory authorities.

United States Drug Development Process

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA") and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state and local statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other things, the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, FDA Form 483, untitled letters, warning letters and other types of enforcement-related letters, requesting product recalls, product seizures, changes to the conditions surrounding marketing approval such as labeling changes or changes to a Risk Evaluation and Mitigations Strategies ("REMS") program, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, debarment, restitution, disgorgement of profits or civil or criminal investigations and penalties. Any agency or judicial enforcement action could have a material adverse effect on us. The FDA may also prevent the import or export of products manufactured in non-compliant facilities or under non-compliant conditions. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies, some in accordance with the FDA's current Good Laboratory Practices ("GLP"), the Animal Welfare Act administered and enforced by the United States Department of Agriculture and other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an institutional review board ("IRB") before each clinical trial may be initiated at each clinical site;
- performance of adequate and well-controlled human clinical trials under protocols submitted to the FDA and reviewed and approved by each IRB, conducted in accordance with federal regulations and according to GCP to establish the safety and efficacy of the proposed drug for its intended use;
- preparation and submission to the FDA of an NDA (and the FDA's acceptance for filing of the NDA);
- completion of registration batches and validation of the manufacturing process to show ability to consistently produce quality batches of product;

- satisfactory completion of an FDA Advisory Committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current good manufacturing practice ("cGMP") to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCP and the integrity of the clinical data;
- payment of user fees and procurement of FDA approval of the NDA;
- FDA review and approval of the NDA; and
- compliance with any post-approval requirements, including, as applicable, REMS and post-approval trials required by the FDA.

Once a pharmaceutical candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies, to assess the initial safety and quality profile of the product. Animal studies must be performed in compliance with federal regulations and requirements, including, as applicable, GLP and the Animal Welfare Act. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. The sponsor will also include a protocol detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated, if the trial lends itself to an efficacy evaluation. Some preclinical testing may continue even after the IND is submitted. A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If during this 30-day period the FDA does not raise any concerns or issues that must be addressed prior to the commencement of clinical trials or does not impose a clinical hold, the IND becomes effective 30 days following the FDA's receipt of the IND and the clinical trial proposed in the IND may begin. Clinical holds also may be imposed by the FDA at any time before or during clinical trials due to safety concerns, non-compliance or other reasons.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCP. They must be conducted under protocols detailing the objectives of the trial, dosing procedures, subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and progress reports detailing the results of the clinical trials must be submitted at least annually. In addition, timely safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse reactions, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol, or animal test results that suggest a significant risk to human subjects. An IRB at each institution participating in the clinical trial must review and approve each protocol before a clinical trial commences at that institution and must also approve the consent form that must be provided to each trial subject or his or her legal representative, monitor the trial until completed and otherwise comply with IRB regulations. Foreign trials conducted under an IND must meet the same requirements that apply to trials being conducted in the United States. The FDA may inspect foreign clinical sites to ensure data integrity and compliance with GCP. Data from a foreign trial not conducted under an IND may be submitted in support of an NDA if the trial was conducted in accordance with GCP and the FDA is able to validate the data.

Human clinical trials are typically conducted in three sequential phases:

- *Phase 1:* The product candidate is initially introduced into humans. Phase 1 clinical trials are typically conducted in healthy human subjects, but in some situations are conducted in patients with the target disease or condition. Phase 1 clinical trials are generally designed to evaluate the safety, dosage tolerance, absorption, metabolism, distribution and excretion of the product candidate in humans, and, if possible, to gain early evidence of effectiveness.
- *Phase 2:* This phase involves trials in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product candidate for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- *Phase 3:* This phase involves trials undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical trial sites. These trials are intended to establish the overall risk-benefit ratio of the product candidate and provide, if appropriate, an adequate basis for product approval and product labeling. Generally, the FDA requires two adequate

and well controlled Phase 3 clinical trials to demonstrate the efficacy of the product candidate, although a single Phase 3 clinical trial with other confirmatory evidence may be sufficient in certain instances.

The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. In some cases, clinical trials are also monitored by an independent group of qualified experts organized by the trial sponsor. These groups are often referred to as data monitoring committees. This group typically provides recommendations to the trial sponsor for whether or not a trial may move forward at designated check points. These decisions are based on the data monitoring committee's independent review of data from the ongoing trial. Phase 1, Phase 2 and Phase 3 testing may not be completed successfully within any specified period, if at all. Further, success in either preclinical studies or early-stage clinical trials does not assure success in later-stage clinical trials. In general, sponsors of most interventional clinical trials that are not Phase 1, are required to submit certain clinical trial information for inclusion in the public clinical trial registry and results data bank maintained by the National Institutes of Health, which are publicly available at http://clinicaltrials.gov. Sponsors are generally also obligated to disclose the results of these clinical trials after completion. Competitors and others may use this publicly-available information to gain knowledge regarding the design and progress of our development programs.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if SAEs occur. Written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies or animal or in vitro testing that suggest a significant risk for human subjects and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and FDA to reach agreement on the next phase of development. Sponsors typically use the end of Phase 2 meeting to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trial that they believe will support approval of the new drug.

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

United States Review and Approval Processes

The results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling, and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product for a specific indication. The submission of an NDA is subject to the payment of user fees under the Prescription Drug User Fee Act, as amended ("PDUFA") ; a waiver of such fees may be obtained under certain limited circumstances. The sponsor under an approved NDA is also subject to annual program user fees. Program fees are assessed for each approved prescription drug product identified in an approved application, with up to five program fees per application. These fees are typically modified annually. The FDA conducts a preliminary review of a submitted NDA within 60 days from receipt to ensure that the application is sufficiently complete for substantive review before it accepts the application for filing. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA's PDUFA performance goals generally provide for action on an NDA within 10 months of the 60-day filing date. That deadline can be extended under certain circumstances, including by the FDA's requests for additional information. The targeted action date can also be shortened to within 6 months of the 60-day filing date for products that are granted priority review designation because they are intended to treat serious or life-threatening conditions and demonstrate the potential to address unmet medical needs. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended

use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured. In addition, the FDA often will conduct a bioresearch monitoring inspection of the clinical trial sites involved in conducting pivotal trials to ensure data integrity and compliance with applicable GCP requirements. The FDA may refer the NDA to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. The approval process is lengthy and often difficult, and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data and information. Even if such data and information are submitted, the FDA may ultimately decide that the NDA does not satisfy the regulatory criteria for approval. Data obtained from clinical trials are not always conclusive, and the FDA may interpret data differently than we interpret the same data.

At the end of the review period, the FDA may issue an approval letter following satisfactory completion of all aspects of the review process, or the FDA may issue a complete response letter ("CRL"), which generally outlines the deficiencies in the submission and may require additional clinical or other data or impose other conditions that must be met in order to secure final approval of the NDA. If and when deficiencies outlined in a CRL have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA may issue an approval letter. The FDA's PDUFA review goal is to review such resubmissions within two or six months of receipt, depending on the type of information included. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval and deny approval of a resubmitted NDA.

NDAs receive either standard or priority review. An application for a drug that treats a serious condition and, if approved, would provide a significant improvement in the safety or effectiveness of the treatment, prevention or diagnosis of disease may qualify for priority review. Priority review for an NDA for a new molecular entity means the FDA will review the NDA within six months from the date that the NDA is accepted for filing by FDA. The FDA has ten months in which to complete its initial review of a standard new molecular entity NDA. The FDA does not always meet its goal dates and in certain circumstances, the goal date may be extended. Priority review does not change the standard for approval, but may expedite the approval process.

Product candidates may qualify for review and approval under the 21 CFR Part 314, Subpart H accelerated approval pathway if the candidates are intended to treat a serious or life-threatening condition, provide meaningful therapeutic benefit over existing treatments, and demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on an intermediate clinical endpoint. In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that is thought to predict clinical benefit, such as how a patient feels, functions, or survives, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. As a condition of accelerated approval, the FDA requires that a sponsor of a drug receiving accelerated approval perform confirmatory adequate and well-controlled post-marketing clinical trials. Approval of a product may be withdrawn if these trials fail to verify clinical benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with the product. Accelerated approval does not change the standards for approval. All promotional materials for drug candidates approved under the accelerated approval pathway are subject to prior review by the FDA. If a sponsor fails to conduct any required post-approval trial with "due diligence," the FDA may withdraw approval of the product.

Further, on December 29, 2022, Congress enacted the Consolidated Appropriations Act of 2023, which included the Food and Drug Omnibus Reform Act ("FDORA"). Under FDORA, the FDA must specify the conditions for any post-approval trials by the date of the accelerated approval and the agency has flexibility in setting forth such conditions, which may include enrollment targets, clinical trial protocol and milestones – including the target date of trial completion. The FDA may also require, as appropriate, that certain post-approval trials be underway prior to accelerated approval or within a specified time from the date of approval. Accelerated approval sponsors must submit progress reports every six months on required post-approval trials.

An approval letter authorizes commercial marketing of the product candidate with specific prescribing information for specific indications. If a product receives regulatory approval, the approval may be further limited to specific diseases, dosages or patient populations, or the indications for use may otherwise be limited, which could restrict the commercial value of the product. In addition, the FDA may require a sponsor to conduct additional (i.e., Phase 4) testing which involves clinical trials designed to further assess a drug's safety and effectiveness after NDA approval, and may require testing and surveillance programs to monitor the safety of approved products which have been commercialized.

The Food and Drug Administration Safety and Innovation Act ("FDASIA") which was enacted in 2012, made permanent the Pediatric Research Equity Act ("PREA"), which requires a sponsor to conduct pediatric studies for most drug applications and supplements to applications, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, such original NDAs and supplements thereto must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must assess the safety

and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product has been assessed to be safe and effective. The sponsor or FDA may request a deferral of pediatric studies for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric studies are complete or that additional safety or effectiveness data needs to be collected before the pediatric studies begin. The FDA may send a non-compliance letter to any sponsor that fails to submit the required assessment, maintain a current deferral or submit a request for approval of a pediatric formulation.

Patent Term Restoration and Regulatory Exclusivities

Depending upon the timing, duration and specifics of FDA approval of our product candidates, some of our United States patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND, and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application, except that the period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension, and the extension must be applied for prior to expiration of the patent and within 60 days of approval. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

The Hatch-Waxman Act also provides periods of regulatory exclusivity for products that would serve as a reference listed drug ("RLD") for an abbreviated new drug application ("ANDA") or application submitted under section 505(b)(2) of the FDCA, or 505(b)(2) application. If a product is a new chemical entity ("NCE")—generally meaning that the active moiety has never before been approved in any drug—there is a period of five years from the product's approval during which the FDA may not accept for filing any ANDA or 505(b)(2) application for a drug with the same active moiety. An ANDA or 505(b)(2) application may be submitted after four years, however, if the sponsor of the application makes a "Paragraph IV" certification.

A product that is not an NCE may qualify for a three-year period of exclusivity if the NDA or supplement to an approved NDA contains new clinical data (other than bioavailability studies), derived from trials conducted by or for the sponsor, that were necessary for approval. In that instance, the exclusivity period does not preclude filing or review of an ANDA or 505(b)(2) application; rather, the FDA is precluded from granting final approval to the ANDA or 505(b)(2) application until three years after approval of the RLD. Additionally, the exclusivity applies only to the conditions of approval that required submission of the clinical data.

Once the FDA accepts for filing an ANDA or 505(b)(2) application containing a Paragraph IV certification, the applicant must within 20 days provide notice to the RLD NDA holder and patent owner that the application has been submitted and provide the factual and legal basis for the applicant's assertion that the patent is invalid or not infringed. If the NDA holder or patent owner files suit against the ANDA or 505(b)(2) applicant for patent infringement within 45 days of receiving the Paragraph IV notice, the FDA is prohibited from approving the ANDA or 505(b)(2) application for a period of 30 months or the resolution of the underlying suit, whichever is earlier. If the RLD has NCE exclusivity and the notice is given and suit filed during the fifth year of exclusivity, the regulatory stay extends until seven and a half years after the RLD approval. The FDA may approve the proposed product before the expiration of the regulatory stay if a court finds the patent invalid or not infringed or if the court shortens the period because the parties have failed to cooperate in expediting the litigation.

Pediatric exclusivity is another type of marketing exclusivity available in the United States. The FDASIA made permanent the Best Pharmaceuticals for Children Act ("BPCA"), which provides for an additional six months of marketing exclusivity if a sponsor conducts clinical trials in children in response to a written request from the FDA ("Written Request"). If the Written Request does not include trials in neonates, the FDA is required to include its rationale for not requesting those trials. The FDA may request trials on approved or unapproved indications in separate Written Requests. The issuance of a Written Request does not require the sponsor to undertake the described trials.

Expedited Programs

The FDA maintains several programs to facilitate and expedite the development and review of drug applications that are intended for the treatment of a serious or life-threatening disease or condition that meet certain other criteria, including Fast Track Designation, Breakthrough Designation, Priority Review (discussed above in United States Review and Approval Processes), and the Accelerated Approval pathway (discussed above in United States Review and Approval Processes). Under the Fast Track Designation program, the sponsor of a new drug candidate may request that the FDA

designate the drug candidate for a specific indication as a fast track drug concurrent with, or after, the filing of the IND for the drug candidate. The FDA must determine if the drug candidate qualifies for fast track designation within 60 days of receipt of the sponsor's request. Under the Fast Track Designation program, the FDA may grant fast track designation for a product candidate if it is intended to treat a serious or life-threatening condition and nonclinical or clinical data demonstrate the potential to address an unmet medical need. Features of Fast Track Designation include more frequent interactions with the review team, and the possibility of rolling review.

Under the Breakthrough Designation Program, FDA may grant a drug Breakthrough Therapy Designation if it is intended to treat a serious condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on a clinically significant endpoint over available therapies. Features of Breakthrough Therapy Designation include intensive guidance on an efficient drug development program, an organizational commitment by the agency involving senior managers in a proactive, cross-disciplinary review of the drug application, and the possibility of rolling review.

Post-Approval Requirements

Once an approval is granted, products are subject to continuing regulation by the FDA. The FDA may withdraw the approval if, among other things, compliance with regulatory standards is not maintained or if safety or efficacy problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on product marketing or even withdrawal of approval for the product application. If new safety issues are identified following approval, the FDA may require the NDA sponsor to take certain measures, such as revising the approved labeling to reflect the new safety information, conducting post-market studies or clinical trials to assess the new safety information, and/or implementing or changing a REMS program to mitigate newly-identified risks. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further FDA review and approval. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws and regulations. Manufacturers and other parties involved in the drug supply chain for prescription drug products must also comply with product tracking and tracing requirements and notify the FDA of counterfeit, diverted, stolen and intentionally adulterated products or products that are otherwise unfit for distribution in the United States. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our product candidates. Future inspections by the FDA and other regulatory agencies may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct.

Any drug products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the drug, providing the FDA with updated safety and efficacy information, drug sampling and distribution requirements, complying with certain electronic records and signature requirements, and complying with FDA promotion and advertising requirements. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label.

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

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of foreign countries or economic areas, such as the EU, before we may commence clinical trials or market products in those countries or areas. The approval process and

requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Under the EU regulatory systems, a company may submit a marketing authorization application ("MAA") either under the centralized procedure or one of the national procedures, depending on the type of product. The centralized procedure provides for the grant of a single marketing authorization by the EC that is valid throughout the EU and in the additional countries of the European Economic Area (Iceland, Liechtenstein and Norway) ("EEA"). The centralized procedure is compulsory for medicinal products produced by certain biotechnological processes; advanced therapy medicinal products (gene therapy, somatic cell therapy and tissue engineered products); medicinal products containing new active substances for specific indications such as the treatment of HIV/AIDS, cancer, neurodegenerative disorders, diabetes, viral diseases and other immune dysfunctions; and designated orphan medicines. For medicines that do not fall within one of the mandatory categories, an applicant still has the option of submitting an application for a centralized marketing authorization as long as the medicine concerned contains a new active substance not yet authorized in the EU, is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health in the EU. Under the centralized procedure, an MAA is submitted to the EMA where it will be evaluated by the CHMP. The CHMP is responsible for conducting an initial assessment of whether a product meets the required quality, safety and efficacy requirements, and whether a product has a positive benefit/risk ratio. Under the centralized procedure, the maximum timeframe for the evaluation of an MAA by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Clock stops may extend the timeframe of evaluation of an MAA considerably beyond 210 days. Where the CHMP gives a positive opinion, it provides the opinion together with supporting documentation to the EC, who makes the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's recommendation. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of an MAA under the accelerated assessment procedure is 150 days, excluding clock stops, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that the application is no longer appropriate to conduct an accelerated assessment. The initial marketing authorization is valid for five years, but once renewed is usually valid for an unlimited period, unless the EC decides, on justified grounds relating to pharmacovigilance (e.g. exposure of an insufficient number of patients to the medicinal product concerned), to mandate one additional five-year renewal.

In specific circumstances, applicants may obtain a CMA prior to having the full clinical data normally required for a standard marketing authorization where (i) the benefit-risk balance of the product is positive, (ii) it is likely that the applicant will be able to provide comprehensive clinical data, (iii) the product addresses an unmet medical need and (iv) the benefit to public health of the immediate availability of the medicinal product on the market outweighs the risk inherent in the fact that additional data are still required. A CMA may contain specific obligations to be fulfilled by the marketing authorization holder following grant of the marketing authorization, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. CMAs are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions and/or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a CMA.

There are also two other possible routes to authorize products for therapeutic indications in several countries in the EU, which are available for products that fall outside the scope of the centralized procedure:

- Decentralized procedure—Using the decentralized procedure, an applicant may apply for simultaneous authorizations in more than one EU Member State for a medicinal product that has not yet been authorized in any EU Member State and that does not fall within the mandatory scope of the centralized procedure.
- Mutual recognition procedure—In the mutual recognition procedure, a medicine is first authorized in one EU Member State, in accordance with the national procedures of that country. Following this, additional marketing authorizations can be sought from other EU Member States in a procedure whereby the countries concerned recognize the validity of the original, national marketing authorization.

In both cases, as with the centralized procedure, the competent authorities of the EU Member States assess the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy before granting the marketing authorization.

When conducting clinical trials in the EU, we must adhere to the provisions of the EU Clinical Trials Regulation (EU) No 536/2014 ("EU CTR"). The EU CTR requires, among other things, that the prior authorization of an ethics committee and the submission and approval of a clinical trial authorization application be obtained in each applicable EU Member State before commencing a clinical trial in that EU Member State. The EU CTR replaced the previous EU Clinical Trials Directive and aims to simplify and streamline the approval of clinical trials in the EU. For example, the EU CTR

implements a coordinated procedure for authorization of clinical trials (through a centralized EU portal known as the Clinical Trials Information System) that is similar to the mutual recognition procedure for marketing authorization of medicinal products, and includes obligations on sponsors to publish clinical trial results.

As in the United States, it may be possible in foreign countries to obtain a period of market and/or data exclusivity that would have the effect of postponing the entry into the marketplace of a competitor's generic or biosimilar product. For example, in the EU, if any of our products receive marketing approval in the EU, we expect that we will benefit from eight years of data exclusivity and an additional two years of marketing exclusivity. An additional one-year extension of marketing exclusivity is possible if during the data exclusivity period we obtain an authorization for one or more new therapeutic indications that is deemed to bring a significant clinical benefit compared to existing therapies for the indication. The data exclusivity period begins on the date of the product's first marketing authorization in the EU and prevents biosimilars or generics from referencing the pharmacological, toxicological and clinical data contained in the dossier of the reference product when applying for a generic marketing authorization for a period of eight years. After eight years, a biosimilar or generic MAA may be submitted and the sponsoring companies may rely on the data for the reference product. However, even with a market authorization a biosimilar or generic medicine cannot launch in the EU until two years after the data exclusivity expires (or a total of ten years after the first marketing authorization in the EU of the innovator product), or three years later (or a total of eleven years after the first marketing authorization in the EU of the innovator product) if the marketing authorization holder obtains marketing authorization for a new indication with significant clinical benefit within the eight year data exclusivity period.

If a marketing authorization for a medicinal product in the EU is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the EU's stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization trials and additional monitoring obligations.
- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive (EU) 2017/1572, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with EU GMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU.
- The marketing and promotion of authorized products, including industry-sponsored continuing medical education and advertising directed toward the prescribers of products and/or the general public, are strictly regulated in the EU. Direct-to-consumer advertising of prescription medicines is prohibited across the EU.

Much like the Anti-Kickback Statue prohibition in the United States, the provision of benefits or advantages to physicians or other health care professionals to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to induce or reward improper performance generally is usually governed by the national anti-bribery laws of EU Member States, and the Bribery Act 2010 in the United Kingdom ("UK"). Infringement of these laws could result in substantial fines and imprisonment. EU Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision has been transposed into the Human Medicines Regulations 2012 and so remains applicable in the UK despite its departure from the EU.

Payments made to physicians or other healthcare professionals in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

The aforementioned EU rules are generally applicable in the EEA.

The EC introduced legislative proposals in April 2023 that, if implemented, will replace the current regulatory framework in the EU for all medicines (including those for rare diseases and for children). In April 2024, the European Parliament adopted its position on the legislative proposals and, in June 2025, the Council of the European Union adopted

its position. A common position on the text has been agreed upon on December 11, 2025, in the context of subsequent inter-institutional trilogue negotiations. The proposed revisions remain to be adopted, and are not expected to become applicable before 2028.

The UK formally left the EU on January 31, 2020. As a result of the Northern Ireland protocol, following the UK leaving the EU, the EMA remained responsible for approving novel medicines for supply in Northern Ireland under the EU centralized procedure, and a separate authorization was required to supply the same medicine in Great Britain (England, Wales and Scotland). On February 27, 2023, the UK government and the EC announced a political agreement in principle to replace the Northern Ireland Protocol with a new set of arrangements, known as the "Windsor Framework." The Windsor Framework was approved by the EU-UK Joint Committee on March 24, 2023, and the medicines aspects of the Windsor Framework have applied since January 1, 2025. This new framework fundamentally changes the previous system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the UK. In particular, the Medicines and Healthcare products Regulatory Agency (the "MHRA") is now responsible for approving all medicinal products destined for the UK market (i.e., Great Britain and Northern Ireland), and the EMA no longer has any role in approving medicinal products destined for Northern Ireland under the EU centralized procedure. A single UK-wide marketing authorization is granted by the MHRA for all novel medicinal products to be sold in the UK, enabling products to be sold in a single pack and under a single authorization throughout the UK. In addition, the new arrangements require all medicines placed on the UK market to be labelled "UK only," indicating they are not for sale in the EU.

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, an accelerated assessment procedure and new routes of evaluation for novel products and biotechnological products. On January 1, 2024, the MHRA put in place a new international recognition framework which means that the MHRA may have regard to decisions on the approval of marketing authorizations made by the EMA and certain other regulators when determining an application for a new UK marketing authorization.

Coverage and Reimbursement

Significant uncertainty exists regarding the coverage and reimbursement status of products approved by the FDA and other government authorities. In the United States, sales of any products for which we may receive regulatory approval for commercial sale will depend in significant part on the availability and adequacy of coverage and reimbursement from third-party payors. Third-party payors include federal and state government authorities, managed care providers, private health insurers and other organizations. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. One third-party payor's decision to cover a product does not ensure that other payors will also provide coverage for the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list which might not include all of the FDA-approved products for a particular indication. Moreover, a payor's decision to provide coverage for a 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.

Factors payors consider in determining reimbursement are based on whether the product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Third-party payors are increasingly challenging the prices charged for, examining the medical necessity of, and assessing the cost-effectiveness of medical products and services, in addition to their safety and efficacy. Our drug candidates may not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. A decision by a third-party payor not to cover a product could reduce physician ordering and patient demand for the product.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for a product for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In addition, sales of our products in other countries are also dependent, in large part, on complex coverage and reimbursement mechanisms and programs in those countries. In some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU provides options for its Member States to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. An EU Member State may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the EU do not follow price structures of the United States and generally tend to be significantly lower.

U.S. Healthcare Reform

The U.S. government and state legislatures have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. For example, the Patient Protection and Affordable Care Act, as amended the ACA, contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales for branded prescription drugs to federal health care programs. Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. For example, the Budget Control Act of 2011 and subsequence legislation, among other things, created measures for spending reductions by Congress that include aggregate reductions of Medicare payments to providers of 2% per fiscal year, which remain in effect through 2031. The U.S. American Taxpayer Relief Act of 2012 further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. On March 11, 2021, former President Biden signed the American Rescue Plan Act of 2021 into law, which eliminated the statutory Medicaid drug rebate cap, set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. These laws and regulations may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Further, on May 30, 2018, the Right to Try Act was signed into law. The Right to Try Act, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

The Inflation Reduction Act of 2022 ("IRA") includes several provisions that may impact our business, depending on how various aspects of the IRA are implemented. Provisions that may impact our business include a $2,000 out-of-pocket cap for Medicare Part D beneficiaries, the imposition of new manufacturer financial liability on most drugs in Medicare Part D, permitting the U.S. government to negotiate Medicare Part B and Part D pricing for certain high-cost drugs and biologics without generic or biosimilar competition, requiring companies to pay rebates to Medicare for drug prices that increase faster than inflation, and delay until January 1, 2031 the implementation of the U.S. Department of Health and Human Services ("HHS") rebate rule that would have limited the fees that pharmacy benefit managers ("PBMs") can charge. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one orphan designation and for which the only approved indication is for that disease or condition. Under the One Big Beautiful Bill Act of 2025, this restriction was eliminated; and effective for the 2028 initial price applicability year, all orphan drugs, regardless of the number of orphan drug designations or indications, are exempt from the Medicare drug price negotiation program. The implementation of the IRA is currently subject to ongoing litigation challenging the constitutionality of the IRA's Medicare drug price negotiation program. The effect of the IRA on our business and the healthcare industry in general continues to evolve and we may discover adverse impacts on our company or our industry. The IRA is anticipated to have significant effects on the pharmaceutical industry and may reduce the prices we can charge and reimbursement we can receive for our product, among other effects.

On December 2, 2020, the HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through PBMs, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between PBMs and manufacturers. Implementation of this change and new safe

harbors for point-of-sale reductions in price for prescription pharmaceutical products and PBM service fees are currently under review by the current United States presidential administration and may be amended or repealed. Further, on December 31, 2020, the Centers for Medicare & Medicaid Services ("CMS") published a new rule, effective January 1, 2023, requiring manufacturers to ensure the full value of co-pay assistance is passed on to the patient or these dollars will count toward the Average Manufacturer Price and Best Price calculation of the drug ("Accumulator Rule"). On May 17, 2022, the U.S. District Court for the District of Columbia granted the Pharmaceutical Research and Manufacturers of America's (PhRMA) motion for summary judgment invalidating the Accumulator Rule. We cannot predict how the implementation of and any further changes to this rule will affect our business. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the current United States presidential administration may reverse or otherwise change these measures. Both the current United States presidential administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

On April 15, 2025, the Trump Administration published Executive Order 14273, "Lowering Drug Prices by Once Again Putting Americans First," which generally directs the federal government to take measures to reduce drug prices, including eliminating the so-called "pill penalty" under the IRA that creates a distinction between small molecule and large molecule products for purposes of determining when a drug may be eligible for drug price negotiation. On May 12, 2025, the Trump Administration published Executive Order 14297, "Delivering Most-Favored-Nation Prescription Drug Pricing to American Patients" which generally, among other things, directs the federal government to establish and communicate most-favored-nation price targets to pharmaceutical manufacturers to bring prices for American patients in line with comparably developed nations. Further, the Executive Order directs the federal government to support regulatory paths to allow direct-to-patient sales for companies that meet these targets. It also states that the Administration will take additional aggressive action (for example, examining whether marketing approvals should be modified or rescinded or opening the door for individual drug importation waivers) should manufacturers fail to offer American consumers the most-favored-nation lowest price. It also directs the Secretary of Commerce and the U.S. Trade Representative to "take all necessary and appropriate action to ensure foreign countries are not engaged in any act, policy, or practice that may be unreasonable or discriminatory or that may impair United States national security . . . including by suppressing the price of pharmaceutical products below fair market value in foreign countries." Notably, a similar "Most Favored Nation" pricing rule enacted under the first Trump Administration was subject to an injunction resulting from judicial challenges to the rule, which was formally rescinded by the former Biden Administration in August 2021.

On November 6, 2025, CMS announced a new drug payment model designed to make Most Favored Nation (MFN)-level prices available to state Medicaid programs via manufacturer rebates. Referred to as the "GENErating cost Reductions fOr U.S. Medicaid Model" ("GENEROUS"), the initiative is designed to run from 2026 through 2030 and is voluntary for both manufacturers and state Medicaid programs. Under the model, participating states will be able to access MFN-level prices for participating manufacturers' drugs through CMS-negotiated supplemental rebates tied to an MFN net price benchmark.

On December 19, 2025, CMS proposed a mandatory Center for Medicare and Medicaid Innovation ("CMMI") drug payment model to test whether alternative methods for calculating Medicare rebates, based on international pricing metrics rather than inflation-based metrics, reduce costs for Medicare fee-for-service ("FFS") beneficiaries and the Medicare program while preserving quality of care. The Guarding U.S. Medicare Against Rising Drug Costs ("GUARD") Model, would test an alternative approach to calculating rebates for certain Medicare Part D products using international pricing benchmarks. The GUARD Model would begin on January 1, 2027, and run through December 31, 2033. Public comments on the Proposed Payment Models are due by February 23, 2026.

Federal and state legislatures and health agencies may continue to focus on additional health care reform measures in the future that will impose additional constraints on prices and reimbursements for our marketed products. In addition, an emphasis on cost containment measures in the United States has increased and we expect will continue to increase the pressure on pharmaceutical pricing.

There have been several Congressional inquiries and proposed and enacted federal and state legislation and regulatory initiatives designed to, among other things, bring more transparency to product pricing, evaluate the relationship between pricing and manufacturer patient programs, and reform government healthcare program reimbursement methodologies for drug products. At the federal level, President Trump reversed some of former President Biden's executive orders, including rescinding Executive Order 14087 entitled "Lowering Prescription Drug Costs for Americans." President Trump may issue new executive orders designed to impact drug pricing. A number of these and other proposed measures may require authorization through additional legislation to become effective.

Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including by requiring pharmaceutical manufacturers to report to state agencies when they introduce new drugs to market with prices over a certain threshold, or when they increase the price of a drug over a certain threshold. If healthcare policies or reforms intended to curb healthcare costs are

adopted, the prices that we charge for any approved product may be limited, our commercial opportunity may be limited and/or our revenues from sales of our product and any future products, if approved, may be negatively impacted.

It is possible that the above-mentioned measures, as currently enacted or may be amended in the future, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, and new payment methodologies and additional downward pressure on coverage and payment and the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of additional cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our approved product or products. We cannot be sure whether additional legislative changes will be enacted in the United States or outside of the United States, or whether regulatory changes, guidance or interpretations will be changed, or what the impact of such changes on our product candidates, if any, may be.

Other Healthcare Laws

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our business operations and any current or future arrangements with third-party payors, healthcare providers and physicians may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we develop, market, sell and distribute any drugs for which we obtain marketing approval. In the United States, these laws include, without limitation, state and federal anti-kickback, false claims, physician transparency and patient data privacy and security laws and regulations, including but not limited to those described below.

- The federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing any remuneration (including any kickback, bride or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward or in return for, either the referral of an individual for, or the purchase order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid. A person or entity need not have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs;
- The federal civil and criminal false claims laws, including the civil False Claims Act (“FCA”), which prohibit individuals or entities from, among other things, knowingly presenting or causing to be presented, to the federal government, claims for payment or approval that are false, fictitious or fraudulent; knowingly making, using or causing to be made or used a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. In addition, the government may assert that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act. The FCA also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery;
- The federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer or remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary’s selection of a particular provider, practitioner or supplier of services reimbursable by Medicare or a state health care program, unless an exception applies. The government may also assert that a claim including items or services resulting from a violation of the federal Anti-Kickback statute constitutes a false or fraudulent claim under federal civil monetary penalties laws;
- The Health Insurance Portability and Accountability Act of 1996 (“HIPAA”) imposes criminal and civil liability for knowingly and willfully executing a scheme or attempting to execute a scheme, to defraud any healthcare benefit program, including private payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense or falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or

payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity need not have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH") and their respective implementing regulations, imposes, among other things, specified requirements on covered entities and their business associates relating to the privacy and security of individually identifiable health information including mandatory contractual terms and required implementation of technical safeguards of such information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates in some cases, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;
- The Physician Payments Sunshine Act, enacted as part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the "ACA") imposed new annual reporting requirements for certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, for certain payments and "transfers of value" provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other licensed health care practitioners and teaching hospitals, as well as ownership and investment interests held by such physicians and their immediate family members; and
- Analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party-payors, including private insurers, and may be broader in scope than their federal equivalents; state and foreign laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to drug pricing and payments and other transfers of value to physicians and other healthcare providers and restrict marketing practices or require disclosure of marketing expenditures and pricing information; state and local laws that require the registration of pharmaceutical sales representatives; state and foreign laws that govern the privacy and security of health information in some circumstances. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the PhRMA Code on Interactions with Healthcare Professionals. These data privacy and security laws may differ from each other in significant ways and often are not pre-empted by HIPAA, which may complicate compliance efforts.

In addition, pharmaceutical manufacturers may also be subject to federal and state consumer protection and unfair competition laws and regulations, which broadly regulate marketplace activities and that potentially harm consumers.

The distribution of drugs and biological products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

In the United States, to help patients afford our approved product, we may use programs to assist them, including patient assistance programs and co-pay coupon programs for eligible patients. Government enforcement agencies have shown increased interest in pharmaceutical companies' product and patient assistance programs, including reimbursement support services, and a number of investigations into these programs have resulted in significant civil and criminal settlements. In addition, at least one insurer has directed its network pharmacies to no longer accept co-pay coupons for certain specialty drugs the insurer identified. Our co-pay coupon programs could become the target of similar insurer actions. In addition, in November 2013, CMS issued guidance to the issuers of qualified health plans sold through the ACA's marketplaces encouraging such plans to reject patient cost-sharing support from third parties and indicating that CMS intends to monitor the provision of such support and may take regulatory action to limit it in the future. CMS subsequently issued a rule requiring individual market qualified health plans to accept third-party premium and cost-sharing payments from certain government-related entities. In September 2014, the Office of Inspector General (the "OIG") of the HHS issued a Special Advisory Bulletin warning manufacturers that they may be subject to sanctions under the federal anti-kickback statute and/or civil monetary penalty laws if they do not take appropriate steps to exclude Part D beneficiaries from using co-pay coupons. Accordingly, companies exclude these Part D beneficiaries from using co-pay coupons. It is possible that changes in insurer policies regarding co-pay coupons and/or the introduction and enactment of new legislation or regulatory action could restrict or otherwise negatively affect these patient support programs, which could result in fewer patients using affected products, and therefore could have a material adverse effect on our sales, business and financial condition.

Third party patient assistance programs that receive financial support from companies have become the subject of enhanced government and regulatory scrutiny. The OIG has established guidelines that suggest that it is lawful for pharmaceutical manufacturers to make donations to charitable organizations who provide co-pay assistance to Medicare patients, provided that such organizations, among other things, are bona fide charities, are entirely independent of and not controlled by the manufacturer, provide aid to applicants on a first-come basis according to consistent financial criteria and do not link aid to use of a donor's product. However, donations to patient assistance programs have received some negative publicity and have been the subject of multiple government enforcement actions, related to allegations regarding their use to promote branded pharmaceutical products over other less costly alternatives. Specifically, in recent years, there have been multiple settlements resulting out of government claims challenging the legality of their patient assistance programs under a variety of federal and state laws. It is possible that we may make grants to independent charitable foundations that help financially needy patients with their premium, co-pay and co-insurance obligations. If we choose to do so, and if we or our vendors or donation recipients are deemed to fail to comply with relevant laws, regulations or evolving government guidance in the operation of these programs, we could be subject to damages, fines, penalties or other criminal, civil or administrative sanctions or enforcement actions. We cannot ensure that our compliance controls, policies and procedures will be sufficient to protect against acts of our employees, business partners or vendors that may violate the laws or regulations of the jurisdictions in which we operate. Regardless of whether we have complied with the law, a government investigation could impact our business practices, harm our reputation, divert the attention of management, increase our expenses and reduce the availability of foundation support for our patients who need assistance.

The full scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform. Federal and state enforcement bodies have continued to increase their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other related governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, disgorgement, exclusion from government funded healthcare programs, such as Medicare and Medicaid, reputational harm, additional oversight and reporting obligations if we become subject to a corporate integrity agreement or similar settlement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to similar actions, penalties and sanctions. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from its business.

Pharmaceutical Price Reporting

A number of government pricing programs create certain price reporting obligations. Under the Medicaid Drug Rebate program, a participating manufacturer is required to pay a rebate to each state Medicaid program for its covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by the state Medicaid program as a condition of having federal funds being made available for drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data reported by the manufacturer on a monthly and quarterly basis to CMS. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug, which, in general, represents the lowest price available from the manufacturer to any wholesaler, retailer, provider, health maintenance organization, nonprofit entity, or governmental entity in the United States in any pricing structure, calculated to include all sales and associated rebates, discounts, and other price concessions.

The ACA (addressed further above in the section titled "—U.S. Healthcare Reform") made significant changes to the Medicaid Drug Rebate Program, and CMS issued a final regulation to implement the changes to the Medicaid Drug Rebate Program under the ACA. CMS also issued a final regulation that modified prior Medicaid Drug Rebate Program regulations to permit reporting multiple best price figures with regard to value based purchasing arrangements; and provide definitions for "line extension," "new formulation," and related terms, with the practical effect of expanding the scope of drugs considered to be line extensions that are subject to an alternative rebate formula.

Federal law requires that a manufacturer also participate in the 340B Drug Pricing program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B program requires participating manufacturers to agree to charge no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs to a specified "covered entities," including community health centers and other entities that receive certain federal grants, as well as hospitals that serve a disproportionate share of low-income patients. The 340B ceiling price is calculated using a statutory formula, which is based on the average manufacturer price and rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate Program.

Further, the IRA establishes a Medicare Part D inflation rebate schemes (the first rebate period is in fourth quarter 2022 through third quarter 2023) and a drug price negotiation program, with the first negotiated prices to take effect in 2026. It also makes several changes to the Medicare Part D benefit, including the creation of a new manufacturer discount program in place of the current coverage gap discount program (beginning in 2025).

In order to be eligible to have its products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by the Department of Veterans Affairs ("VA"), Department of Defense ("DoD"), Public Health Service, and Coast Guard (the "Big Four Agencies") and certain federal grantees, a manufacturer is required to participate in the VA Federal Supply Schedule ("FSS") pricing program, established under Section 603 of the Veterans Health Care Act of 1992. Under this program, the manufacturer is obligated to make its covered drugs available for procurement on an FSS contract and charge a price to the Big Four Agencies that is no higher than the Federal Ceiling Price ("FCP"), which is a price calculated pursuant to a statutory formula. The FCP is derived from a calculated price point called the "non-federal average manufacturer price" ("Non-FAMP"), which the manufacturer calculates and reports to the VA on a quarterly and annual basis. Pursuant to applicable law, knowing provision of false information in connection with a Non-FAMP filing can subject a manufacturer to significant penalties for each item of false information. The FSS contract also contains extensive disclosure and certification requirements. Under Section 703 of the National Defense Authorization Act for FY 2008, the manufacturer is required to pay quarterly rebates to DoD on utilization of its innovator products that are dispensed through DoD's Tricare network pharmacies to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non-FAMP and FCP for the calendar year that the product was dispensed.

In addition, at the state level, legislatures have increasingly passed legislation and implemented regulations similar to those under consideration at the federal level, as well as laws designed to control pharmaceutical and biotherapeutic product pricing, including restrictions on pricing or reimbursement at the state government level, limitations on discounts to patients, marketing cost disclosure and transparency measures, restrictions or other limitations on patient assistance, and, in some cases, policies to encourage importation from other countries (subject to federal approval) and bulk purchasing. Certain states are also pursuing cost containment efforts through Prescription Drug Affordability Boards ("PDABs") and similar entities. While many PDABs have been granted authority to promote drug price transparency and reporting, some states have granted PDABs more expansive authority, including to set Upper Payment Limits ("UPLs") on select, high price drugs. The adoption and implementation of UPLs may put downward pressure on drug prices and impact our company's future revenues.

Human Capital

As of December 31, 2025, we had 915 full-time employees, including 258 engaged in research, development and medical affairs, 526 in commercial activities and 131 in general and administrative functions. In 2025, we added a significant number of employees to support our commercial operations in both the United States and Europe. In addition, we have added employees in research and development as we continue to expand our pipeline activities. None of our employees are covered by collective bargaining agreements and we consider relations with our employees to be good. We also retain consultants on an as-needed basis.

We believe that our future success will be shaped by our continued ability to attract and retain highly skilled employees. We provide our employees with a competitive total rewards package inclusive of salaries, bonuses and equity ownership. We also provide robust benefits designed to promote well-being across all aspects of their lives, including health care, disability, retirement investment options and paid time off. In addition, we believe that continued growth and development are essential to the professional well-being of our team. As our organization and capabilities grow, we aim to ensure that we provide our team members with the guidance and resources they need to develop as professionals and to support our business.

As a growing global commercial-stage biopharmaceutical company, we value our workforce and believe it contributes to our long-term success and ability to execute our objectives of delivering innovative therapies to patients in need. Our team is unified by four core values—focus on the patient, having an owner mindset, the relentless pursuit of innovation and commitment to collaboration. We strive to ensure that these core values guide our employee-related endeavors, including our onboarding initiatives, continuous feedback process and recognition program.

General Information

We were incorporated in Delaware in March 2000. Our principal executive offices are located at 200 Barr Harbor Drive, Suite 200, West Conshohocken, PA 19428. Our internet website address is www.madrigalpharma.com. No portion of our website is incorporated by reference into this Annual Report.

We advise you to read this Annual Report in conjunction with other reports and documents that we file from time to time with the SEC. In particular, please read our definitive proxy statement, which will be filed with the SEC in connection with our 2026 annual meeting of stockholders, our quarterly reports on Form 10-Q and any current reports on

Form 8-K that we may file from time to time. You may obtain copies of these reports after the date of this Annual Report directly from us or from the SEC at its website at www.sec.gov. We make our periodic and current reports available on our internet website, free of charge, as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC.

We have adopted a Corporate Code of Conduct and Ethics, Corporate Governance Guidelines and written charters for our Audit Committee, Compensation Committee, Nominating and Corporate Governance Committee and Science and Technology Committee. Each of the foregoing is available on our website at www.madrigalpharma.com under "Investors & Media—Corporate Governance." In accordance with SEC rules, we intend to disclose any amendment (other than any technical, administrative or other non-substantive amendment) to the above code, or any waiver of any provision thereof with respect to any of our executive officers, on our website within four business days following such amendment or waiver. In addition, we may use our website as a means of disclosing material non-public information and for complying with our disclosure obligations under Regulation Fair Disclosure promulgated by the SEC. These disclosures will be included on our website under the "Investors & Media" section.

Item 1A. Risk Factors

You should carefully consider the risks described below, together with all of the other information included in or incorporated by reference into this Annual Report and in other documents we file with the SEC, before making an investment decision. The risks and uncertainties described below are not intended to be exhaustive and are not the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us or that we do not currently believe are material to an investor may also harm our business, and it is not possible to predict the impact that any factor or combination of factors may have on our business, prospects, financial condition and results of operations. If any of the events, contingencies, circumstances or conditions described in the following risk factors actually occur, our business, financial condition or our results of operations could be materially and adversely affected, which may cause the trading price of our common stock to decline and you may lose part or all of the value of any of our shares that you hold.

Risks Related to the Commercialization and Continued Approval of Rezdiffra

Our prospects are highly dependent on the success of our only approved product, Rezdiffra, which was approved in the United States under the Subpart H accelerated approval pathway for new drugs for serious or life-threatening illnesses and has received a CMA in the EU. If we are unable to successfully commercialize or maintain approval for Rezdiffra, our business, financial condition, results of operations and prospects and the value of our common stock will be materially adversely affected.

In March 2024, the FDA granted accelerated approval for Rezdiffra in conjunction with diet and exercise for the treatment of adults with noncirrhotic MASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis), and in August 2025, the EC granted a CMA for Rezdiffra in the EU. We have invested, and continue to invest, significant efforts and financial resources in the launch of Rezdiffra. We have never, as an organization, launched or commercialized any other product, and there is no guarantee that we will continue to successfully commercialize Rezdiffra. There are numerous examples of failures to meet high expectations of market potential, including by pharmaceutical companies with more experience and resources than us. We believe that the commercial success of Rezdiffra depends on many factors, including the following:

- our ability to effectively educate healthcare providers and patients on the risks of MASH and the potential clinical benefits of Rezdiffra;
- the efficacy, cost, approved use, and side-effect profile of Rezdiffra relative to competitive treatment regimens for the treatment of MASH;
- Rezdiffra may compete with the off-label use of currently marketed products and other therapies in development that may in the future obtain approval for MASH;
- the effectiveness of our commercial strategy for the marketing of Rezdiffra, including our pricing strategy and the effectiveness of our efforts to obtain and maintain adequate third-party reimbursements;
- developing, maintaining and successfully monitoring commercial manufacturing arrangements for Rezdiffra with third-party manufacturers to ensure they meet our standards and those of regulatory authorities, including the FDA, which extensively regulate and monitor pharmaceutical manufacturing facilities;
- our ability to negotiate and enter into any additional commercial, supply and distribution contracts to support commercialization efforts, and to hire and manage additional qualified personnel;
- our ability to meet the demand for commercial supplies of Rezdiffra at acceptable costs;
- the acceptance of Rezdiffra by physicians, patients and third-party payors;
- our ability to remain compliant with laws and regulations that apply to us and our commercial, promotional and medical activities;
- the actual market-size, ability to identify targeted patients and the demographics of patients eligible for Rezdiffra, which may be different than what we currently expect;
- the occurrence of any side effects, adverse reactions or misuse, or any unfavorable publicity in these areas;
- our ability to obtain, maintain or enforce our patents and other intellectual property rights; and
- the effect of recent or potential health care legislation in the United States.

While we believe that Rezdiffra has a commercially competitive profile, we cannot accurately predict the amount of revenue that would be generated from the sale of Rezdiffra. If we do not effectively commercialize Rezdiffra, we will not be able to execute our business plan and may not be able to achieve profitability. If our revenues, market share or other indicators of market acceptance of Rezdiffra do not meet the expectations of investors or public market analysts, the market price of our common stock would likely decline.

We obtained regulatory approval of Rezdiffra through the Subpart H accelerated approval pathway in the United States and Rezdiffra has received a CMA in the EU. Full approvals will be contingent on the completion of trials to successfully confirm the clinical benefit of Rezdiffra. Failure to obtain full approval or otherwise meet our post-marketing requirements and commitments would have a material adverse effect on our business.

The FDA approved Rezdiffra under the accelerated approval pathway for new drugs for serious or life-threatening illnesses and the EC granted a CMA for Rezdiffra in the EU. The approvals were supported by 52-week data from the Phase 3 MAESTRO-NASH trial, which achieved both primary endpoints—MASH resolution with no worsening of fibrosis and an improvement in fibrosis by at least one stage with no worsening of the NAFLD activity score. In connection with the FDA's accelerated approval, we have agreed to certain post-marketing commitments, including completing our MAESTRO-NASH trial to demonstrate a clinical benefit of Rezdiffra on composite endpoints. Our MAESTRO-NASH trial is ongoing as a 54-month outcomes trial designed to generate confirmatory outcomes data that, if positive, is expected to verify a clinical benefit and support the full approval of Rezdiffra in the U.S. Additionally, full approval could also be based on results from our MAESTRO-NASH OUTCOMES trial that will noninvasively measure progression to liver decompensation events in patients with compensated MASH cirrhosis. Positive data from our MAESTRO-NASH OUTCOMES trial is expected to support the full approval of Rezdiffra in noncirrhotic MASH in the U.S. and support approval for patients with compensated cirrhosis (F4c), expanding the eligible patient population for Rezdiffra. We have agreed to submit results from these trials to the EMA in support of transitioning the CMA into a standard marketing authorization for Rezdiffra in the EU. Failure to meet post-marketing commitments and requirements, and in particular, any failure to obtain positive data from any studies designed to confirm clinical benefit, could result in negative regulatory action and/or withdrawal of such approvals. The recently enacted FDORA has expanded FDA's expedited withdrawal procedures for drugs approved through the accelerated approval pathway if a sponsor fails to conduct any required post-approval study with due diligence.

A CMA is granted on the basis of less comprehensive clinical data than is normally required and is valid for one year, renewable annually, and subject to specific post-authorization obligations, such as clinical studies. If we fail to complete these obligations on time, if new data do not confirm a positive benefit-risk profile, or if new safety, efficacy or quality issues arise, the EC may decline to renew, vary, suspend or revoke the CMA or decline to convert it to a standard marketing authorization based on a respective recommendation by the EMA. Any such action may limit or prevent commercialization of Rezdiffra in the EU and could have a material adverse effect on our business. There is no assurance that the EC will grant full approval of Rezdiffra in the EU or that any such approval will be on commercially acceptable terms.

The commercial success of Rezdiffra will depend on the degree of market acceptance by physicians, patients, third-party payors and others in the health care community.

Despite receiving FDA and EC approval of Rezdiffra, our product may not gain, or over time may not retain, market acceptance by physicians, patients, third-party payors or others in the health care community. Rezdiffra was the first product approved by the FDA and EC for the treatment of MASH. Accordingly, we must educate healthcare providers and patients on the risks of MASH and the potential clinical benefits and appropriate use of Rezdiffra. If Rezdiffra does not achieve and maintain an adequate level of acceptance, it is likely that we will not generate significant revenue or become

profitable. The degree of market acceptance of Rezdiffra is also dependent on a number of additional factors, including the following:

- the willingness of physicians to prescribe, and our target patient population to use, Rezdiffra;
- the pricing of Rezdiffra;
- the efficacy and potential advantages of Rezdiffra compared to other treatment regimens;
- the ability of patients to tolerate Rezdiffra;
- sufficient third-party insurance coverage and reimbursement;
- the ability of the patient to pay out-of-pocket costs for Rezdiffra;
- the timing of market introduction of competitive products and treatments; and
- any publicity concerning Rezdiffra or any potential competitive products.

Our efforts to educate physicians, patients, third-party payors and others in the health care community on the potential benefits of Rezdiffra will require significant resources and may not be successful.

If the sales and marketing capabilities we have established for the commercialization of Rezdiffra are not effective, Rezdiffra may not be successfully commercialized.

While many of our officers and employees have experience commercializing drug products with prior companies, we have never as an organization engaged in commercial activities prior to the approval of Rezdiffra. We have hired and trained a commercial team and developed the organizational infrastructure we believe we need to support the commercial success of Rezdiffra in the U.S. and EU, and we continue to invest time and financial resources in optimizing this infrastructure. Factors that may inhibit our efforts to maintain and further develop commercial capabilities include:

- an inability to retain an adequate number of effective commercial personnel;
- an inability to adequately train commercial personnel, who may have limited experience with our company or our product, to deliver a consistent message regarding Rezdiffra and be effective in educating physicians regarding its potential benefits;
- an inability to equip commercial field personnel with compliant and effective materials, including marketing literature to help them educate physicians and healthcare providers regarding Rezdiffra and educate payors on the safety, efficacy and effectiveness profile of Rezdiffra to support favorable coverage decisions; and
- unforeseen costs and expenses associated with maintaining and further developing an independent commercial organization.

If we are not successful in maintaining our commercial infrastructure, of if our commercial capabilities are not effective, we will encounter difficulty in achieving, maintaining or increasing projected sales of Rezdiffra, which would adversely affect our business and financial position.

If we are unable to obtain or maintain adequate coverage and reimbursement from government or third-party payors for Rezdiffra or, if approved, any other product candidates, our prospects for generating revenue may be adversely affected.

Our ability to successfully commercialize Rezdiffra and any future product candidate, if approved, will depend in part on the extent to which coverage and reimbursement for these drugs will be available from third party payors, including government authorities (such as Medicare and Medicaid programs in the U.S.), managed care organizations and private health insurers. See the section titled “Business—Government Regulation—Coverage and Reimbursement” in this Annual Report for more information.

In the United States and other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Without third party payor reimbursement, patients may not be able to obtain or afford prescribed medications. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to successful commercialization. Our ability to successfully commercialize Rezdiffra and any additional products in the future will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. In addition, coverage and reimbursement guidelines by third party payors may have a significant impact on the prescribing physicians’ willingness and ability to prescribe Rezdiffra or

any other future product. The demand for, and the commercial success of, Rezdiffra could be materially harmed if state Medicaid programs, the Medicare program, other healthcare programs in the U.S. or elsewhere, or third party commercial payors in the U.S. or elsewhere, deny reimbursement for Rezdiffra or provide reimbursement only on unfavorable terms.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular drugs. For example, third party payors may require prior authorization for, and require reauthorization for continuation of, prescription products or impose step edits, which require prior use of another medication, prior to approving coverage for a particular product. We cannot predict actions that third party payors may take, or whether they will limit the access and level of reimbursement for Rezdiffra or refuse to provide any approvals or coverage. In addition, net prices for drugs may also be reduced by mandatory discounts or rebates required by government healthcare programs or private payors. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for drugs. We cannot be sure that coverage will be available or maintained for Rezdiffra or any drug candidate that we commercialize and, if coverage is available, the level of reimbursement.

Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. The availability of coverage and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford treatments. Pharmacy benefit managers ("PBMs"), other similar organizations and payors can limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication, exclude drugs from their formularies in favor of competitor drugs or alternative treatments, place drugs on formulary tiers with higher patient co-pay obligations, and/or mandate stricter utilization criteria. Formulary exclusion effectively encourages patients and providers to seek alternative treatments, make a complex and time-intensive request for medical exemptions, or pay 100% of the cost of a drug. In addition, in many instances, certain PBMs, other similar organizations and third party payors may exert negotiating leverage by requiring incremental rebates, discounts or other concessions from manufacturers in order to maintain formulary positions, which could result in higher gross to net deductions for affected products. The market for PBM services has become highly concentrated and vertically integrated, giving these entities further leverage in negotiating rebates, discounts or other concessions. In this regard, we have entered into agreements with PBMs and payor accounts to provide rebates to those entities related to formulary coverage for Rezdiffra, but we cannot guarantee that we will be able to agree to coverage terms with other PBMs and other third party payors. Payors could decide to exclude Rezdiffra from formulary coverage lists, impose step edits that require patients to try alternative treatments before authorizing payment for Rezdiffra, or impose a moratorium on coverage for Rezdiffra while the payor makes a coverage decision. An inability to maintain adequate formulary positions could increase patient cost-sharing and cause some patients to determine not to use Rezdiffra. Any delays or unforeseen difficulties in reimbursement approvals could limit patient access, depress therapy adherence rates, and adversely impact our ability to successfully commercialize Rezdiffra. In addition, PBMs and other third-party payors could implement alternative funding programs that could have an impact on product revenue. Further, prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs. If we are unsuccessful in maintaining broad coverage for Rezdiffra, our anticipated revenue from and growth prospects for Rezdiffra could be negatively affected.

The pricing of pharmaceutical products has come under increasing scrutiny as part of a global trend toward healthcare cost containment. Resulting changes in healthcare law and policy, including changes to Medicare, may impact our business in ways that we cannot currently predict, which could have a material adverse effect on our business and financial condition.

The United States and several foreign jurisdictions are considering, or have already enacted, a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payers in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access to healthcare. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. We expect to experience pricing pressures in connection with the sale of any products that we develop due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative proposals. See the section titled "Business—Government Regulation—U.S. Healthcare Reform" in this Annual Report for more information.

The continuing efforts of the government, insurance companies, managed care organizations and other payers of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for any of our product candidates, if approved;
- the ability to set a price that we believe is fair for any of our product candidates, if approved;
- our ability to generate revenues and achieve or maintain profitability;

- the level of taxes that we are required to pay; and
- the availability of capital.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical and biologic products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

In addition to the ACA, the U.S. government continues to seek to adopt healthcare policies and reforms intended to curb healthcare costs, such as federal or state controls on payment for drugs (including under Medicare, Medicaid, and commercial health plans). The IRA, among other things, establishes Medicare Part B and Part D inflation rebate schemes. Failure to timely pay a Part B or Part D inflation rebate is subject to a civil monetary penalty. The IRA also creates a drug price negotiation program under which the prices for Medicare units of certain high Medicare spend drugs and biologics without generic or biosimilar competition will be capped by reference to, among other things, a specified non-federal average manufacturer price, starting in 2026. Failure to comply with requirements under the drug price negotiation program is subject to an excise tax and/or a civil monetary penalty. The IRA further makes changes to the Medicare Part D benefit, including a limit on annual out-of-pocket costs, and a change in manufacturer liability under a new discount program which could negatively affect the profitability of our product candidates. Failure to pay a discount under this new program will be subject to a civil monetary penalty. Congress continues to examine various policy proposals that may result in pressure on the prices of prescription drugs in the government health benefit programs. The effect of the IRA on our business and the healthcare industry in general continues to evolve and we may discover adverse impacts on our company or our industry. The IRA is anticipated to have significant effects on the pharmaceutical industry and may reduce the prices we can charge and reimbursement we can receive for our product, among other effects.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs.

We expect that the healthcare reform measures that have been adopted and may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product and could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

Federal legislative and regulatory efforts to implement reference pricing or most-favored-nation pricing models could impact our product revenues and harm our business.

On May 12, 2025, President Trump issued an executive order calling on pharmaceutical manufacturers to voluntarily reduce the prices of medicines in the U.S. and directing the Secretary of Health and Human Services (HHS) to communicate most-favored-nation (MFN) price targets to pharmaceutical manufacturers to align prices with those in comparably developed nations and, in the event significant progress towards MFN pricing is not delivered, to propose rulemaking to impose MFN pricing.

Since the May 12, 2025 order, the Trump administration has continued to exert pressure on drug manufacturers to implement MFN pricing, including by suggesting that the administration may impose significant tariffs on pharmaceuticals if such manufacturers do not reach agreements to implement MFN pricing. Further, in November 2025, the Centers for Medicare & Medicaid Services (CMS) introduced the GENEROUS (GENErating cost Reductions fOr U.S. Medicaid) Model, a voluntary Medicaid payment initiative under which participating drug manufacturers may voluntarily offer supplemental rebates to participating state Medicaid programs that are intended to provide such Medicaid programs with an MFN price for the manufacturers' products. Additionally, in December 2025, CMS announced proposals for new mandatory demonstration payment models through two proposed rules under its Center for Medicare and Medicaid Innovation ("CMMI") authority, the Global Benchmark for Efficient Drug Pricing (GLOBE) for Medicare Part B and Guarding U.S. Medicare Against Rising Drug Costs (GUARD) for Medicare Part D. If finalized, these models would impose additional mandatory rebates on manufacturers of certain Medicare Part B and Medicare Part D drugs, for select

Medicare populations intended to represent 25% of Medicare patients, if the Medicare prices for such products exceed those paid in economically comparable countries. Both the GLOBE and GUARD models have proposed seven-year testing periods, with the GLOBE model proposed to begin on October 1, 2026 and the GUARD model proposed to begin on January 1, 2027.

If the GLOBE and GUARD models are finalized as proposed under CMMI authority, we could be required to pay additional rebates on products reimbursed by Medicare for the covered populations during the applicable model periods. In addition, if MFN pricing or similar reference pricing policies are enacted or implemented in the U.S. outside of the CMMI framework and applied more broadly, we could be required to pay rebates on products on utilization by a broader portion of U.S. patients to align with prices in certain reference countries. We currently derive the substantial portion of our revenue from U.S. sales, and any requirement to pay additional rebates in the U.S. to match international reference prices would impact our overall net revenue.

MFN pricing models in the U.S. could also affect our international pricing strategy and future decisions on reimbursement and commercialization in certain jurisdictions. If our U.S. pricing becomes tied to international reference prices, we may face decisions regarding pricing in foreign markets that could result in reduced patient access internationally, affect our relationships with foreign regulatory authorities and payers, or impact our ability to obtain or maintain reimbursement approvals in ex-U.S. markets.

These reforms remain subject to change, potential legal challenges, or expansion through additional rulemaking or sub-regulatory guidance, creating uncertainty for our overall pricing strategy. It remains to be seen whether and how these drug pricing initiatives will apply to Rezdiffra, how they will affect the broader pharmaceutical industry, and whether similar reform measures may be adopted in the future.

Like all medicinal products, Rezdiffra remains subject to ongoing regulatory review, and if we fail to comply with regulations or satisfy our post-approval commitments, we could lose our approval and the sale of Rezdiffra could be suspended.

Even though we received FDA accelerated approval and EC CMA for Rezdiffra, the manufacturing, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, sampling, and record keeping related to our product will remain subject to extensive regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP regulations, and GCPs for any clinical trials that we conduct post-approval, all of which may result in significant expense and limit our ability to commercialize Rezdiffra. As such, we and our contract manufacturers will be subject to periodic review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA or other marketing application and previous responses to inspection observations.

Further, the FDA and other regulatory agencies closely regulate the post-approval marketing and promotion of drugs to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. In the current administration, the FDA has increased its enforcement scrutiny over prescription drug advertising, particularly direct-to-consumer product promotion and advertising. The FDA and other regulatory agencies impose stringent restrictions on manufacturers' communications regarding off-label use, and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing by the FDA and other federal and state enforcement agencies, including the United States Department of Justice. Violation of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may also lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

For certain commercial prescription drug products, manufacturers and other parties involved in the supply chain must also meet chain of distribution requirements and build electronic, interoperable systems for product tracking and tracing and for notifying the FDA and regulators in other territories of counterfeit, diverted, stolen and intentionally adulterated products or other products that are otherwise unfit for distribution in the United States or other territories, respectively. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control. The FDA may also require a REMS program as a condition of approval of Rezdiffra or any future product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Regulatory authorities in the EU also have broad discretion to impose additional conditions, require labelling changes, restrict indications or distribution, require additional monitoring or risk minimization measures, or suspend or withdraw authorizations based on new safety, quality or efficacy information,

including information arising from real-world use. Other regulatory elements may also be added by other health authorities throughout the world.

If we fail to comply with the regulatory requirements of the FDA, the EMA and other applicable domestic and foreign regulatory authorities, or previously unknown problems with Rezdiffra, manufacturer, or manufacturing process are discovered, we could be subject to administrative or judicially imposed sanctions, including:

- restrictions on marketing or manufacturing of Rezdiffra;
- withdrawal of Rezdiffra from the market;
- holds on clinical trials;
- warning letters or untitled letters;
- civil or criminal penalties;
- fines;
- injunctions;
- product seizures or detentions;
- pressure to initiate voluntary product recalls;
- suspension or withdrawal of regulatory approvals; and
- refusal to approve supplements to approved applications.

If any of these events occur, our ability to sell Rezdiffra may be impaired, and we may incur substantial additional expense to comply with regulatory requirements, which could adversely affect our business, financial condition and results of operations.

Rezdiffra could develop unexpected safety or efficacy concerns, which would likely have a material adverse effect on us.

The regulatory approvals for Rezdiffra were supported by 52-week data from the MAESTRO-NASH trial and additional safety data from the Phase 3 MAESTRO-NAFLD-1 and MAESTRO-NAFLD-OLE extensions trials. Rezdiffra will now be used by more patients, potentially for longer periods of time, and we and others (including regulatory agencies and private payors) will collect extensive information on the efficacy and safety of Rezdiffra by monitoring its use in the marketplace. In addition, we are generating confirmatory data regarding the longer-term use of Rezdiffra in two ongoing trials. New safety or efficacy data from both market surveillance and our clinical trials may result in negative consequences including the following:

- Suspension or withdrawal of regulatory approval;
- Modification to product labeling or promotional statements, such as additional boxed or other warnings or contraindications, or the issuance of additional “Dear Doctor Letters” or similar communications to healthcare professionals;
- Required changes in the dosing of Rezdiffra;
- Imposition of additional post-marketing surveillance, post-marketing clinical trial requirements, distribution restrictions or other risk management measures, such as a REMS or a REMS with elements to assure safe use;
- Suspension or termination of ongoing clinical trials or refusal by regulators to grant full approval or approve pending marketing applications or supplements to approved applications;
- Suspension of, or imposition of restrictions on, our operations, including costly new manufacturing requirements with respect to Rezdiffra; and
- Voluntary or mandatory product recalls or withdrawals from the market and costly product liability claims.

Any of the foregoing circumstances could negatively impact Rezdiffra’s market acceptance and would likely materially adversely affect our business.

We operate in a highly competitive and changing environment, and if we are unable to adapt to our environment, we may be unable to compete successfully.

The biopharmaceutical industry has undergone and is likely to continue to experience rapid and significant change. Our future success will depend in large part on our ability to maintain a competitive position with respect to these technologies and to obtain and maintain protection for our intellectual property. Compounds, products or processes that we develop may become obsolete before we recover any expenses incurred in connection with their development. We face substantial competition from pharmaceutical, biotechnology and other companies, universities and research institutions with respect to MASH, and will face substantial competition with respect to future product candidates we may develop in MASH and other disease areas. Relative to us, many of these entities have substantially greater capital resources, research and development staffs, facilities and experience in conducting clinical studies, obtaining regulatory approvals, and manufacturing and marketing pharmaceutical products.

There are over 140 drugs in development for the potential treatment of MASH by companies ranging in size from private biotech companies to large pharmaceutical organizations. See the section titled "Business—Competition" in this Annual Report for more information.

Our ability to compete successfully will depend on, among other things, our ability to:

- effectively commercialize Rezdiffra;
- discover and/or in-license medicines that are differentiated from other products in the market;
- obtain required regulatory approvals;
- obtain patent and/or proprietary protection for our products and technologies; and
- attract and retain high-quality research, development and commercial personnel.

If we are unable to compete successfully, it will materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

Rezdiffra was approved for treatment in a limited population of patients with MASH with moderate to advanced liver fibrosis, and additional clinical trials and regulatory applications will be required to expand its indication. We may not be successful in these trials or in obtaining such regulatory approval, which may materially adversely affect our prospects and the value of our common stock.

The FDA granted accelerated approval of, and the EC granted a CMA for, Rezdiffra for the treatment of MASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis). A key component to our corporate strategy is to expand the target patient population for Rezdiffra. We have fully enrolled our Phase 3 MAESTRO-NASH OUTCOMES trial. In this trial, we are evaluating progression to liver decompensation events in patients with compensated MASH cirrhosis (F4c) treated with Rezdiffra versus placebo. A positive outcome is expected to support the full approval of Rezdiffra for noncirrhotic MASH in the U.S. and also expand the eligible patient population for Rezdiffra with an additional indication in patients with compensated MASH cirrhosis. We cannot guarantee positive results in this trial. If we are unable to expand the indication for use of Rezdiffra, our prospects and the value of our common stock may be materially adversely affected.

If we do not obtain regulatory approval of Rezdiffra in foreign jurisdictions, we will not be able to market Rezdiffra in other jurisdictions, which will limit our commercial revenues.

While Rezdiffra has been approved by the FDA and EC for the treatment of noncirrhotic MASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis), it has not been approved in any other jurisdiction for this indication or for any other indication. In order to market Rezdiffra for other indications or in other jurisdictions, we must obtain regulatory approval for each of those indications and in each of the applicable jurisdictions, and we may never be able to obtain such approval. In order to market any products outside of the United States and EU, we must establish and comply with numerous and varying regulatory requirements of other countries regarding clinical trial design, safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals could result in significant delays, difficulties and costs for us and may require additional preclinical studies or clinical trials, which would be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. If we fail to comply with regulatory requirements in international markets or to

obtain and maintain required approvals, our target market will be reduced and our ability to realize the full market potential of Rezdiffra will be harmed.

EU pricing and reimbursement regulations may materially affect our ability to market and receive coverage for Rezdiffra in the EU Member States.

Our ability to successfully commercialize Rezdiffra in the EU, which has received a CMA from the EC and which we have launched in Germany, will depend on the pricing and reimbursement terms we are able to secure and maintain in the EU Member States in which we plan to launch. Pricing and reimbursement decisions are made at the Member State level in the EU and the policies, evidentiary requirements, and assessment methodologies governing drug pricing and reimbursement vary widely from country to country. For example, an EU Member State may restrict the range of medicinal products for which their national health insurance systems provide reimbursement and may approve a specific price for the medicinal product, while others may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Pricing negotiations with governmental authorities can take considerable time after receiving marketing authorization in the EU Member States and this may negatively impact our anticipated timelines for launch in key markets in the EU.

In addition, as we have received a CMA from the EC, it may be more difficult to obtain reimbursement approval in certain EU Member States and we may not be able to obtain a satisfactory price for Rezdiffra through the benefit and value assessments conducted by the Health Technology Assessment bodies in the EU Member States based on the clinical data that we have to date. We may be required to provide additional evidence (including comparative effectiveness, real-world evidence, registries, or other post-launch commitments) before we can be granted reimbursement, or we may be required to seek reimbursement for a narrower sub-population than the authorized label in order to obtain commercially viable pricing and reimbursement terms.

If we are unable to secure reimbursement, if reimbursement is limited in scope or population, or if pricing is set at levels that are not commercially sustainable in any EU Member States, it may not be commercially viable for us to launch in such countries. Even if we are able to launch in such countries, unsatisfactory pricing and reimbursement terms would impact our revenues from sales of Rezdiffra and the potential profitability of Rezdiffra in those countries would be negatively affected. In particular, we may not be able to obtain pricing for Rezdiffra in the EU Member States which is similar to our intended price for the U.S. market.

If the FDA or other applicable regulatory authorities approve generic products that compete with Rezdiffra, the sales of Rezdiffra would be adversely affected.

Once an NDA or marketing authorization application outside the United States is approved, the product covered thereby becomes a "listed drug" that can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application in the United States or equivalent marketing authorization application outside the United States. Agency regulations and other applicable regulations and policies provide incentives to manufacturers to create modified, non-infringing versions of a drug to facilitate the approval of an abbreviated new drug application or other application for generic substitutes in the United States and in nearly every pharmaceutical market around the world. These manufacturers might only be required to conduct a relatively inexpensive study to show that their product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use, or labeling, as our product and that the generic product is bioequivalent to our product, meaning it is absorbed in the body at the same rate and to the same extent as our product. These generic equivalents, which must meet the same quality standards as branded pharmaceuticals, would be significantly less costly than our product to bring to market, and companies that produce generic equivalents are generally able to offer their products at lower prices. Thus, after the introduction of a generic competitor, a significant percentage of the sales of any branded product are typically lost to the generic product. Accordingly, competition from generic equivalents to Rezdiffra would materially adversely affect our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made.

We currently rely on a limited number of specialty pharmacies for distribution of Rezdiffra in the United States, and the loss of one or more of these specialty pharmacies or their failure to effectively distribute Rezdiffra could materially harm our business.

Rezdiffra is currently only available for distribution through a limited number of specialty pharmacies in the United States. These specialty pharmacies account for substantially all of our revenue in the U.S. A specialty pharmacy is a pharmacy that specializes in the dispensing of medications for complex or chronic conditions that often require a high level of patient education and ongoing management. The use of specialty pharmacies involves certain risks, including, but not limited to, risks that these specialty pharmacies:

- may not serve a significant portion of our expected patient population;

- may not provide us accurate or timely information regarding their inventories, the number of patients using Rezdiffra or complaints about Rezdiffra;
- reduce their efforts or discontinue to sell or support Rezdiffra, particularly if competing therapies enter the marketplace;
- do not devote the resources necessary to sell Rezdiffra or support patients;
- are be unable to satisfy financial obligations to us or others; or
- will cease operations.

If one or more of our specialty pharmacies do not fulfill their contractual obligations to us, or refuse or fail to adequately serve patients, or their agreements are terminated without adequate notice, shipments of Rezdiffra, and associated revenues, could be adversely affected. We expect that it would take a significant amount of time if we were required to replace one or more of our specialty pharmacies. In addition, if we determine to modify our distribution strategy, we may experience disruptions in the distribution of Rezdiffra, which could adversely impact our business.

If estimates of the size of the potential market for Rezdiffra is overstated or data we have used to identify physicians is inaccurate, our ability to earn revenue to support our business could be materially adversely affected.

We have relied on external sources, including market research funded by us and third parties, and internal analyses and calculations to estimate the potential market opportunities for Rezdiffra. The externally sourced information used to develop these estimates has been obtained from sources we believe to be reliable, but we have not verified the data from such sources, and their accuracy and completeness cannot be assured. With respect to Rezdiffra, our internal analyses and calculations are based upon management's understanding and assessment of numerous inputs and market conditions. These understandings and assessments necessarily require assumptions subject to significant judgment and may prove to be inaccurate. As a result, our estimates of the size of these potential market for Rezdiffra could prove to be overstated, perhaps materially.

In addition, we are relying on third-party data to identify the physicians who treat the majority of MASH patients in the United States and to determine how to deploy our resources to market to those physicians; however, we may not be marketing to the appropriate physicians and may therefore be limiting our market opportunity.

In addition, our market opportunity could be reduced if a regulator limits the proposed treatment population for any future product candidate, similar to the limited population for which Rezdiffra was approved. In either circumstance, even if we obtain regulatory approval, we may be unable to commercialize the product on a scale sufficient to generate significant revenue from such product candidates, which could have a material adverse effect on our business, financial condition, results of operations and prospects and the value of our common stock.

Product liability lawsuits brought against us could cause us to incur substantial liabilities and could limit commercialization of Rezdiffra or any future product candidates that we may develop.

We face an inherent risk of product liability lawsuits related to the testing of any product candidates in human clinical trials and an even greater risk in connection with the commercialization of Rezdiffra. Product liability claims may be brought against us or our partners by participants enrolled in our clinical trials, patients, healthcare providers or others using, administering or selling any approved product. If we cannot successfully defend ourselves against any such claims, we may incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for Rezdiffra or any of our future approved products;
- injury to our reputation;
- withdrawal of clinical trial participants;
- termination of clinical trial sites or entire trial programs;
- significant litigation costs;
- substantial monetary awards to or costly settlements with patients or other claimants;
- product recalls or a change in the indications for which products may be used;
- loss of revenue;
- diversion of management and scientific resources from our business operations; and
- the inability to commercialize our product candidates.

We are highly dependent upon consumer perceptions of us and the safety and quality of Rezdiffra and any future product we commercialize. We could be adversely affected if we are subject to negative publicity. We could also be adversely affected if any of our products or any similar products distributed by other companies prove to be, or are asserted to be, harmful to patients. Also, because of our dependence upon consumer perceptions, any adverse publicity associated with illness or other adverse effects resulting from patients' use or misuse of our products or any similar products distributed by other companies could have a material adverse impact on our results of operations.

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we may need to further increase our insurance coverage as we begin additional clinical trials or if we successfully commercialize additional drug candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to Product Development and Regulatory Approval

Pharmaceutical research and development is very expensive, time-consuming and difficult to design and implement and involves uncertain outcomes. Furthermore, the results of preclinical studies and earlier clinical trials are not always predictive of future results. Any product candidate that we advance into clinical trials may not have favorable results in later clinical trials or receive regulatory approval.

Drug development is an expensive, high-risk, lengthy, complicated, resource intensive process. In order to successfully develop products, we must, among other things:

- identify potential product candidates;
- submit for and receive regulatory approval to perform clinical trials;
- conduct appropriate preclinical and clinical trials, including confirmatory clinical trials, according to good laboratory practices and GCP and disease-specific expectations of the FDA and other regulatory bodies;
- select and recruit clinical investigators and subjects for our clinical trials;
- obtain and correctly interpret data establishing adequate safety of our product candidates and demonstrating with statistical significance that our product candidates are effective for their proposed indications, as indicated by the achievement of specified endpoints;
- receive regulatory approvals for marketing;
- manufacture the product candidates according to cGMP and other applicable standards and regulations.

We will be required to demonstrate through adequate and well-controlled clinical trials that our product candidates are safe and effective, with a favorable benefit-risk profile, for use in our target indications before we can seek regulatory approvals for commercial sale. Clinical trials are expensive, difficult to design and implement, can take many years to complete and are uncertain as to outcome. Delay or failure can occur at any stage of development, including after commencement of any of our clinical trials. In addition, success in early clinical trials does not mean that later clinical trials will be successful, because later-stage clinical trials may be conducted in broader patient populations and involve different study designs. Furthermore, our ongoing and future trials will need to demonstrate sufficient safety and efficacy in large patient populations for approval by regulatory authorities. Companies frequently suffer significant setbacks in advanced clinical trials, even after earlier clinical trials have shown promising results, and we cannot be certain that we will not face similar setbacks. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. In addition, only a small percentage of drugs under development result in the submission of an NDA to the FDA and even fewer are approved for commercialization.

We cannot be certain that any of our ongoing or future clinical trials will be successful, and any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications.

Additionally, our clinical trials may utilize an "open-label" trial design. An "open-label" clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject

to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results with any of our product candidates when studied in a controlled environment with a placebo or active control.

In addition, there are many other difficulties and uncertainties inherent in pharmaceutical research and development that could significantly delay or otherwise materially impair our ability to develop future product candidates, including the following:

- conditions imposed by regulators, ethics committees or institutional review boards for preclinical testing and clinical trials relating to the scope or design of our clinical trials, including selection of endpoints and number of required patients or clinical sites;
- restrictions placed upon clinical trials and clinical trial sites, including with respect to potential clinical holds or suspension or termination of clinical trials due to, among other things, potential safety or ethical concerns or noncompliance with regulatory requirements;
- failure by third-party contractors, contract research organizations, clinical investigators, clinical laboratories, or suppliers to comply with regulatory requirements or meet their contractual obligations in a timely manner; and
- greater than anticipated cost of our clinical trials.

Failure to successfully develop future product candidates for any of these reasons may materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

If we fail to successfully develop and commercialize our other product candidates, we may be unable to grow our business.

We plan to evaluate the development and commercialization of therapies beyond Rezdiffra, including MGL-2086, ervogastat and our siRNA programs. We may choose to in-license or acquire additional product candidates to treat patients suffering from disorders with high unmet medical needs and limited treatment options. These product candidates will require additional, time-consuming development efforts prior to commercial sale, including preclinical studies, clinical trials and approval by the FDA and/or applicable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, be successfully commercialized, be widely accepted in the marketplace, or be more effective than other commercially available alternatives.

Interim, topline and preliminary data from our clinical trials that we announce or publish from time to time may change as more data become available, may be interpreted differently if additional data are disclosed, and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or topline data from our clinical trials, which may be based on a preliminary analysis of data in a summary or topline format, and the results and related findings may change as additional data become available, may be interpreted differently if additional data are disclosed at a later time and are subject to audit and verification procedures that could result in material changes in the final data. If additional results from our clinical trials are not viewed favorably, our ability to obtain approval for and commercialize our approved drug and drug candidates, our business, operating results, prospects, or financial condition may be harmed and our stock price may decrease.

We make assumptions, estimates, calculations, and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the preliminary or topline results that we report may differ from future results of the same trials, or different conclusions or considerations may qualify such results, once additional data have been disclosed and/or are received and fully evaluated. Such data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we published. As a result, preliminary and topline data should be viewed with caution until the final data are available. We may also disclose interim data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Differences between preliminary or interim data and final data could significantly harm our business prospects.

Further, other parties, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions, or analyses or may interpret or weigh the importance of data differently, which could impact the particular program or commercialization of the particular drug candidate or product, and our business in general. In addition, in regards to the information we publicly disclose regarding a particular study or clinical trial, such as topline data, others may not agree with what we determine is the material or otherwise appropriate information to include in such disclosure, and any information we determine not to disclose, or to disclose at a later date, such as at a medical meeting may ultimately be deemed significant with respect to future decisions, conclusions, views, activities, or otherwise regarding a particular drug, drug candidate, or our business. If the interim, topline or preliminary data that we report differ from actual results or are interpreted differently once additional data are disclosed at a later date, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for and commercialize our drug candidates, our business, operating results, prospects, or financial condition may be harmed or our stock price may decline.

If clinical trials or regulatory approval processes are prolonged, delayed or suspended, we may be unable to advance the development of or commercialize our product candidates on a timely basis, which would require us to incur additional costs and delay our receipt of any revenue from potential product sales.

We cannot predict whether we will encounter problems with any of our completed, ongoing or planned clinical trials that will cause us or any regulatory authority to delay, suspend, or terminate those clinical trials or delay the analysis of data derived from them. A number of events, including but are not limited to any of the following, could delay or impede completely the completion of our ongoing and planned clinical trials and negatively affect our ability to obtain regulatory approval for, and to market and sell, a particular product candidate:

- conditions imposed on us by the FDA, the EMA or other regulatory authorities regarding the scope or design of our clinical trials;
- insufficient supply of our product candidates or other materials necessary to conduct and complete our clinical trials;
- slow enrollment and retention rate of subjects in our clinical trials;
- challenges in identifying or recruiting sufficient trial sites or investigators for clinical trials; and
- serious and unexpected drug-related side effects related to the product candidate being tested.

Commercialization of any future product candidates may be delayed by the imposition of additional conditions on our clinical trials by the FDA or any other applicable foreign regulatory authority or the requirement of additional supportive trials by the FDA or such foreign regulatory authority.

We do not know whether our ongoing clinical trials will need to be restructured, will enroll an adequate number of patients on time, or will be completed on schedule, if at all, or whether future clinical trials will begin as planned or have similar future challenges. Delays in the initiation, enrollment or completion of our clinical trials will result in increased development costs for our product candidates, and our financial resources may be insufficient to fund any incremental costs. In addition, if our clinical trials are delayed, our competitors may be able to bring products to market before we do and the commercial viability of our product candidates could be limited.

If we inadvertently fail to comply with foreign regulatory requirements governing human clinical trials and marketing approval for drugs, we could be prevented from selling our drug candidates in such foreign markets, which may adversely affect our operating results and financial condition.

The requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement for marketing products outside the United States vary greatly from country to country and may require additional testing. We expect that our future clinical development of our drug candidates will involve a number of clinical trials in foreign jurisdictions, particularly in Europe. We have limited experience in obtaining foreign regulatory approvals. The time required to obtain approvals outside the United States may differ from that required to obtain FDA approval. We may not obtain foreign regulatory approvals on a timely basis, if at all. Approval by the FDA does not guarantee approval by regulatory authorities in other countries, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Failure to comply with these regulatory requirements or obtain required approvals could impair our ability to develop foreign markets for our drug candidates and may have a material adverse effect on our results of operations and financial condition.

We may in the future conduct certain clinical trials for our product candidates outside of the U.S. However, the FDA may not accept data from such trials, in which case our development plans will be delayed, which could materially harm our business.

We may conduct one or more of our clinical trials for our product candidates outside the U.S. Although the FDA may accept data from clinical trials conducted outside the U.S., acceptance of this data is subject to certain conditions imposed by the FDA. Where data from foreign clinical trials are intended to serve as the basis for marketing approval in the U.S., the FDA will not approve the application on the basis of foreign data alone unless those data are applicable to the U.S. population and U.S. medical practice; the studies were performed by clinical investigators of recognized competence; and the data are considered valid without the need for an on-site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. For studies that are conducted only at sites outside of the U.S. and not subject to an IND, the FDA generally does not provide advance comment on the clinical protocols for the studies, and therefore there is an additional potential risk that the FDA could determine that the study design or protocol for a non-U.S. clinical trial was inadequate, and require us to conduct additional clinical trials. In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. There can be no assurance the FDA will accept data from clinical trials conducted outside off the U.S. If the FDA does not accept data from our clinical trials of our product candidates, we would likely need to conduct additional clinical trials, which would be costly and time consuming and could delay or halt our development of our product candidates. Additionally, recent policy proposals in the U.S., if enacted in the future, may make acceptance by the FDA or inclusion in a marketing application of foreign data more difficult or costly. These and other risks associated with our potential international operations may materially adversely affect our ability to develop our product candidates and attain or maintain profitable operations, which could have a material adverse effect on our business and results of operations.

We depend on enrollment of patients in our clinical trials. If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

Identifying and qualifying patients to participate in clinical trials is critical to our success. We may not be able to initiate, continue, or complete clinical trials required by the FDA or foreign regulatory agencies if we are unable to locate, enroll and maintain a sufficient number of eligible patients to participate. The timing to conduct and complete clinical trials, is affected by many factors, including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials, and clinicians' and patients' perceptions as to the potential advantages and disadvantages of the product candidate being studied in relation to other available therapies. Delays in patient enrollment for our clinical trials could increase costs and delay commercialization and sales, if any, of our products. With respect to our MAESTRO-NASH OUTCOMES trial, our inability to maintain a sufficient number of eligible patients enrolled in the trial could restrict our ability to commercialize Rezdiffra in a broader population of patients with noncirrhotic MASH. Once enrolled, patients may elect to discontinue participation in a clinical trial at any time. For example, patients in our ongoing MAESTRO-NASH trial may elect to discontinue their participation in the trial now that Rezdiffra is an approved product and is commercially available. If patients elect to discontinue participation in our clinical trials at a higher rate than expected, we may be unable to generate the data required by regulators for approval. Enrollment delays in these clinical trials may result in increased development costs for our planned or future product candidates, which would cause the value of our Company to decline and limit our ability to obtain additional financing.

Breakthrough therapy or priority review by the FDA for any product candidate may not lead to faster development, regulatory review or approval processes, and it does not increase the likelihood that our product candidates will receive marketing approval.

We may seek breakthrough therapy designation or priority review for future product candidates if supported by the results of clinical trials. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Priority review is intended to speed the FDA marketing application review timeframe for drugs that treat a serious condition and, if approved, would provide a significant improvement in safety or effectiveness.

For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development. Sponsors of drugs that are breakthrough therapies may also be able to submit marketing applications on a rolling basis, meaning that the FDA may review portions of a marketing application before the sponsor submits the complete application to the FDA, if the sponsor pays the user fee upon submission of the first portion of the marketing application. For applications that receive priority

review, the FDA's marketing application review goal is shortened to six months, as opposed to ten months under standard review.

Designation as a breakthrough therapy or priority review product is within the discretion of the regulatory agency. Accordingly, even if we believe one of our future product candidates meets the criteria for designation as a breakthrough therapy or priority review product, the agency may disagree and instead determine not to make such designation. In any event, the receipt of such a designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional regulatory procedures and does not assure ultimate marketing approval by the agency. In addition, regarding breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification as a breakthrough therapy or, for priority review products, decide that the period for FDA review or approval will not be shortened.

Risks Related to our Business Operations, Employee Matters and Managing Growth

Our failure to successfully in-license, acquire, develop and market additional product candidates could impair our ability to grow our business.

As part of our business strategy, we may effect acquisitions or licenses to obtain additional product candidates, technologies, capabilities or personnel. The success of this strategy depends partly upon our ability to identify and select promising pharmaceutical product candidates, negotiate licensing or acquisition agreements with their current owners and finance these arrangements. The process of proposing, negotiating and implementing a license or acquisition of a product candidate is lengthy and complex. Other companies, including some with substantially greater financial and other resources, may compete with us for the license or acquisition of product candidates. Moreover, we may devote resources to potential acquisitions or licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. Additionally, we may not be able to acquire the rights to additional product candidates on terms that we find acceptable, or at all.

Any strategic transactions we enter into may not be clinically or commercially successful, and may require financing or a significant amount of cash, which could adversely affect our business.

Entering into strategic transactions involves a number of operational risks, including:

- failure to achieve expected synergies;
- the possibility that our acquired technologies, products and product candidates may not be clinically or commercially successful;
- difficulty and expense of assimilating the operations, technology and personnel of any acquisition;
- the inability to maintain any acquired company's relationship with key third parties, such as alliance partners; and
- diversion of our management's attention from our core business.

We also may enter into collaborative relationships that would involve our collaborators conducting proprietary development programs. Disagreements with collaborators may develop over the rights to our intellectual property, and any conflict with our collaborators could limit our ability to obtain future collaboration agreements and negatively influence our relationship with existing collaborators. If we make one or more significant acquisitions or enter into a significant collaboration in which the consideration includes cash, we may be required to use a substantial portion of our available cash or need to raise additional capital, which could adversely affect our financial condition.

We are dependent upon retaining and attracting key personnel, the loss of whose services could materially adversely affect our business, financial condition, results of operations, prospects and the value of our common stock.

We are highly dependent on principal members of our senior management team and our scientific, clinical, sales and medical staff. These executives and employees each have significant pharmaceutical industry experience. The loss of any senior member of our management team or scientific and commercial staff could have a material adverse effect on our business and stock price. Our management and other employees may voluntarily terminate their employment with us at any time. The loss of the services of these or other key personnel, or the inability to attract and retain additional qualified personnel, could result in delays to development or approval of any future product candidates, loss of sales of Rezdiffra or any future product, if approved, and diversion of management resources. Competition for qualified personnel is intense, and the process of hiring and integrating such qualified personnel is often lengthy. We may be unable to recruit such personnel on a timely basis, if at all, which would negatively impact our development and commercialization programs.

Our employees, contractors, vendors and partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading laws, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of fraud or other misconduct by our employees, contractors, vendors or partners. Misconduct by these parties could include failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with federal and state healthcare fraud and abuse laws and regulations, to report financial information or data timely, completely or accurately, or to disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Third-party misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Business Conduct and Ethics, but it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent misconduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us resulting from this misconduct and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

We expect to continue to expand our development and commercialization capabilities, and as a result, we may encounter challenges in managing our growth, which could disrupt our operations.

We are in the process of expanding our commercial operations in Europe for Rezdiffra and are seeking to continue to expand our development pipeline. We expect to continue to experience growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs, quality, commercial compliance, medical affairs, and sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. We may not be able to effectively manage the expansion of our operations, which could delay the execution of our business plans or disrupt our operations.

We enter into various contracts in the normal course of our business in which we indemnify the other party to the contract. In the event we have to perform under these indemnification provisions, such performance could have a material adverse effect on our business, financial condition and results of operations.

In the normal course of business, we periodically enter into academic, commercial, service, collaboration, licensing, consulting and other agreements that contain indemnification provisions. With respect to our academic and other research agreements, we typically indemnify the institution and related parties from losses arising from claims relating to the products, processes or services made, used, sold or performed pursuant to the agreements for which we have secured licenses and from claims arising from our or our potential sublicensees' exercise of rights under the agreements. With respect to our commercial agreements, we indemnify our vendors from any third-party product liability claims that could result from the production, use or consumption of our product, as well as for alleged infringements of any patent or other intellectual property right by a third party.

Should our obligation under an indemnification provision exceed applicable insurance coverage or if we are denied insurance coverage, our business, financial condition and results of operations could be adversely affected. Similarly, if we are relying on a collaborator to indemnify us and the collaborator is denied insurance coverage or the indemnification obligation exceeds the applicable insurance coverage, and if the collaborator does not have other assets available to indemnify us, our business, financial condition and results of operations could be adversely affected.

Risks Related to Our Dependence on Third Parties

If the third parties on which we rely for the conduct of our clinical trials and results do not perform our clinical trial activities in accordance with our agreements, GCP and related regulatory requirements, we may be unable to obtain regulatory approval for our product candidates or commercialize our products.

We use clinical research organizations ("CROs") and other third-party service providers to conduct and oversee our clinical trials and expect to continue to do so for the foreseeable future. We rely heavily on these parties for successful execution of our clinical trials. Nonetheless, we are responsible for confirming that each of our clinical trials is conducted in accordance with FDA requirements and our general investigational plan and protocol.

The FDA requires us and our third-party service providers to comply with GCP for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate, and that the trial participants are adequately protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements.

Third parties may not complete activities on schedule or may not conduct our clinical trials in accordance with regulatory or GCP requirements, our agreements or the respective trial plans and protocols. In addition, third parties may not be able to repeat their past successes in clinical trials. We also rely on third parties to select and enter into agreements with clinical investigators to conduct clinical trials to support approval of our product candidates. The failure of these third parties to adequately carry out their obligations could delay or prevent the development and approval of our product candidates and commercialization of our products or result in enforcement action against us.

If our relationship with these third-party providers terminates, we may not be able to enter into arrangements with alternative providers or do so on commercially reasonable terms. Switching or adding additional third-party providers involves substantial cost and requires management time and focus, and could delay development and commercialization of our product candidates and approved products. Though we intend to carefully manage our relationships with our third-party providers, we may encounter challenges or delays in the future and any such delays or challenges may have a negative impact on our business and financial condition.

We have relied on, and expect to continue to rely on, third-party manufacturers to produce Rezdiffra and any future product candidates.

We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of Rezdiffra or any product candidates, and we lack the resources and the capabilities to do so. As a result, we currently rely, and expect to rely on third-party manufacturers to supply our product candidates for our clinical trials as well as our commercial supply of Rezdiffra. Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured Rezdiffra or our product candidates ourselves. For example, if we do not maintain our key manufacturing relationships, we may fail to find replacement manufacturers or develop our own manufacturing capabilities, which could negatively impact our commercial operations or delay or impair our ability to obtain regulatory approval for our product candidates and substantially increase our costs or deplete profit margins, if any. If we do find replacement manufacturers, we may not be able to enter into agreements with them on terms and conditions favorable to us and there could be a substantial delay before new facilities could be qualified and registered with the FDA and other foreign regulatory authorities.

Even if we are able to establish and maintain arrangements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- manufacturing delays if our third-party manufacturers give greater priority to the supply of other products over Rezdiffra or any other future product candidates or otherwise do not satisfactorily perform according to the terms of the agreement between us;
- limitations on supply availability resulting from capacity and scheduling constraints of third-parties, or as a result of economic or political developments, including the ongoing conflicts in Ukraine and the Middle East and global economic instability;
- the possible breach of manufacturing agreements by third-parties because of factors beyond our control;
- the possible termination or non-renewal of the manufacturing agreements by a third-party, at a time that is costly or inconvenient to us; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

The FDA and other foreign regulatory authorities require manufacturers to register manufacturing facilities. The FDA and corresponding foreign regulators also inspect these facilities to confirm compliance with cGMPs. Contract manufacturers may face manufacturing or quality control problems that may cause drug substance production and shipment delays or may cause contractors not to be able to maintain compliance with the applicable cGMP requirements. Any failure to comply with cGMP requirements or other FDA, EMA, or comparable foreign regulatory requirements could adversely affect our clinical research activities and our ability to develop our product candidates and market our products following approval, including Rezdiffra.

Our current and anticipated future dependence upon others for the manufacture of Rezdiffra and any product candidate may adversely affect our future profit margins, if any, and our ability to develop our product candidates and commercialize any products that receive regulatory approval on a timely basis.

If any third-party manufacturer of Rezdiffra or any other future product candidates is unable to increase the scale of its production of such product or product candidates or increase the product yield of its manufacturing, then our costs to manufacture such product or product candidate may increase and any commercialization may be delayed.

In order to produce sufficient quantities to meet the demand for our clinical trials and commercialization of Rezdiffra in the United States and any subsequent commercialization of Rezdiffra in other jurisdictions, if approved, or any other future product candidates that we may develop, our third-party manufacturers will be required to increase their production and optimize their manufacturing processes while maintaining the quality of the product. The transition to larger scale production could be difficult. In addition, if our third party manufacturers are not able to optimize their manufacturing processes to increase the product yield for Rezdiffra or any other future product candidates, or if they are unable to produce increased amounts of such product candidates while maintaining the quality of the product and compliance with cGMPs, then we may not be able to meet the demands of clinical trials or market demands, which could decrease our ability to generate profits and have a material adverse impact on our business and results of operation.

Using specialty distributors to market and sell Rezdiffra in certain jurisdictions outside of the United States subjects us to certain risks.

Outside of the United States, we may enter into distribution agreements with specialty distributors to commercialize Rezdiffra. We may be unable to enter into appropriate supply, marketing, and distribution arrangements on favorable terms, if at all. Our use of distributors in these markets to market and sell Rezdiffra involves certain risks, including, but not limited to, risks that these organizations will not comply with applicable laws and regulations, not effectively sell or support Rezdiffra or reduce or discontinue their efforts to sell or support Rezdiffra, not devote the resources necessary to market and sell Rezdiffra in the volumes and within the time frame we expect, not be able to satisfy financial obligations to us or others, not provide us with accurate or timely information regarding their inventories of Rezdiffra or the number of patients who are using Rezdiffra, or not provide us with accurate or timely information regarding serious adverse events and/or product complaints. Any such events may result in regulatory actions that may include suspension or termination of the distribution and sale of Rezdiffra in a certain country, loss of revenue, and/or reputational damage, which could harm our results of operations and business.

Risks Related to Our Financial Position and Need for Capital

We have a limited operating history and currently only have one commercial product, Rezdiffra, which may make it difficult to evaluate the prospects for our future viability.

Our operations to date have been primarily limited to conducting research and development activities, including preclinical studies and clinical trials and, more recently, preparing for commercialization of and commercializing Rezdiffra. We have not yet demonstrated an ability to generate revenues on a long term sustained basis, or to conduct sales and marketing activities necessary for successful longer term product commercialization. Initial sales of Rezdiffra may not be predictive of long-term commercial results.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. Accordingly, you should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by companies in the early commercial stage, especially pharmaceutical companies such as ours. Any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history with these activities.

We have a history of operating losses, expect to incur operating losses in the future and may never achieve or maintain profitability.

As of December 31, 2025, we had an accumulated deficit of $2,090.5 million. Losses have principally resulted from costs incurred from our commercialization efforts, in our preclinical studies and clinical trials, research and development programs and from our selling, general and administrative expenses. As of December 31, 2025, we had cash, cash equivalents, restricted cash and marketable securities of approximately $988.6 million. Despite our recent launch of Rezdiffra in the United States and Germany, we expect to continue to incur operating losses as we:

- support our sales and marketing efforts for Rezdiffra;
- fulfill our post-marketing commitments and clinical trials of Rezdiffra, as required by the FDA;
- initiate or continue clinical trials of any future product candidates;
- seek to acquire or in-license additional product candidates;

- seek regulatory approvals and, if approved, commercialize Rezdiffra in foreign markets;
- add operational, financial and management information systems and personnel, including personnel to support commercialization of Rezdiffra and product candidate development and to help us comply with our obligations as a public company; hire and retain additional personnel, such as clinical, quality control, scientific, commercial and administrative personnel;
- maintain, expand and protect our intellectual property portfolio; and
- add equipment and physical infrastructure to support our research and development.

We may never achieve profitability. Furthermore, even if we achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Because of the numerous risks and uncertainties associated with developing and commercializing Rezdiffra and any future product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if ever.

We have a limited history of recognizing revenue from product sales and may not be able to achieve or maintain long-term sustainable profitability.

Our ability to generate revenue and achieve profitability depends on our ability to successfully obtain and maintain the regulatory approvals necessary to commercialize our products, including our commercialization of Rezdiffra in the United States and EU. Our ability to recognize revenues from product sales depends heavily on our success in:

- obtaining and delivering supply of Rezdiffra;
- satisfying post-marketing requirements;
- obtaining reimbursement for our product from private insurance or government payors;
- completing research, preclinical studies and clinical development of any future product candidates;
- seeking and obtaining full U.S. approvals and foreign marketing approvals for Rezdiffra and for other product candidates for which we may complete clinical trials;
- obtaining and maintaining market acceptance of our product and any product candidates, if approved;
- launching and commercializing product candidates for which we obtain marketing approval;
- addressing any competing technological and market developments;
- implementing additional internal systems and infrastructure;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter;
- maintaining, defending, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how; and
- attracting, hiring and retaining qualified personnel.

Other than Rezdiffra, we have not yet launched any other approved products for commercial sale. We anticipate continuing to incur significant costs associated with seeking full approval of Rezdiffra in the United States and European Union and the commercialization of Rezdiffra, and even if another product candidate we may develop is approved for commercial sale, we anticipate incurring significant costs associated the commercialization of any such approved product candidate. Even though we generate revenues from the sale of Rezdiffra, we may not be able to achieve or maintain long-term sustainable profitability unless Rezdiffra is fully approved in the United States and European Union and is approved in other jurisdictions or for additional indications or our future product candidates are approved. Because of the uncertainties and risks associated with these activities, we are unable to accurately and precisely predict the timing and amount of revenues, the extent of any future losses or if we might sustain profitability.

Our failure to remain profitable may depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. If we suffer losses as we have in the past, investors may not receive any return on their investment and may lose their entire investment.

We may need to raise additional capital to fund our operations, but we face uncertainties with respect to our ability to access capital. If we are unable to raise capital if and when needed, we could be forced to delay, reduce or eliminate our drug development activities or commercialization efforts.

Our operations have consumed substantial amounts of capital since our inception and we may require additional working capital in the future. We expect to use substantial financial resources to, among other things, commercialize Rezdiffra, conduct additional trials and seek regulatory approvals, establish commercialization capabilities in Europe and fund potential strategic transactions. The amount and timing of any expenditure needed to fund our operations will depend on numerous factors, including:

- the costs associated with commercializing Rezdiffra;
- the type, number, scope, progress, expansion costs, results of and timing of our ongoing and future clinical trials or the need for additional clinical trials;
- the costs of obtaining, maintaining and enforcing our patents and other intellectual property rights;
- the timing and costs of maintaining marketing approvals for Rezdiffra in the United States and European Union;
- the number of other product candidates that we may pursue and such product candidate's development requirements;
- the timing of obtaining regulatory approval for any potential future product candidates;
- the costs and timing of obtaining or maintaining manufacturing for Rezdiffra;
- the costs and timing of building and maintaining our commercial infrastructure;
- the terms and timing of establishing and maintaining collaborations, license agreements and other strategic transactions;
- our headcount growth and associated costs as we expand our research and development efforts, increase our office space and establish a commercial infrastructure;
- costs associated with any new product candidates that we may develop, in-license or acquire;
- the effect of competing technological and market developments; and
- the ongoing costs of operating as a public company.

Some of these factors are outside of our control. These and other circumstances may cause us to delay certain research activities and related clinical expenses, but such delays will not alter our need to raise additional funding. As a result, we may need to raise substantial additional funds in the future. We may seek additional funding through future debt and equity financings, as well as potential additional collaborations or strategic partnerships with other companies or through non-dilutive financings. Additional funding may not be available to us on acceptable terms, or at all. In addition, the terms of any financing may adversely affect the holdings or the rights of our stockholders or have a potential restrictive effect on how we operate our business. In addition, market perception that we need to issue additional shares, the issuance of additional shares by us, or the possibility of such issuance, may cause the market price of our shares to decline.

If we are unable to obtain additional funding on a timely basis, our business may be materially and adversely affected. We also could be required to seek funds through arrangements with collaborative partners or otherwise that may require us to relinquish rights to our product candidates or otherwise agree to terms unfavorable to us.

Our quarterly and annual operating results may fluctuate in the future. As a result, we may fail to meet or exceed the expectations of research analysts or investors, which could cause our stock price to decline and negatively impact our financing or funding ability, as well as negatively impact our ability to exist as a standalone company.

Our financial condition and operating results have varied in the past and will continue to fluctuate from quarter-to-quarter and year-to-year in the future due to a variety of factors, many of which are beyond our control, such that the results of any of our prior quarterly or annual periods should not be relied upon as indications of our future operating performance. Additionally, a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

Our Financing Agreement contains restrictive and financial covenants that may limit our operating flexibility.

On July 17, 2025, we entered into a Financing Agreement with certain funds managed by Blue Owl Corporation as the lenders (the "Lenders") and LSI Financing LLC as the administrative agent (as amended, the "Financing Agreement"). Under the Financing Agreement, the Lenders have committed up to $500.0 million in senior secured credit facilities, consisting of (a) an initial term loan in an aggregate principal amount equal to $350.0 million (the "Initial Term Loan") and (b) delayed draw term loan commitments in an aggregate principal amount not to exceed $150.0 million (the loans thereunder, if any, the "Delayed Draw Term Loans"). In addition, the Financing Agreement includes an uncommitted incremental facility in an aggregate principal amount not to exceed $250.0 million (the loans thereunder, if any, the "Incremental Term Loans", together with the Initial Term Loan and any Delayed Draw Term Loans, collectively the "Term Loans"), subject to the satisfaction of certain terms and conditions set forth in the Financing Agreement. Our obligations under the Financing Agreement are secured by a security interest in substantially all of our assets. Until we have repaid such indebtedness, the Financing Agreement subjects us to various terms, conditions and covenants. These include financial reporting obligations, and certain limitations on indebtedness, liens (including a negative pledge on intellectual property and other assets), investments, distributions (including dividends), collateral, investments, distributions, transfers, mergers or acquisitions, taxes, corporate changes, and deposit accounts. Additionally, the Financing Agreement contains affirmative and restrictive covenants, including maintenance of a minimum unrestricted cash balance of $100.0 million. Our business may be adversely affected by these restrictions on our ability to operate our business. If we raise any additional debt financing, as permitted by the Financing Agreement and if pursued and secured by the Company, the terms of such additional debt could further restrict our operating and financial flexibility.

We may not be able to generate sufficient cash flow or sales to pay the principal and interest under the Term Loans. Furthermore, our future working capital, borrowings or equity financing could be unavailable to repay or refinance the amounts outstanding under the Term Loans. In the event of a liquidation, the Lenders would be repaid all outstanding principal and interest prior to distribution of assets to unsecured creditors, and the holders of our common stock would receive a portion of any liquidation proceeds only if all of our creditors then existing were first repaid in full.

Our failure to comply with the covenants or other terms of the Financing Agreement, including as a result of events beyond our control, could result in a default under the Financing Agreement that could materially and adversely affect our business.

We may be required to repay the outstanding indebtedness under the Financing Agreement if an event of default occurs under the Financing Agreement or, if applicable, any future debt facility. The Loan Agreement includes customary events of default, including payment defaults, breaches of covenants following any applicable cure period, the occurrence of certain events that could reasonably be expected to have a "material adverse effect" as set forth in the Financing Agreement and cross acceleration. We may not have enough available cash or be able to raise additional funds through equity or debt financings to repay such indebtedness at the time any such event of default occurs. In this case, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant to others rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Our business, financial condition and results of operations could be materially adversely affected as a result of any of these events.

Risks Related to Government Regulation

Government healthcare reform could materially increase our costs, which could materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

The pharmaceutical industry is highly regulated and changes in or revisions to laws and regulations that make gaining regulatory approval, reimbursement and pricing more difficult or subject to different criteria and standards may adversely impact our business, operations or financial results.

There have been a number of legal challenges and certain changes to the ACA since it was enacted. On January 28, 2021, an executive order was issued to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including, among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. Further, on February 10, 2021, the federal government's support for overturning the ACA was withdrawn. It is unclear how the Supreme Court ruling, other such litigation and the healthcare reform measures of the Biden Administration will impact the ACA. It is difficult to predict the future legislative landscape in healthcare and the effect on our business, results of operations, financial condition and prospects. Changes to the ACA, to the Medicare or Medicaid programs, or to the ability of the federal government to negotiate or otherwise affect drug prices, or other federal

legislation regarding healthcare access, financing or legislation in individual states, could affect our business, financial condition, results of operations and prospects and the value of our common stock. We may face similar challenges to gaining regulatory approval and sufficient reimbursement and pricing due to government healthcare reform in the EU, and other jurisdictions. It remains unclear how any new legislation or regulation might affect the prices we may obtain for Rezdiffra or any future product candidates for which regulatory approval is obtained.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional rebate requirements, penalties, or other sanctions, which could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

Under the Medicaid Drug Rebate program, a participating manufacturer is required to pay a rebate to each state Medicaid program for its covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by the state Medicaid program as a condition of having federal funds being made available for drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data reported by the manufacturer on a monthly and quarterly basis to CMS. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug, which, in general, represents the lowest price available from the manufacturer to any wholesaler, retailer, provider, health maintenance organization, nonprofit entity, or governmental entity in the United States in any pricing structure, calculated to include all sales and associated rebates, discounts, and other price concessions. If we fail to pay the required rebate amount or report pricing data on a timely basis, we may be subject to civil monetary penalties and/or termination from the Medicaid Drug Rebate program. Additionally, civil monetary penalties can be applied if we are found to have knowingly submitted any false price or product information to the government, if we fail to submit the required price data on a timely basis, or if we misclassify or misreport product information. CMS could also decide to terminate our Medicaid drug rebate agreement, in which case federal payments may not be available under Medicaid or Medicare Part B for our covered outpatient drugs. See the section titled "Business—Government Regulation—Pharmaceutical Price Reporting" in this Annual Report for more information.

The ACA (addressed further above in the section titled "Business—Government Regulation—U.S. Healthcare Reform") made significant changes to the Medicaid Drug Rebate Program, and CMS issued a final regulation to implement the changes to the Medicaid Drug Rebate Program under the ACA. Our failure to comply with these price reporting and rebate payment options, as well as pharmaceutical benefit manager "accumulator" programs, could negatively impact our financial results.

If we are found to have knowingly and intentionally charged 340B covered entities more than the statutorily mandated ceiling price, we could be subject to significant civil monetary penalties and/or such failure also could be grounds for HRSA to terminate our agreement to participate in the 340B program, in which case our covered outpatient drugs would no longer be eligible for federal payment under the Medicaid or Medicare Part B program.

Further, the IRA established a Medicare Part D inflation rebate scheme and a drug price negotiation program, with the first negotiated prices to take effect in 2026. It also makes several changes to the Medicare Part D benefit, including the creation of a new manufacturer discount program in place of the current coverage gap discount program (beginning in 2025). Manufacturers may be subject to civil monetary penalties for certain violations of the negotiation and inflation rebate provisions and an excise tax during a noncompliance period under the negotiation program. Drug manufacturers may also be subject to civil monetary penalties with respect to their compliance with the new Part D manufacturer drug discount program.

Pricing and rebate calculations are complex, vary across products and programs, and are often subject to interpretation by the manufacturer, governmental agencies, and courts. A manufacturer that becomes aware that its Medicaid reporting for a prior quarter was incorrect, or has changed as a result of recalculation of the pricing data, is obligated to resubmit corrected data up to three years after those data originally were due. Restatements and recalculations increase the costs for complying with the laws and policies governing the Medicaid Drug Rebate program and could result in an overage or underage in our rebate liability for past quarters. They also may affect the 340B ceiling price and therefore liability under the 340B program.

Finally, in order to be eligible to have its products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by the Big Four Agencies and certain federal grantees, a manufacturer is required to participate in the VA FSS pricing program, established under Section 603 of the Veterans Health Care Act of 1992. If we overcharge the government in connection with the FSS contract or Tricare Retail Pharmacy Rebate Program, whether due to a misstated FCP or otherwise, we will be required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against us under the False Claims Act and other laws and regulations. Unexpected refunds to the government, and any response to government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Under Section 703 of the National Defense Authorization Act, a manufacturer is required to pay quarterly rebates to DoD on utilization of its innovator products that are dispensed through DoD's Tricare network pharmacies to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non-FAMP and FCP for the calendar year that the product was dispensed. A manufacturer that overcharges the government in connection with the FSS contract or Tricare Retail Pharmacy Rebate Program, whether due to a misstated FCP or otherwise, is required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against us under the False Claims Act and other laws and regulations.

If we are found in violation of federal or state "fraud and abuse" laws, we may be required to pay a penalty or may be suspended from participation in federal or state healthcare programs, which may adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

In the United States, we are subject to various federal and state healthcare "fraud and abuse" laws, including anti-kickback laws, false claims laws and other laws intended to reduce fraud and abuse in federal and state healthcare programs. Although we seek to structure our business arrangements in compliance with all applicable requirements, these laws are broadly written, and it is often difficult to determine precisely how the law will be applied in specific circumstances. Accordingly, it is possible that our practices may be challenged under these laws. Violations of fraud and abuse laws may be punishable by criminal and/or civil sanctions, including fines or exclusion or suspension from federal and state healthcare programs such as Medicare and Medicaid and debarment from contracting with the U.S. government, and our business, financial condition, results of operations and prospects and the value of our common stock may be adversely affected. Our reputation could also suffer. In addition, private individuals have the ability to bring actions on behalf of the government under the federal False Claims Act as well as under the false claims laws of several states. See the section titled "Business—Government Regulation—Other Healthcare Laws" in this Annual Report for more information.

Under the ACA and certain state laws, we are required to report information on payments or transfers of value to any U.S. physicians, physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, or certified nurse-midwives (in each case who are not bona fide employees of the applicable manufacturer that is reporting the payment) and teaching hospitals, which is posted in searchable form on a public website. Failure to submit required information may result in civil monetary penalties.

Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state. In addition to the federal government, some states, as well as other countries, including France, require the disclosure of certain payments to healthcare professionals. HIPAA, state, and foreign privacy laws may limit access to information identifying those individuals who may be prospective users or limit the ability to market to them. Some of these laws are new or ambiguous as to what is required to comply with their requirements, and we could be subject to penalties if it is determined that we have failed to comply with an applicable legal requirement.

We are subject to anti-corruption laws and trade control laws, as well as other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures, legal expenses, and negative publicity which could adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

Our operations are currently subject to anti-corruption laws, including the U.S. Foreign Corrupt Practices Act ("FCPA"). In addition, if we expand sales of Rezdiffra to other jurisdictions, we'll be subject to anti-corruption or similar laws that apply in countries where we do business. The FCPA and these other laws generally prohibit us, our employees and our intermediaries from making prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the U.S. Department of Commerce's Bureau of Industry and Security, the U.S. Department of Treasury's Office of Foreign Assets Control, and various non-U.S. government entities, including applicable export control regulations, economic sanctions on countries and persons, customs requirements, currency exchange regulations and transfer pricing regulations (collectively, "Trade Control Laws").

We may not be effective in ensuring our compliance with all applicable anti-corruption laws, including the FCPA or other legal requirements, including Trade Control Laws. If we are not in compliance with the FCPA and other anti-corruption laws or Trade Control Laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and prospects and the value of our common stock. Likewise, even an investigation by US or foreign authorities of potential violations of the FCPA other anti-corruption laws or Trade Control Laws could have an

adverse impact on our reputation, business, financial condition, results of operations and prospects and the value of our common stock.

Disruptions at the FDA and other government agencies caused by the change in presidential administration, funding shortages or potential funding shortages could hinder their ability to hire and retain key leadership and other personnel, delay or prevent new products and services from being developed or commercialized in a timely manner, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to operate, including to review and approve new products, provide feedback on clinical trials and development programs, meet with sponsors and otherwise review regulatory submissions can be affected by a variety of factors, including government budget and funding levels; ability to hire and retain key personnel and accept the payment of user fees; and statutory, regulatory, leadership and policy changes, including as a result of shifting policy priorities of the current presidential administration and political appointees tasked to oversee the agency, among other factors. Average review times at the agency may fluctuate as a result. For example, in 2025, changes and cuts in FDA staffing have been reported as resulting in delays in the FDA's responsiveness or in its ability to review IND submissions or marketing applications. In addition, government funding of other government agencies on which our operations may rely is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies or to otherwise respond to regulatory submissions, which would adversely affect our business. Over the last several years, the U.S. government has shut down multiple times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA and other government employees and stop critical activities. The FDA is currently funded through September 30, 2026. Without appropriation of necessary funding to federal agencies, our business operations related to our product development activities for the U.S. market could be impacted. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Failure to comply with health and data protection laws and regulations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation and/or adverse publicity, and could negatively affect our operating results and business.

We may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA imposes privacy and security obligations on covered entity health care providers, health plans, and health care clearinghouses, as well as their "business associates" – certain persons or covered entities that create, receive, maintain, or transmit protected health information in connection with providing a specified service or performing a function on behalf of a covered entity. We could potentially be subject to criminal penalties if we, our affiliates, or our agents knowingly receive individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA. Failing to take appropriate steps to keep consumers' personal information secure may also constitute unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act (the "FTCA"), 15 U.S.C § 45(a). The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business and the cost of available tools to improve security and reduce vulnerabilities.

Regulators and legislators in the U.S. are also increasingly scrutinizing and restricting certain personal data transfers and transactions involving foreign countries. For example, the Department of Justice's January 28, 2025 rule on "Preventing Access to U.S. Sensitive Personal Data and Government-Related Data by Countries of Concern or Covered Persons" prohibits data brokerage transactions involving certain sensitive personal data categories, including health data, genetic data, and biospecimens, to countries of concern, including China. The regulations also restrict certain investment agreements, employment agreements and vendor agreements involving such data and countries of concern, absent specified cybersecurity controls. Actual or alleged violations of these regulations may be punishable by criminal and/or civil sanctions and may result in exclusion from participation in federal and state programs.

Further, 20 U.S. states have implemented comprehensive laws which govern the privacy and security of personal information. For example, to the extent we collect California resident personal information, we may also be subject to the CCPA. The CCPA, created a comprehensive privacy framework which granted California residents several new rights with regard to their personal information. The CCPA was amended by the California Privacy Rights Act ("CPRA") ballot initiative which as of January 1, 2023 has introduced significant amendments to the CCPA and established and funded a dedicated California privacy regulator, the California Privacy Protection Agency ("CPPA"). Failure to comply with the CCPA may result in, among other things, significant civil penalties and injunctive relief, or statutory or actual damages. In addition, California residents have the right to bring a private right of action in connection with data breaches. These claims may result in significant liability and damages. Similar laws have been passed in numerous other states, adding additional

complexity, variation in requirements, restrictions and potential legal risk, requiring additional investment of resources in compliance programs. The implementation of these laws may impact our strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies. These laws and regulations are evolving and may impose limitations on our business activities.

The existence of comprehensive privacy laws in different states in the country may make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance. There are also states that are specifically regulating health information. For example, Washington's My Health My Data Act, which became effective on March 31, 2024, regulates the collection and sharing of health information and has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data. In addition, other states have proposed and/or passed legislation that regulates the privacy and/or security of certain specific types of information. For example, a small number of states, including Texas and Illinois, have passed laws that regulate biometric data specifically. These various privacy and security laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products. State laws are changing rapidly and there are discussions in the U.S. Congress of new comprehensive federal data privacy laws to which we could become subject to, if enacted.

All of these evolving compliance and operational requirements impose significant costs, such as costs related to organizational changes, implementing additional protection technologies, training employees and engaging consultants and legal advisors, which are likely to increase over time. The obligations to comply with new privacy laws may require us, among other things, to update our notices and develop new processes internally and with our third-party collaborators, service providers, contractors or consultants to facilitate consumer rights requests, and such laws may impose restrictions on our processing of personal information that may impact the way we operate our business. Any failure or perceived failure by us to comply with any applicable federal, state or foreign laws and regulations relating to data privacy and security could result in damage to our reputation, as well as proceedings or litigation by governmental agencies or other third parties, including class action privacy litigation in certain jurisdictions, which would subject us to significant fines, sanctions, awards, injunctions, penalties or judgments. We may be subject to fines, penalties, or private actions in the event of non-compliance with such laws. The CCPA, the CPRA or other domestic privacy and data protection laws and regulations may increase our compliance costs and potential liability. In addition, such requirements may require us to modify our data processing practices and policies, utilize management's time and/or divert resources from other initiatives and projects. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

European data collection is governed by restrictive regulations governing the use, processing and cross-border transfer of personal information.

Outside the United States, our clinical trial programs and operations implicate international data protection laws, including the EU General Data Protection Regulation ("EU GDPR") including the EU GDPR in such form as implemented into the laws of the UK ("UK GDPR", collectively with EU GDPR, "GDPR"). The GDPR increases our responsibility and liability in relation to the processing of personal data of individuals located in the EU. The GDPR, together with the national legislation of the EU member states governing the processing of personal data, places numerous obligations on companies, including requirements relating to processing health and other sensitive data, where required obtaining consent of the individuals to whom the personal data relates, having legal bases or conditions for processing, requiring disclosures to individuals regarding data processing activities, requiring that safeguards are implemented to protect the security and confidentiality of personal data, responding to individuals' requests to exercise their rights, limiting retention periods for personal data, creating mandatory data breach notification requirements in certain circumstances, requiring that certain measures (including contractual requirements) are put in place when engaging third-party processors, appointing data protection officers, conducting data protection impact assessments, ensuring certain accountability measures are in place and record keeping. Companies that fail to comply with the GDPR may face temporary or definitive bans on data processing and other corrective actions; fines of up to €20 million under the EU GDPR, or £17.5 million under the UK GDPR, or 4% of annual global revenue, whichever is greater; or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests.

Although the UK is regarded as a third country under the EU GDPR, the EC has now issued a decision recognizing the UK as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EU to the UK remain unrestricted. In December 2025, the EC adopted a decision to extend the validity of the UK adequacy decision for six years until December 2031, determining that the UK continues to offer a level of data protection that is "essentially equivalent" to the EU standards. This follows the UK's adoption of the Data (Use and Access) Act 2025 (the "DUAA") in June 2025. The respective provisions and enforcement of the EU GDPR and UK GDPR may further diverge in the future and create additional regulatory challenges and uncertainties. This lack of clarity on future UK laws and regulations and their interaction with EU laws and regulations could add legal risk, complexity and

cost to our handling of personal data and our privacy and data security compliance programs and could require us to implement different compliance measures for the UK and the EEA. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the UK to countries not regarded by the UK as providing adequate protection. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing.

Specifically regarding the transfer of personal data outside of the EU and UK, adequate safeguards must be implemented in compliance with EU and UK data protection laws. There are currently various mechanisms that may be used to transfer personal data from the EEA and UK to the United States in compliance with law, such as the EEA's standard contractual clauses, the UK's International Data Transfer Agreement / Addendum, and the EU-U.S. Data Privacy Framework ("Framework") and the UK extension thereto (which allows for transfers to relevant U.S.-based organizations who self-certify compliance and participate in the Framework). When relying on certain mechanisms, such as the EEA's standard contractual clauses, companies are required to conduct transfer impact assessments. Our ability to continue to transfer personal data outside of the EU, the UK or Switzerland may become significantly more expensive and may subject us to increased scrutiny and liability under the GDPR or similar local laws, and we may experience operating disruptions if we are unable to conduct these transfers in the future.

Risks associated with operations outside of the United States could adversely affect our business.

Following the receipt of a CMA by the EC, we launched Rezdiffra in Germany in September 2025. International operations and business expansion plans are subject to numerous additional risks, including:

- multiple, conflicting and changing laws and regulations such as tax laws, privacy regulations, tariffs, export and import restrictions, employment, immigration and labor laws, regulatory requirements, and other governmental approvals, permits and licenses, compliance with which can increase in complexity as we enter into additional jurisdictions;
- difficulties in staffing and managing operations in diverse countries and difficulties in connection with assimilating and integrating any operations and personnel we might acquire into our company;
- risks associated with obtaining and maintaining, or the failure to obtain or maintain, regulatory approvals for the sale or use of our products in various countries;
- complexities associated with managing government payor systems, multiple payor-reimbursement regimes or patient self-pay systems;
- financial risks, such as longer payment cycles, difficulty obtaining financing in foreign markets, difficulty enforcing contracts and intellectual property rights, difficulty collecting accounts receivable and exposure to foreign currency exchange rate fluctuations;
- general political and economic conditions in the countries in which we operate, including inflation, political or economic instability, terrorism and political unrest and geopolitical events; and
- public health risks, including epidemics and pandemics, and related effects on new patient starts, clinical trial activity, regulatory agency response times, supply chain, travel and employee health and availability.

Risks Related to Our Intellectual Property

Our success depends on our ability to protect our intellectual property and our proprietary technologies.

Our success depends on our ability to protect our intellectual property and our proprietary technologies. Our commercial success depends in part on our ability to obtain and maintain patent and/or trade secret protection for our product, product candidates, proprietary technologies, and their uses, as well as our ability to freely operate without infringing upon the proprietary rights of others.

We can provide no assurance that our patent applications or those of our licensors will result in additional patents being issued or that issued patents will afford sufficient protection against competitors with similar technologies, nor can we provide any assurance that the patents issued will not be infringed, designed around or invalidated by third parties. Even issued patents may later be found unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. This failure to properly protect the intellectual property rights relating to our product or product candidates could have a material adverse effect on our financial condition and results of operations. While we own patents and have licensed rights to issued patents in the United States and other jurisdictions for resmetirom and its use, we cannot be certain

that the claims in issued patents will not be found invalid or unenforceable if challenged. We cannot be certain that the claims in owned and licensed patent applications covering our product and product candidates will be considered patentable by the United States Patent and Trademark Office ("USPTO") and valid by courts in the United States or by the patent offices and courts in foreign jurisdictions. Even if we owned and licensed patent applications covering our product and product candidates, the patents may not be enforced against competitors. For example, a formulation patent may not be enforced against those making and marketing a product that has the same active pharmaceutical ingredient in a different formulation that is not claimed in the formulation patent. Method-of-use patents protect the use of a product for the specified method or for treatment of a particular indication. This type of patent may not be enforced against competitors making and marketing a product that has the same active pharmaceutical ingredient but is used for a method not claimed in the patent. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products "off-label." Although off-label prescriptions may infringe, induce, or contribute to the infringement of method-of-use patents, the practice is common and such infringement may be difficult to prevent or prosecute.

Our composition-of-matter patent licensed from Roche relating to resmetirom is scheduled to expire in the United States in 2026. Our co-owned patents and pending patent applications that cover our particular solid form, dosage, method of manufacturing, and uses of resmetirom to treat various indications are scheduled to expire in 2033. Our patent directed to Rezdiffra's commercial weight-threshold dosing regimen is scheduled to expire in the United States in 2045. Our pending patent applications that cover various solid forms of resmetirom, combination therapy, method of use, and method of manufacturing, if issued, are expected to expire between 2037 and 2045. While patent term adjustments or patent term extensions could result in later expiration dates for each of these patents, there can be no assurances that we will receive any patent adjustments or patent term extensions. The patent application process and patent maintenance and enforcement are subject to numerous risks and uncertainties, and there can be no assurance that we or any of our future development partners will be successful in protecting our product and product candidates by obtaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process and after a patent has issued. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case;
- patent applications may not result in any patents being issued;
- patents may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- we and our licensor(s) may not have been the first to make the inventions covered by pending patent applications or issued patents;
- we and our licensor(s) may not have been the first to file patent applications for our product or product candidates or the compositions developed, or for their uses;
- others may independently develop identical, similar or alternative products or compositions and uses thereof;
- we and our licensor(s)' disclosures in patent applications may not be sufficient to meet the statutory requirements for patentability;
- others may design around our owned and licensed patent claims to produce competitive products which fall outside of the scope of the patents;
- others may identify prior art or other bases which could invalidate our or our licensor(s)' patents;
- our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where us and our licensor(s) do not have patent rights, and then use the information learned from such activities to develop competitive products for sale in major commercial markets;
- there may be significant pressure on the United States government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and

- countries other than the United States may have patent laws less favorable to patentees than those upheld by United States courts, allowing foreign competitors a better opportunity to create, develop and market competing products.

In addition, we rely on the protection of our trade secrets and proprietary know-how. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants and advisors, we cannot provide any assurances that any of these parties would not breach the agreements to disclose any proprietary information, including trade secrets, and we may not be able to obtain adequate remedies for such breaches. Further, third parties may still obtain this information by other means, such as breaches of our physical or computer security systems. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. Moreover, third parties may come upon this or similar information lawfully and independently. We would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. Further, intellectual property rights have limitations and do not necessarily address all potential threats to our competitive position. If any of these events occurs or if we otherwise lose protection for our trade secrets or proprietary know-how, our business may be harmed.

Our rights to develop and commercialize resmetirom are subject in part to the terms and conditions of the Roche Agreement.

Pursuant to the terms of the Roche Agreement, we assumed control of all development and commercialization of resmetirom and hold exclusive worldwide rights for all potential indications. Under the Roche Agreement, Roche exclusively licensed certain patent rights and know-how relating to resmetirom in exchange for consideration consisting of an upfront payment, milestone payments tied to the achievement of product development and regulatory milestones, and royalty payments based on net sales of products containing resmetirom, including Rezdiffra, or another licensed product, subject to certain reductions. Pursuant to the Roche Agreement, our obligation to pay Roche royalties in a given country will expire on the last to occur of (i) the expiration of the last valid claim of a licensed patent covering the manufacture, use or sale of products containing resmetirom in a given country, or (ii) ten years after the first sale of a product containing resmetirom in such country.

We do not have, nor have we had, any material disputes with Roche regarding the Roche Agreement. However, if there is any future dispute between us and Roche regarding the parties' rights under the Roche Agreement, our ability to develop and commercialize resmetirom, or any other product candidate covered by the Roche Agreement, may be materially harmed. Any uncured, material breach under the Roche Agreement could result in our loss of exclusive rights to resmetirom and may lead to a complete termination of the Roche Agreement and force us to cease product development efforts for resmetirom.

We may fail to comply with any of our obligations under agreements pursuant to which we license rights or technology, which could result in the loss of rights or technology that may be material to our business.

We have entered into license agreements for MGL-2086, ervogastat and our siRNA programs, and may enter into additional license agreements in the future. Licensing of intellectual property is important to our business and involves complex legal, business and scientific issues. Disputes may arise regarding intellectual property subject to a license agreement, including but not limited to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by us and our licensors and collaborators; and
- the priority of invention of patented technology.

If disputes over intellectual property and other rights that we have licensed or acquired from third parties prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product or product candidates.

If we do not obtain protection under the Hatch-Waxman Act and similar foreign legislation by extending the term of patents covering our product or product candidates, our business may be materially harmed.

Depending upon the timing, duration and conditions of FDA marketing approval of our products, one or more of our United States patents may be eligible for limited patent term extension under Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product may not extend beyond the current patent expiration dates and competitors may obtain approval to market competing products sooner. As a result, our revenue could be potentially materially reduced. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

On September 16, 2011, the Leahy-Smith America Invents Act (the "Leahy-Smith Act") was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a "first inventor to file" system in which the first inventor to file a patent application will be entitled to the patent. Third parties are allowed to submit prior art before the issuance of a patent by the USPTO, and a patent may become subject to post-grant proceedings including opposition, derivation, reexamination, *inter partes* review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position.

Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts.

The biotechnology industry has been characterized by frequent litigation regarding patent and other intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we have and are developing products and product candidates. As the biotechnology industry expands and more patents are issued, the risk increases that our product and product candidates may be subject to claims of infringement of the patent rights of third parties. Because patent applications are maintained in secrecy until the application is published, we may be unaware of third party patents that may be infringed by commercialization of resmetirom or our other product candidates. Moreover, because patent applications can take many years to issue, there may be currently-pending patent applications that may later result in issued patents that our product and product candidates may infringe. In addition, identification of third party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. Any claims of patent infringement asserted by third parties would be time consuming and could likely:

- result in costly litigation;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing resmetirom for MASH or our other product candidates until the asserted patent expires or is held finally invalid or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis; or
- require us to enter into royalty or licensing agreements.

Although no third party has asserted a claim of patent infringement against us as of the filing date of this report, others may hold proprietary rights that could prevent resmetirom or our other product candidates from being marketed. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to our

product and product candidates or processes could subject us to potential liability for damages and require us to obtain a license to continue to manufacture or market resmetirom or our other product candidates. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. In addition, we cannot be sure that we could redesign our product or product candidates or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing resmetirom or our other product candidates, which could harm our business, financial condition and operating results.

Moreover, we may be subject to a third party preissuance submission of prior art to the USPTO or in addition to interference proceedings, may become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review or other post-grant proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future products and product candidates.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged in court.

If we or any of our future development partners were to initiate legal proceedings against a third party to enforce a patent directed at our product or one of our product candidates, or one of our future product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement or insufficient written description. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product or product candidate. Such a loss of patent protection would have a material adverse impact on our business.

Interference proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our product candidates to market.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

We may not be successful in obtaining or maintaining necessary rights to our product and product candidates through acquisitions and in-licenses.

We currently have rights to the intellectual property, through licenses from third parties and under patents that we own or co-own, to develop and market our product and product candidates. Because our programs may require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license, or use these proprietary rights. For example, our product or product candidates may require specific formulations to work effectively and efficiently and the rights to these formulations may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes, or other third party intellectual property rights from third parties that

we identify as necessary for our product or product candidates. The licensing and acquisition of third party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources, and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

We may collaborate with U.S. and foreign academic institutions and industry collaborators to accelerate our preclinical or clinical research. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

If we are unable to successfully obtain rights to required third party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of that program and our business and financial condition could suffer.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third parties to research and develop and to manufacture our product and product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Any of these could impair our competitive position.

In addition, these agreements typically restrict the ability of our advisors, employees, third party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. For example, any academic institution that we may collaborate with in the future will usually expect to be granted rights to publish data arising out of such collaboration, provided that we are notified in advance and given the opportunity to delay publication for a limited time period in order for us to secure patent protection of intellectual property rights arising from the collaboration, in addition to the opportunity to remove confidential or trade secret information from any such publication. In the future we may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

We may not be able to protect our intellectual property rights throughout the world.

While we have licensed from Roche issued patents directed at resmetirom, and have filed our own patent applications and have obtained our own issued patents, in the United States and other countries, filing, prosecuting and

defending patents on resmetirom in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries may not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing their inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with resmetirom, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Risks Related to Ownership of Our Common Stock

The price of our common stock has been, and may continue to be, volatile.

Historically, the market price of our common stock has fluctuated over a wide range, and it is likely that the price of our common stock will continue to be volatile in the future. The closing price of our common stock has ranged from $267.56 to $602.83 per share during the year ended December 31, 2025. The market price of our common stock could be impacted due to a variety of factors, including global market or financial developments; prevailing macroeconomic conditions, including potential recession or economic downturns; U.S. market events (including the potential for unusual market trading activity following external short interest developments or social media activity); the outbreak of war or hostilities; MASH therapeutic company developments or FDA developments, regardless of whether occurring generally or specifically as to our clinical trials and development programs; industry-wide events and the following events or developments:

- the losses we may incur, including increased losses resulting from costs associated with increases in our clinical trial activity;
- our cash position and rate of expenditures;
- our ability to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- product revenue;
- regulatory decisions, including our ability to receive full regulatory approval for Rezdiffra and our ability to receive regulatory approval for any future product candidates;
- changes in laws or regulations applicable to Rezdiffra and any other future product candidates, including but not limited to clinical trial requirements for approvals;
- our ability to successfully commercialize Rezdiffra and any other future product candidates, if approved;
- developments in patent or other proprietary rights owned or licensed by us, our collaborative partners or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- the progress and results of our clinical trials;
- public or regulatory concern as to the safety and efficacy of MASH products developed by us or others or public safety generally;

- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- introduction of new products or services offered by us or our competitors, or the release or publication of clinical trial results from competing product candidates;
- changes in the market valuations of similar companies;
- our ability to obtain coverage and adequate reimbursement of Rezdiffra and any future product candidates, if approved;
- our ability to effectively manage our growth;
- actual or anticipated variations in quarterly operating results;
- announcements of significant acquisitions, strategic partnerships, joint ventures, or capital commitments by us or our competitors;
- any changes to our relationship with any manufacturers, suppliers, licensors, future collaborators or other strategic partners;
- our ability to obtain adequate product supply for any approved drug product or inability to do so at acceptable prices;
- changes to the structure of healthcare payment systems;
- our ability to establish collaborations, if needed;
- additions or departures of key scientific or management personnel;
- litigation;
- issuances of debt or equity securities;
- sales of our common stock by us or our stockholders in the future or the perception that such sales may occur;
- trading volume of our common stock;
- changes in accounting practices;
- effectiveness of our internal controls; and
- other events or factors, many of which are beyond our control.

In addition, due to one or more of the foregoing factors in one or more future quarters, our results of operations may fall below the expectations of securities analysts and investors. In the event any of the foregoing occur, the market price of our common stock could be highly volatile and may materially decline.

Anti-takeover provisions in our restated certificate of incorporation (our "Charter"), our Restated Bylaws (our "Bylaws") and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management, which may depress the trading price of our common stock.

Provisions in our Charter and Bylaws may delay or prevent a merger, acquisition or other change of control that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our Charter and Bylaws:

- provide for a classified board of directors with three classes;
- permit our board of directors to issue certain shares of preferred stock, with any rights, preferences and privileges as they may designate (including the right to approve an acquisition or other change in our control);
- provide that the authorized number of directors may be changed only by resolution of the board of directors;
- provide that our board of directors or any individual director may only be removed with cause and by the affirmative vote of the holders of at least 80% of the voting power of all of our then-outstanding shares of capital stock entitled to vote at an election of directors, voting together as a single class;

- provide that all vacancies, including newly created directorships, may, except as otherwise required by law, be filled only by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide notice in writing in a timely manner and also specify requirements as to the form and content of a stockholder's notice;
- do not provide for cumulative voting rights (therefore allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose);
- provide that special meetings of our stockholders may be called only by the board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors; and
- provide that the Court of Chancery of the State of Delaware (or, in the event that the Delaware Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware or other state courts of the State of Delaware) is the sole and exclusive forum for the any stockholder to bring: (i) any derivative action or proceeding brought on our behalf; (ii) any action or proceeding asserting a claim of breach of a fiduciary duty owed by any of our current or former directors, officers or other employees to us or our stockholders; (iii) any action or proceeding asserting a claim against us or any of our current or former directors, officers or other employees, arising out of or pursuant to any provision of the Delaware General Corporation Law, our Charter or our Bylaws or (iv) any action asserting a claim governed by the internal affairs doctrine, in all cases to the fullest extent permitted by law and subject to the court's having personal jurisdiction over any indispensable parties.

The amendment of any of these provisions, with the exception of the ability of our board of directors to issue shares of preferred stock and designate any rights, preferences and privileges thereto, would require approval by the holders of at least 80% of our then-outstanding common stock.

In addition, as a Delaware corporation, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits, with some exceptions, stockholders owning 15% or more of our outstanding voting stock from merging or combining with us for a certain period of time. A Delaware corporation may opt out of this provision by express provision in its original certificate of incorporation or by amendment to its certificate of incorporation or bylaws approved by its stockholders. However, we have not opted out of this provision.

Although we believe these provisions together provide for an opportunity to receive higher bids by requiring potential acquirers to negotiate with our board of directors, such provisions would apply even if the offer may be considered beneficial by some stockholders. These and other provisions in our charter and bylaws and under Delaware law could make it more difficult for stockholders or potential acquirors to obtain control of our board of directors or initiate actions that are opposed by our then-current board of directors, and could delay or impede a merger, tender offer or proxy contest involving our company. The existence of these provisions could negatively affect the price of our common stock and limit opportunities for you to realize value in a corporate transaction.

Our bylaws provide that the Court of Chancery of the State of Delaware and the federal district court of the United States for the District of Delaware will be the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our bylaws provide that, to the fullest extent permitted by law and subject to the court's having personal jurisdiction over any indispensable parties, the Court of Chancery of the State of Delaware is the exclusive forum for (i) any derivative action or proceeding brought on our behalf; (ii) any action or proceeding asserting a claim of breach of a fiduciary duty owed by any of our current or former directors, officers or other employees to us or our stockholders; (iii) any action or proceeding asserting a claim against us or any of our current or former directors, officers or other employees, arising out of or pursuant to any provision of the Delaware General Corporation Law, our Charter or our Bylaws or (iv) any action asserting a claim governed by the internal affairs doctrine.

This exclusive forum provision may limit a stockholder's ability to bring a claim in a judicial forum that such stockholder finds favorable for disputes with us or our directors, officers or other employees, which may discourage lawsuits against us and our directors, officers and other employees. If a court were to find such exclusive forum provision

to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving the dispute in other jurisdictions, which could seriously harm our business.

Future sales and issuances of our common stock or rights to purchase common stock could result in additional dilution of the percentage ownership of our stockholders and could cause our share price to fall.

Significant additional capital may be needed in the future to continue our planned operations. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. We have in the past used, and currently have the ability to use, an "at-the-market" ("ATM") sales program to raise capital by selling our securities through a sales agent up to established limits, and have also issued shares of our common stock in registered offerings and shares of convertible preferred equity to institutional investors in registered and private direct offerings. We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital or convertible securities, through any ATM program, public equity offering, direct offering, private offering or otherwise, our stockholders may experience substantial dilution. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

Funds affiliated with Baker Bros. Advisors LP hold a significant portion of our total outstanding shares of common stock (including shares of our common stock issuable upon conversion of shares of our Series A Convertible Preferred Stock and Series B Convertible Preferred Stock and pre-funded warrants), and any sale of such shares into the market, or a perception that such sales could occur, in the future could cause the market price of our common stock to drop significantly.

Based on a Schedule 13D/A filed with the SEC on March 25, 2024 and subsequent filings with the SEC, 667, L.P. and Baker Brothers Life Sciences, L.P., funds affiliated with Baker Bros. Advisors LP ("Baker Bros."), reported an ownership interest in (i) Madrigal common stock and (ii) other Madrigal securities with limitations on conversion or exercise to common stock. If such limitations did not exist, Baker Bros. would be deemed to beneficially own 7,219,498 shares of our common stock (which includes 1,969,797 shares of common stock issuable upon the conversion of our Series A Convertible Preferred Stock and 400,000 shares of common stock issuable upon the conversion of our Series B Convertible Preferred Stock, each of which are common stock equivalents with no voting rights, that are convertible into shares of common stock on a 1-for-1 basis only to the extent that after giving effect to such conversion the holders thereof and their affiliates and any persons who are members of a Section 13(d) group with such holders or their affiliates would beneficially own (in the aggregate, for purposes of Rule 13d-3 under the Exchange Act) no more than 4.99% of the outstanding common stock. The Series B Convertible Preferred Stock beneficial ownership limitation may be increased or decreased up to 19.99% at the holder's election, provided that any such increase will not be effective until the 61st day after such notice is provided to us. The Series A Convertible Preferred Stock beneficial ownership limitation may be increased or decreased to any other percentage provided that any such increase or decrease will not be effective until the 61st day after such notice is provided to us (the "Beneficial Ownership Limitations"). The 7,219,498 total shares also include 2,705,790 pre-funded warrants. Without such limitations on conversion or exercise, Baker Bros. total ownership would represent approximately 26% of our total outstanding shares of common stock as of December 31, 2025 on a fully exercised or as-converted to common stock basis. The pre-funded warrants are only exercisable to the extent that, after giving effect to such exercise, the holders thereof, together with their affiliates and any members of a Section 13(d) group with such holders, would beneficially own, for purposes of Rule 13d-3 under the Exchange Act, no more than 9.99% of the outstanding shares of our common stock (the "Maximum Percentage"). By written notice to us, holders of the pre-funded warrants may from time to time increase or decrease the Maximum Percentage to any other percentage not in excess of 19.99%. Any such increase in the Maximum Percentage will not be effective until the 61st day after such notice is provided to us. In addition, the 7,219,498 total shares includes 6,220 shares underlying vested restricted stock units and 2,210 shares underlying vested stock options granted to representatives of Baker Bros. that serve on our Board of Directors. Sales of a substantial number of shares of our common stock in the public market by Baker Bros., or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales by Baker Bros., or any perception that such sales may occur, may have on the prevailing market price of our common stock.

Sales of a significant number of shares of our common stock in the public markets or significant short sales of our common stock, or the perception that such sales could occur, could depress the market price of our common stock and impair our ability to raise capital.

As of December 31, 2025, there were a number of investors or investor groups that held a significant beneficial ownership interest in our common stock. Based on a Schedule 13D/A filed on December 12, 2025 by each of Dr. Paul Friedman, a member of our board of directors, and Dr. Rebecca Taub, a member of our board of directors and our former

Chief Medical Officer and President of Research and Development, they collectively beneficially own 1,814,831 shares (7.8%) of our common stock (the "Friedman/Taub Holdings"). Based on a Schedule 13D/A filed with the SEC on March 25, 2024 and subsequent SEC filings, funds affiliated with Baker Bros. Advisors LP beneficially owned (for SEC reporting purposes) 9.99% of our common stock and maintained an ownership interest in up to 7,219,498 shares of our common stock subject to exercise or conversion limits such as the Beneficial Ownership Limitation and the Maximum Percentage (the "Baker Bros. Holdings"), as described in the preceding paragraph. Based on a Schedule 13G/A filed with the SEC on February 14, 2024, funds affiliated with Avoro Capital Advisors LLC reported beneficial ownership of 2,288,888 shares of our common stock, including pre-funded warrants to purchase 400,000 shares of common stock that are subject to the Maximum Percentage (the "Avoro Holdings"). In addition, as of December 31, 2025, there are: 2,034,771 shares of our common stock issuable upon the exercise of outstanding stock options or the vesting of restricted stock units and performance stock units (assuming the maximum outcome of the performance conditions) under our 2015 Stock Plan, as amended, 2023 Inducement Plan and 2025 Inducement Plan; pre-funded warrants to purchase shares of common stock pursuant to outstanding pre-funded warrants as described above and 19,454 shares of our common stock issuable upon the exercise of outstanding vested warrants held by our former creditors consisting of Hercules Capital Inc. ("Hercules") and affiliates. In addition, there are other institutional investors (including funds affiliated with Janus Henderson Group plc, which reported beneficial ownership of 1,842,690 shares of our common stock (8.3%) in a Schedule 13G/A filed with the SEC on November 14, 2025) who from time to time file Schedule 13Gs (or amendments thereto) or Form 13Fs reflecting substantial beneficial ownership of our outstanding common stock.

Sales of a substantial number of shares of our common stock by one or more of the investors or groups listed above or other equity-related securities in the public markets could depress the market price of our common stock and impair our ability to raise capital. If there are significant sales or short sales of our stock, the price decline that could result from this activity may cause the share price to decline further, which, in turn, may cause long holders of our common stock to sell their shares, thereby contributing to sales of common stock in the market. See the risk factor titled "The price of our common stock has been, and may continue to be, volatile." for additional information. Such sales or short sales also may impair our ability to raise capital through the sale of additional shares in the future at a time and price that our management deems acceptable, if at all.

We do not anticipate paying cash dividends on our common stock, and accordingly, stockholders must rely on stock appreciation, if any, for any return on their investment.

We have never declared or paid any cash dividend on our common stock and do not anticipate paying cash dividends on our common stock in the future. As a result, the only return to stockholders will be appreciation in the price of our common stock, which may never occur. Investors seeking cash dividends should not invest in our common stock.

If securities analysts publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock depends in part on the research and reports that industry or securities analysts publish about us or our business. If one or more of the analysts who may cover us issues an adverse opinion about our company, our stock price would likely decline. If one or more of these analysts ceases research coverage of us or fails to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

General Risk Factors

We incur significant costs as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives.

As a public company, we incur significant and ongoing legal, accounting and other expenses. We are subject to the reporting requirements of the Securities Exchange Act of 1934, which require, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and the Nasdaq Stock Market ("Nasdaq") to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act (the "Dodd-Frank Act") was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that required the SEC to adopt additional rules and regulations in areas such as "say on pay" and proxy access. Stockholder activism, the current political environment and regulatory reform may lead to changes in regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We expect to continue to incur substantial costs to comply with the rules and regulations applicable to public companies. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. Any increased costs will decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

A failure of our information technology infrastructure and cybersecurity threats may adversely affect our business and operations.

Our information technology infrastructure is subject to threats from cybersecurity incidents, data breaches, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. In addition, the information technology systems of our current or future third-party collaborators, service providers, contractors and consultants are subject to similar threats, and we depend in part on third-party security measures over which we do not have full control to protect against data security incidents. Attacks on information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and such attacks are being conducted by increasingly sophisticated and organized groups and individuals with a wide range of motives and expertise. Attempts to disrupt or gain unauthorized access to our and our third-party vendors' information systems from malicious third parties or insider threats may incorporate widely varying and frequently changing tactics, which may be enhanced or facilitated by artificial intelligence. In addition to extracting information (which could be sensitive), such as trade secrets or other intellectual property, such attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, wrongful or accidental conduct by employees or vendors, and social engineering (including phishing attacks) to affect service reliability and/or threaten the confidentiality, integrity and availability of information. A cybersecurity incident, data breach or other adverse event could result in a material disruption of our operations or development programs and/or produce significant reputational, financial, legal, regulatory, business or operational harm. For example, any loss of clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

To the extent that any cybersecurity incident, disruption or data breach results in a loss of or damage to our data or applications or other data or applications relating to our technology, product or product candidates, or inappropriate disclosure of confidential, personal or proprietary information, we could incur liabilities and the further development of and regulatory approval efforts for our product candidates or commercialization of our product could be delayed. Like other companies in our industry, we, and our third party vendors, have experienced threats and cybersecurity incidents related to our data, information technology systems and infrastructure, and the systems of our third-party vendors. Although we have taken steps to enhance our cybersecurity protections and minimize the impact of any future events, we cannot provide any assurances that these security safeguards will be successful, and that future cybersecurity incidents, data breaches or other adverse events will not occur, and to the extent they occur, that such events will not impact our operations or have any material adverse impact on our business.

Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our privacy and data security obligations. In addition, although we maintain cyber liability insurance, this insurance may not cover or be sufficient in type or amount to cover us against claims related to cybersecurity incidents or data breaches.

Any failure or perceived failure by us or the third-party collaborators, service providers or consultants whom we rely to comply with our privacy, confidentiality, data security or similar obligations may result in: governmental investigations, litigation, claims, regulatory enforcement actions, fines, sanctions or other penalties, injunctive relief requiring costly compliance measures, required notification and credit monitoring, public statements against us, or third parties to lose trust in us, any of which could have a material adverse effect on our reputation, business, financial condition or results of operations.

Our use of new and evolving technologies, such as artificial intelligence, may present risks and challenges that can impact our business, including by posing cybersecurity and other risks to our confidential and/or proprietary information, including personal information, and as a result we may be exposed to reputational harm and liability.

We may use and integrate artificial intelligence into our business processes both in our own development and implementation of models and through the adoption of commercially available tools. Use of this technology could pose cybersecurity, data privacy, IT, intellectual property, regulatory, legal, operational, competitive, reputational and other risks and challenges that could affect our business. Specifically, risks related to bias, AI hallucinations, discrimination, harmful content, misinformation, fraud, scams, targeted attacks such as model poisoning or data poisoning, surveillance, data

leakage, loss of consensus reality, inequality, environmental harms, and other harms may flow from our development, use, or deployment of AI technologies.

The rapid evolution of artificial intelligence will require the application of significant resources to design, develop, test and maintain processes to help ensure that artificial intelligence is implemented in accordance with applicable law and regulation and in a socially responsible manner and to minimize any real or perceived unintended harmful impacts. The development of artificial intelligence models requires resources for design, development, testing and maintenance. We must also endeavor to implement artificial intelligence in accordance with applicable law and regulation, in a socially responsible manner and to minimize any real or perceived unintended harmful impacts. If we enable or use models that contain actual or perceived biases, or otherwise draw controversy due to perceived or actual negative societal impact, we may experience brand or reputational harm, competitive harm or legal liability.

In addition, the use of artificial intelligence technologies can give rise to intellectual property risks, including the disclosure or compromise of our confidential information or other proprietary intellectual property through the use of generative AI tools, or the ability to assert or defend ownership rights in intellectual property created with the use of generative artificial intelligence tools.

Further, we expect to see increasing government and supranational regulation related to artificial intelligence use and ethics, which may also significantly increase the burden and cost of research, development and compliance in this area. For example, the EU's Artificial Intelligence Act ("AI Act") originally entered into force on August 1, 2024, and is expected to undergo amendments as introduced in the EU's November 2025 Digital Omnibus on AI. As enacted, the AI Act imposes significant obligations on providers and deployers of high-risk artificial intelligence systems, and encourages providers and deployers of artificial intelligence systems to account for EU ethical principles in their development and use of these systems. The scope of requirements depends on judicial interpretations and forthcoming legislative amendments, and non-compliance can lead to significant fines.

Likewise, in the U.S., the regulatory environment is complex and uncertain. President Trump's Executive Order "Ensuring a National Policy Framework for Artificial Intelligence," effective December 11, 2025, directed federal agency reviews of state AI laws and coordination between White House advisors and Congress to reach a legislative proposal for a uniform federal AI policy framework. At the same time, several states, including Colorado and California, passed laws that regulate various facets of AI, some of which have taken effect and will continue to take effect through 2026 and beyond. These laws address a wide range of AI-related topics, including consequential decisions, transparency, training data, among others, and it remains unclear which requirements, if any, will be superseded by the Executive Order. So far, these efforts have not been successful in curtailing state action on AI regulation, contributing to a complicated legislative patchwork, which may be litigated in state and federal courts. Various federal and state regulators have also issued guidance and focused enforcement efforts on the use of AI in regulated sectors. The FDA, for example, issued guidance on the use of artificial intelligence in medical devices, requiring detailed risk management and review processes to obtain approvals. If we develop or use AI systems that are governed by the these laws or regulations, we will need to meet higher standards of data quality, transparency, and human oversight, and we would need to adhere to specific and potentially burdensome and costly ethical, accountability, and administrative requirements. We may also be subject to significant enforcement or litigation in the event of any perceived non-compliance.

Our vendors may in turn incorporate artificial intelligence tools into their offerings, and the providers of these artificial intelligence tools may not meet existing or rapidly evolving regulatory or industry standards, including with respect to privacy and data security. Further, bad actors around the world use increasingly sophisticated methods, including the use of artificial intelligence, to engage in illegal activities involving the theft and misuse of personal information, confidential information and intellectual property. In addition, the use of generative AI models in our internal or third-party systems may create new attack surfaces or methods for adversaries, which could impact us and our vendors. The integration of AI systems, by us or by our vendors, may increase cybersecurity risk. Any of these effects could damage our reputation, result in the loss of valuable property and information, cause us to breach applicable laws and regulations, and adversely impact our business.

If we fail to maintain proper and effective internal control over financial reporting, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, investors' views of us and, as a result, the value of our common stock.

Pursuant to Section 404 of the Sarbanes-Oxley Act ("Section 404"), our management is required to assess and report annually on the effectiveness of our internal control over financial reporting and to identify any material weaknesses in our internal control over financial reporting. We are also required to comply with the auditor attestation requirements of Section 404(b). The rules governing the standards that must be met for management and our independent registered public accounting firm to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation. In connection with our and our independent registered public accounting firm's evaluations of our internal control over financial reporting, we may need to upgrade systems, including information

technology, implement additional financial and management controls, reporting systems and procedures and hire additional accounting and finance staff.

Any failure to implement required new or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations. In addition, any testing by us or our independent registered public accounting firm conducted in connection with Section 404 may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock. Internal control deficiencies could also result in a restatement of our financial results in the future. We could become subject to stockholder or other third-party litigation, as well as investigations by the SEC, Nasdaq or other regulatory authorities, which could require additional financial and management resources and could result in fines, trading suspensions, payment of damages or other remedies.

Our ability to use net operating loss ("NOL") and tax credit carryforwards and certain built-in losses to reduce future tax payments may be limited by provisions of the Internal Revenue Code.

Our NOLs have been fully offset by a valuation allowance due to uncertainties surrounding our ability to realize these tax benefits.

Our NOLs could expire unused and be unavailable to offset future income tax liabilities because of their limited duration. NOLs generated in taxable years beginning before January 1, 2018 are permitted to be carried forward for 20 taxable years under applicable U.S. federal income tax law. Under current U.S. federal income tax law, NOLs arising in tax years beginning after December 31, 2020 may not be carried back. Moreover, NOLs generated in taxable years beginning after December 31, 2017 may be carried forward indefinitely, but the deductibility of such NOLs generally will be limited in taxable years beginning after December 31, 2020 to 80% of current year taxable income. As of December 31, 2025, the Company had NOLs for U.S. federal and state income tax purposes of approximately $1,179.0 million and $979.5 million, respectively, a portion of which expire beginning in 2031 if not utilized.

Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the "Code"), if a corporation undergoes an "ownership change" (generally defined as a greater than 50% change (by value) in its equity ownership over a rolling three year period), the corporation's ability to use its pre-change NOL carryforwards and other pre-change tax attributes to offset its post-change income may be limited. Similar rules may apply under state tax laws. We experienced a Section 382 ownership change during the year ended December 31, 2017 which imposes annual limitations on our use of pre-change NOL carryforwards and other pre-change tax attributes. We have determined that our research and development credit carryforwards are also limited. We may also experience ownership changes in the future as a result of future transactions in our stock (some of which are outside our control). In addition, we file U.S. federal income tax returns and income tax returns in various state, local, and foreign jurisdictions and we are routinely subject to examination by taxing authorities in those jurisdictions. Tax years beginning in 2021 remain open to examination by the Internal Revenue Service ("IRS"), state, and foreign taxing authorities. To the extent that we have tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon IRS, state, or foreign tax authorities' examination to the extent utilized in a future period. Furthermore, our ability to utilize NOLs of companies that we may acquire in the future may be subject to limitations. There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs or other unforeseen reasons, our existing NOLs could expire or otherwise be unavailable to reduce future income tax liabilities, including for state tax purposes. As a result, if we earn net taxable income, our ability to use the NOLs and tax credits reflected on our balance sheet to offset U.S. federal taxable income may become subject to limitations, which could adversely affect our operating results and financial condition.

Taxing authorities could challenge our historical and future tax positions or our allocation of taxable income among our subsidiaries and we may incur additional tax liabilities.

We operate through various subsidiaries in a number of countries throughout the world. Consequently, we are subject to tax laws, treaties, and regulations in the countries in which we operate, and these laws and treaties are subject to interpretation. We have taken, and will continue to take, tax positions based on our interpretation of such tax laws. Our transfer pricing arrangements are not generally binding on applicable tax authorities. The price charged for products, services, or the royalty rates and other amounts paid for intellectual property rights, could be challenged by the various tax authorities, resulting in additional tax liability, interest, and/or penalties. There can be no assurance that a taxing authority will not have a different interpretation of applicable law and assess us with additional taxes. If we are assessed with additional taxes, this may result in a material adverse effect on our results of operations and/or financial condition.

Changes in tax law could adversely affect our business and financial condition.

The rules dealing with U.S. federal, state, local and international income taxation are constantly under review by persons involved in the legislative process and by the U.S. Internal Revenue Service, the U.S. Treasury Department and international tax authorities. Changes to tax laws (which changes may have retroactive application) could adversely affect the Company or holders of our common stock. In recent years, many such changes have been made, and changes are likely to continue to occur in the future. It cannot be predicted whether, when, in what form or with what effective dates tax laws, regulations and rulings may be enacted, promulgated or issued, which could result in an increase in our tax liability or the tax liability of holders of our common stock or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law.

Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. We urge investors to consult with their legal and tax advisers regarding the implications of potential changes in tax laws on an investment in our common stock.

Volatility in foreign currency exchange rates could have a material adverse effect on our operating results.

As we expand our operations into Europe, we are exposed to risks related to changes in foreign currency exchange rates, primarily between the U.S. dollar, euro and Swiss franc. As we endeavor to expand our presence in international markets, to the extent we are required to enter into agreements denominated in a currency other than the U.S. dollar, results of operations and cash flows may increasingly be subject to fluctuations due to changes in foreign currency exchange rates and may be adversely affected in the future due to changes in foreign currency exchange rates. To date, we have not entered into any hedging arrangements with respect to foreign currency risk. As our international operations grow, we will continue to reassess our approach to manage our risk relating to fluctuations in currency rates. In addition, the current presidential administration has enacted or proposed to enact certain economic and trade policies, including with respect to tariffs, that could impact the global economy and further increase the volatility of foreign exchange rates. Any future volatility in foreign exchange rates is likely to impact our operating results and financial condition.

Business disruptions could seriously harm our operations, future revenues and financial condition and increase our costs and expenses.

Our operations, and those of our CROs, suppliers, and other contractors and consultants, could be subject to geopolitical events, natural disasters, power and other infrastructure failures or shortages, public health crises, pandemics or epidemics, and other natural or man-made disasters or business interruptions. In addition, geopolitical and other events, such as the Russian invasion of Ukraine or the conflicts in the Middle East, could lead to sanctions, embargoes, supply shortages, regional instability, geopolitical shifts, cyberattacks, other retaliatory actions, and adverse effects on macroeconomic conditions, currency exchange rates, and financial markets, which could adversely impact our operations and financial results, as well as those of third parties with whom we conduct business. The occurrence of any of these business disruptions could seriously harm our operations, future revenues and financial condition and increase our costs and expenses.

We may be subject to securities litigation, which is expensive and could divert management attention.

The market price of our common stock may be volatile and, in the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert management's attention from other business concerns, which could seriously harm our business.

Item 1B. Unresolved Staff Comments

None.

Item 1C. Cybersecurity

We are increasingly dependent on sophisticated software applications and computing infrastructure to conduct key operations. We depend on our own systems, networks, and technology as well as the systems, networks and technology of our contractors, consultants, vendors and other business partners.

Cybersecurity Program

We rely on a combination of internally-managed systems and third-party technology environments to support our research, clinical, commercial, and corporate operations. As our business has grown, these systems have become increasingly important to our ability to operate effectively. We therefore maintain a cybersecurity program designed to

support the resilience of our information systems and help prepare for evolving information security risks. Our program includes administrative, physical, and technical safeguards and is informed by industry frameworks, including the National Institute of Standards and Technology Cybersecurity Framework.

We periodically evaluate aspects of our cybersecurity program through risk-based external assessments. We assess cybersecurity risks as part of our broader risk-management processes and consider potential impacts on our operations, financial results and reputation. Cybersecurity training is required when onboarding new employees, and we also provide annual cybersecurity awareness training for employees.

We use a risk-based approach with respect to our evaluation and oversight of third-party service providers that takes into account whether such service providers access, process or store our information or support key business operations. Our due diligence activities may include security questionnaires, reviews of available audit reports and other supporting documentation. We also include appropriate security terms in contracts with third-party service providers, where applicable.

Process for Assessing, Identifying and Managing Material Risks from Cybersecurity Threats

We maintain written information security policies, including an incident response program that outlines processes for identifying, assessing, escalating, and responding to cybersecurity incidents. Designated personnel are responsible for assessing the severity of an incident and associated threat; containing the threat; remediating the threat, including recovery of data and access to systems; and evaluating any applicable legal or regulatory reporting obligations. Our incident response program also provides for post-incident review.

We maintain 24/7 security monitoring through a managed detection and response (“MDR”) provider. We recently expanded our cybersecurity capabilities by adding contracted personnel dedicated to security operations and incident response. These personnel operate under the direction of our Cybersecurity and Chief Information Security Officer ("CISO") within the cybersecurity program overseen by our Chief Information Officer ("CIO"), and work alongside our MDR provider and other third-party specialists.

Governance

Management Oversight

Overall responsibility for our information technology and cybersecurity functions resides with our CIO. Our CIO has more than 25 years of experience as an information technology ("IT") professional overseeing and supporting IT operations in the biopharmaceutical industry, including several years of experience in cybersecurity. Our CISO has over 25 years of experience in IT and security, including more than a decade in the pharmaceutical sector focused on protecting intellectual property and proprietary data.

Our CISO is responsible for the development and execution of our cybersecurity strategy and for overseeing the day-to-day operation of our cybersecurity program, which is carried out by a combination of internal and contracted cybersecurity resources supporting security operations and incident response. In this role, the CISO, together with the CIO, oversees our processes for the prevention, detection, mitigation, and remediation of cybersecurity incidents through established policies, procedures, and reporting mechanisms, and provides regular updates to senior management and the Audit Committee of our Board of Directors (the "Audit Committee"), which oversees cybersecurity-related risk.

Board Oversight

Our Board of Directors has overall responsibility for risk oversight, and the Audit Committee oversees cybersecurity-related risk. The Audit Committee receives reports quarterly, and otherwise as needed, from the CISO and CIO and reviews cybersecurity matters with management, including our cybersecurity risk profile and the steps taken to monitor and mitigate cybersecurity risks.

Cybersecurity Risks

We assess cybersecurity risks as part of our broader risk-management processes and consider potential impacts on our operations, financial results, and reputation. We also maintain cybersecurity insurance providing coverage for certain costs related to cybersecurity incidents that impact our systems, networks and technology.

While we believe we maintain an effective cybersecurity program, the techniques used to infiltrate IT systems continue to evolve. Accordingly, we may not be able to timely detect threats or anticipate and implement adequate security measures.

To date, there have not been any risks from cybersecurity threats, including as a result of any cybersecurity incidents, which have materially affected or are reasonably likely to materially affect us, including our business strategy, results of operations or financial condition. See the section titled "Risk Factors—General Risk Factors—A failure of our information technology infrastructure and cybersecurity threats may adversely affect our business and operations." in this Annual Report for more information.

Item 2. Properties

As of December 31, 2025, we leased approximately 44,347 square-feet of facilities located in West Conshohocken, Pennsylvania, our corporate headquarters. These leases contain extension rights beyond the scheduled lease expiration dates of November 2026 and June 2031, respectively. We lease additional office space in Waltham, Massachusetts. We continue to evaluate our facility requirements and believe that appropriate space will be available to accommodate our future needs.

Item 3. Legal Proceedings

We currently are not a party to any material legal proceedings.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Market Information

Our common stock trades on the Nasdaq Stock Market under the symbol "MDGL."

Holders

As of December 31, 2025, there were approximately 12 holders of record of our common stock. This number does not include "street name" or beneficial holders, whose shares are held of record by banks, brokers, financial institutions and other nominees. In addition, we had two holders of record who owned shares of our Series A Convertible Preferred Stock and Series B Convertible Preferred Stock and three holders of our pre-funded warrants.

Dividends

We have not paid any cash dividends on our common stock. We currently intend to retain all available funds and any future earnings to fund the development and expansion of our business, and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay cash dividends will be at the discretion of our board of directors and will depend on our financial condition, results of operations, contractual restrictions, capital requirements and other factors that our board of directors deems relevant.

Securities Authorized for Issuance Under Equity Compensation Plans

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

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

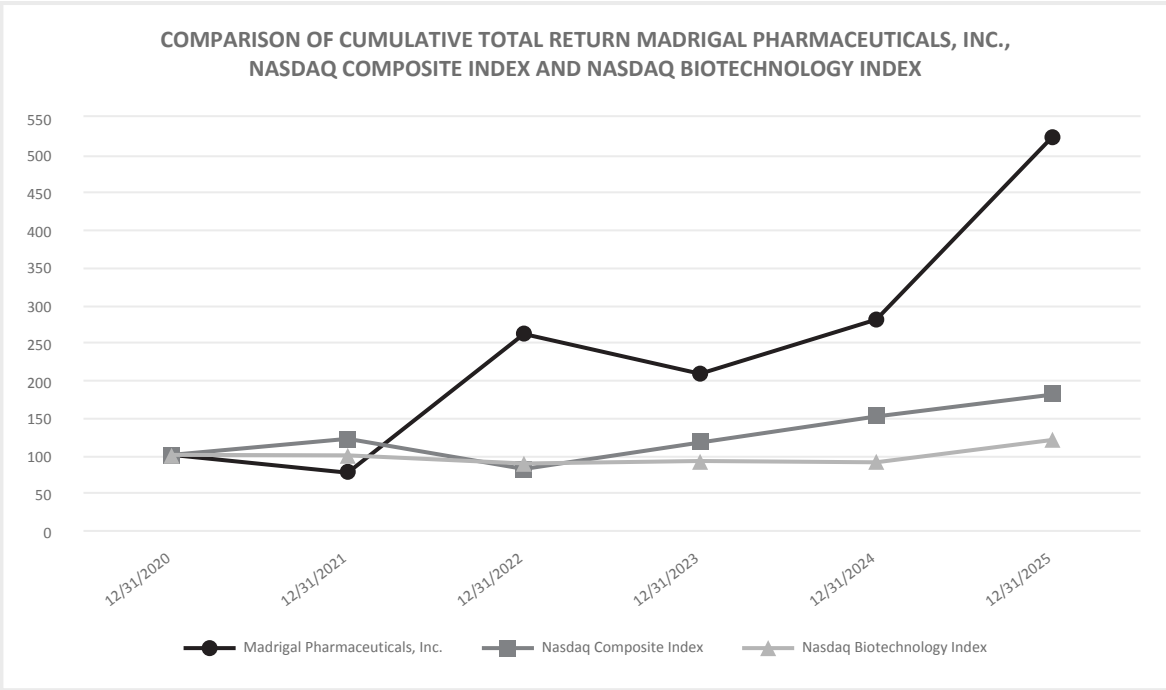
Unregistered Sales of Securities

During the year ended December 31, 2025, we did not issue or sell any unregistered securities.

Stock Performance Graph

The graph set forth below compares the cumulative total stockholder return on our common stock between December 31, 2020 and December 31, 2025, with the cumulative total return of (a) the Nasdaq Biotechnology Index and (b) the Nasdaq Composite Index, over the same period. This graph assumes the investment of $100 on December 31, 2020 in our common stock, the Nasdaq Biotechnology Index and the Nasdaq Composite Index and assumes the reinvestment of dividends, if any.

The comparisons shown in the graph below are based upon historical data. We caution that the stock price performance shown in the graph below is not necessarily indicative of, nor is it intended to forecast, the potential future performance of our common stock.



The above Stock Performance Graph and related information shall not be deemed to be "soliciting material" or to be "filed" with the Securities and Exchange Commission, nor shall such information be incorporated by reference into any future filing under the Securities Act of 1933 or Securities Exchange Act of 1934, each as amended, except to the extent that we specifically request that such information be treated as soliciting material or specifically incorporate it by reference into a filing.

Item 6. [Reserved]

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

The following discussion should be read in conjunction with our audited consolidated financial statements and the notes thereto contained elsewhere in this Annual Report. This discussion contains forward-looking statements that involve risks and uncertainties. As a result of many factors, such as those set forth under the sections titled "Risk Factors," "Cautionary Note Regarding Forward-Looking Statements" and elsewhere herein, our actual results may differ materially from those anticipated in these forward-looking statements.

Executive Overview

We are a biopharmaceutical company focused on delivering novel therapeutics for MASH, a serious liver disease with high unmet medical need that can lead to cirrhosis, liver failure, liver cancer, need for liver transplantation and premature mortality. MASH is the leading cause of liver transplantation in women, the second leading cause of all liver transplantation in the United States and the fastest-growing indication for liver transplantation in Europe. Our medication, Rezdiffra (resmetirom), is a once-daily, oral, liver-directed THR-β agonist designed to target key underlying causes of MASH. In March 2024, Rezdiffra became the first therapy approved by the FDA for patients with MASH and was commercially available in the United States beginning in April 2024. Following receipt of CMA from the EC, we launched Rezdiffra in Germany in September 2025. Rezdiffra was the first medication approved by both the FDA and EC for the treatment of adults with noncirrhotic MASH with moderate to advanced liver fibrosis (F2 to F3 fibrosis). We are also evaluating Rezdiffra in patients with compensated MASH cirrhosis (consistent with F4c fibrosis) in our MAESTRO-NASH OUTCOMES trial, that, if successful, could expand the eligible patient population for Rezdiffra.

In addition, we are advancing a focused pipeline to lead the evolution of MASH treatment for patients for decades to come. Through our business development efforts, we have acquired rights to MGL-2086, an oral GLP-1 receptor agonist, ervogastat, an oral DGAT2 inhibitor, six siRNA programs and additional preclinical MASH candidates. We plan to evaluate these candidates with the goal of delivering best-in-disease therapies for the treatment of MASH. As we continue to build our pipeline, we will evaluate mechanisms that fit scientifically, strategically and commercially to enhance our leading position in MASH care.

See "Part I, Item 1. Business" for a summary of our commercial and clinical activities.

Financial Overview

We have incurred losses since inception, resulting in an accumulated deficit of $2,090.5 million as of December 31, 2025. Prior to generating product revenue from sales of Rezdiffra beginning in April 2024, we financed our operations primarily through public and private offerings of our equity securities and through our credit facilities. We have generated losses principally from costs associated with research and development activities, acquiring, filing and expanding intellectual property rights, establishing a commercial infrastructure to support the launch of Rezdiffra and selling, general and administrative expenses. As a result of planned expenditures to commercialize Rezdiffra, expand our commercial operations in Europe, continue research and development activities, manage and grow our intellectual property portfolio and engage in potential business development transactions and costs associated with general corporate activities, we expect to incur additional operating losses.

Our ability to reduce operating losses and begin to generate positive cash flow from operations depends on a number of factors, including our ability to continue to successfully commercialize Rezdiffra, achieve positive results from our post-approval trials in order to obtain full approval of Rezdiffra in the United States and the European Union, expand the eligible patient population for Rezdiffra and successfully develop and receive regulatory approval for additional therapies. Our financial results may fluctuate from quarter to quarter and will depend on, among other factors, the net sales of Rezdiffra; the scope and progress of our research and development efforts and the timing of certain expenses.

See the section titled "Risk Factors—Risks Related to Our Financial Position and Need for Capital." in this Annual Report for additional information.

Key Components of Our Operating Results

Product Revenue, Net

In March 2024, the FDA approved Rezdiffra for the treatment of noncirrhotic MASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis). We began generating revenue from sales of Rezdiffra in the United States in April 2024. In addition, we launched Rezdiffra in Germany in September 2025. As described in the "Critical

Accounting Policies and Estimates" section below, revenue is recorded net of variable consideration, which includes prompt pay discounts, service fees, returns, chargebacks, rebates and co-payment assistance.

Cost of Sales

Cost of sales includes the cost of manufacturing and distribution of inventory related to sales of Rezdiffra, including royalties payable to Roche. We expect cost of sales to increase in the future, as manufacturing costs incurred prior to regulatory approval were expensed to research and development rather than capitalized as inventory, as approval was considered uncertain.

Research and Development Expenses

Research and development expenses primarily consist of costs associated with our research activities, including the clinical development of our product candidates. We expense our research and development expenses as incurred. We contract with clinical research organizations to manage our clinical trials under agreed upon budgets for each trial, with oversight by our clinical program managers. We account for nonrefundable advance payments for goods and services that will be used in future research and development activities as expenses when the service has been performed or when the goods have been received. Manufacturing expense includes costs associated with drug formulation development and clinical drug production. We do not track employee- and facility-related research and development costs by project, as we typically use our employee and infrastructure resources across multiple research and development programs. We believe that the allocation of such costs would be arbitrary and not be meaningful.

Our research and development expenses consist primarily of:

- salaries and related expense, including stock-based compensation;
- external expenses paid to clinical trial sites, contract research organizations, laboratories, database software and consultants that conduct clinical trials;
- expenses related to development and the production of non-clinical and clinical trial supplies, including fees paid to contract manufacturers;
- expenses related to preclinical activities;
- expenses related to compliance with drug development regulatory requirements;
- other allocated expenses, which include direct and allocated expenses for depreciation of equipment and other supplies; and
- certain upfront and milestone payments payable pursuant to our license agreements.

We expect to continue to incur substantial expenses related to our development activities for the foreseeable future as we conduct our clinical trial programs, manufacturing and toxicology studies. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later stage clinical trials, additional drug manufacturing requirements, and later stage toxicology studies such as carcinogenicity studies. The process of conducting preclinical studies and clinical trials necessary to obtain regulatory approval is costly and time consuming. The probability of success for each product candidate is affected by numerous factors, including preclinical data, clinical data, competition, manufacturing capability and commercial viability.

Completion dates and costs for our clinical development programs as well as our research program can vary significantly for any future product candidate and are difficult to predict. As a result, we cannot estimate with any degree of certainty the costs we will incur in connection with the development of product candidates at this time. We expect that we will make determinations as to which programs and product candidates to pursue and how much funding to direct to each program and product candidate on an ongoing basis in response to the scientific success of research, results of ongoing and future clinical trials, potential collaborative agreements with respect to programs or potential product candidates and ongoing assessments as to each product candidate's commercial potential.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist primarily of salaries, benefits and stock-based compensation expenses for employees, management costs, costs associated with commercial activities, costs associated with obtaining and maintaining our patent portfolio, commercial and marketing activities, professional fees for accounting, auditing, consulting and legal services, and allocated overhead expenses.

We expect that our selling, general and administrative expenses will increase in the future as we expand our operating activities, continue commercialization efforts, including extending operations into new geographies (if approved), maintain and expand our patent portfolio and incur additional costs associated with being a public company and maintaining compliance with exchange listing and SEC requirements.

Interest Income

Interest income consists primarily of interest and dividend income earned on cash equivalents and marketable securities.

Interest Expense

Interest expense consists primarily of interest accrued on principal balances outstanding under our Financing Agreement. We also accrued interest on loans outstanding under our loan facility (the "Hercules Loan Facility") with Hercules until the Hercules Loan Facility was repaid in full and terminated in July 2025.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements which have been prepared in accordance with generally accepted accounting principles in the United States ("GAAP"). The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenue and expenses and the disclosure of contingent assets and liabilities at the date of the financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to gross to net expenses, inventory valuation, accrued research and development expenses and stock-based compensation expenses. We base our estimates on historical experience, known trends and events and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ materially from these estimates under different assumptions or conditions.

Revenue Recognition

Our accounting policy over revenue recognition has a significant impact on our financial results and involves substantial judgment and estimation. The amount of revenue we recognize is impacted by variable consideration, as described in Note 2 "Summary of Significant Accounting Policies," in the accompanying notes to the consolidated financial statements. Our gross to net estimates are based on contracts with customers, government agencies, healthcare providers, industry data, historical information, and other factors. The judgments and estimates involved in determining variable consideration are reviewed each reporting period, as all are subject to adjustments as new information becomes available.

We recognize revenue in accordance with ASC Topic 606 - Revenue from Contracts with Customers ("ASC 606"). Revenue is recognized at the point in time when the customer obtains control of promised goods or services in an amount that reflects the consideration to which we expect to be entitled in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of ASC 606, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligation(s) in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligation(s) in the contract and (v) recognize revenue when (or as) we satisfy its performance obligation(s).

Revenue is recorded net of variable consideration, which includes prompt pay discounts, returns, chargebacks, rebates and co-payment assistance. The variable consideration is estimated based on contractual terms as well as management assumptions. The amount of variable consideration is calculated by using the expected value method, which is the sum of probability-weighted amounts in a range of possible outcomes, or the most likely amount method, which is the single most likely amount in a range of possible outcomes. Estimates are reviewed quarterly and adjusted as necessary.

Accruals are established for gross to net deductions and actual amounts incurred are offset against applicable accruals. We reflect these accruals as either a reduction in the related account receivable from the customer or as a current

liability, depending on the means by which the deduction is settled. Sales deductions are based on management's estimates that involve a substantial degree of judgment.

Prompt Pay: Customers receive a prompt pay discount for payments made within a contractually agreed number of days before the due date.

Returns: We record allowances for product returns as a reduction of revenue at the time product sales are recorded. Product returns are estimated based on forecasted sales and historical and industry data. Returns are permitted in accordance with the return goods policy defined within each customer agreement.

Chargebacks: We estimate obligations resulting from contractual commitments with the government and other entities to sell products to qualified healthcare providers at prices lower than the list prices charged to the customer who directly purchases from us. The customer charges us for the difference between what it pays to us for the product and the selling price to the qualified healthcare providers.

Co-Payment Assistance: Co-payment assistance programs are offered to eligible end-users as price concessions. We use a third-party to administer the co-payment program for pharmacy benefit claims.

Rebates: Our rebates include amounts paid to Medicaid, Medicare, certain commercial payors and other rebate programs. Reserves for rebates are recorded in the same period the related product revenue is recognized. Our estimate for rebates is based on statutory or contractual discount rates, expected utilization or an estimated number of patients on treatment, as applicable.

Inventory

Inventory, which consists of work in process and finished goods, is stated at the lower of cost or estimated net realizable value, using actual cost, based on a first-in, first-out method. The balance sheet classification of inventory as current or non-current is determined by whether it will be consumed within our normal operating cycle. We periodically review our inventory for factors that could impact the future recoverability and realization of future sales, which requires estimates and judgments. We analyze our inventory levels quarterly and write down inventory subject to expiry, in excess of expected requirements or that has a cost basis in excess of its expected net realizable value. These write downs are charged to cost of sales in the accompanying Consolidated Statements of Operations. We capitalize inventory costs when future commercial sale in the ordinary course of business is probable.

Results of Operations

Discussion of Results of Operations

The following table provides comparative results of operations for the years ended December 31, 2025, 2024 and 2023 (in thousands):

	Year Ended December 31,			2025 vs 2024		2024 vs 2023	
	2025	2024	2023	$	%	$	%
Product revenue, net	$ 958,403	$ 180,133	$ —	$778,270	432 %	$180,133	*
Operating expenses:							
Cost of sales	56,148	6,233	—	49,915	801 %	6,233	*
Research and development	388,525	236,718	272,350	151,807	64 %	(35,632)	(13)%
Selling, general and administrative	813,827	435,057	108,146	378,770	87 %	326,911	302 %
Total operating expenses	1,258,500	678,008	380,496	580,492	86 %	297,512	78 %
Loss from operations	(300,097)	(497,875)	(380,496)	197,778	(40)%	(117,379)	31 %
Interest income	37,364	46,654	19,578	(9,290)	(20)%	27,076	138 %
Interest expense	(22,309)	(14,671)	(12,712)	(7,638)	52 %	(1,959)	15 %
Loss on extinguishment of debt	(2,779)	—	—	(2,779)	*	—	*
Other expense, net	(463)	—	—	(463)	*	—	*
Net loss	$(288,284)	$(465,892)	$(373,630)	$177,608	(38)%	$ (92,262)	25 %

*Indicates the percentage change period over period is not meaningful due to zero amount in the prior period.

Revenue

We recorded $958.4 million of product revenue, net for the year ended December 31, 2025, compared to $180.1 million in the corresponding period in 2024. The increase was primary driven by overall increased demand for Rezdiffra in 2025, as well as a full year of commercialization of Rezdiffra in 2025 compared to nine months in 2024 following FDA approval in March 2024.

Cost of Sales

Cost of sales were incurred as a result of sales of Rezdiffra. For the year ended December 31, 2025, we recorded $56.1 million of cost of sales compared to $6.2 million in the corresponding period in 2024. The increase was primary driven by overall increased demand for Rezdiffra in 2025, as well as a full year of commercialization of Rezdiffra in 2025 compared to nine months in 2024 following FDA approval in March 2024.

Research and Development Expense

The following represents our research and development expenses for the years ended December 31, 2025, 2024 and 2023 (in thousands):

	Year Ended December 31,			2025 vs 2024		2024 vs 2023	
	2025	2024	2023	$	%	$	%
Personnel and Internal Expense	$ 73,283	$ 73,418	$ 56,824	$ (135)	— %	$ 16,594	29 %
External Expense	315,242	163,300	215,526	151,942	93 %	(52,226)	(24)%
Total	$ 388,525	$ 236,718	$ 272,350	$ 151,807	64%	$ (35,632)	(13)%

Our research and development expenses were $388.5 million for the year ended December 31, 2025 compared to $236.7 million for the year ended December 31, 2024. Research and development expenses increased by $151.8 million in 2025 primarily due to business development transactions, including $120.0 million upfront expense under the CSPC License Agreement and $50.0 million under the Pfizer License Agreement, partially offset by a reduction in expenses related to clinical trials.

Selling, General and Administrative Expense

Our selling, general and administrative expenses were $813.8 million for the year ended December 31, 2025 compared to $435.1 million for the year ended December 31, 2024. Selling, general and administrative expenses increased by $378.8 million in 2025 primarily due to an increase in commercial activities for Rezdiffra, including a corresponding increase in headcount to support our commercialization efforts.

Interest Income

Our interest income was $37.4 million for the year ended December 31, 2025 compared to $46.7 million for the year ended December 31, 2024. The decrease in interest income was due primarily to higher principal balances and interest rates in 2024.

Interest Expense

Our interest expense was $22.3 million for the year ended December 31, 2025, compared to $14.7 million for the year ended December 31, 2024. The increase in interest expense was primarily the result of a higher average outstanding principal balance during the period after entering into the Financing Agreement.

Comparison of the Years Ended December 31, 2024 and 2023

For discussion of our 2024 results and a comparison with 2023 results, please refer to “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, 2024 that was filed with the SEC on February 26, 2025.

Liquidity and Capital Resources

As of December 31, 2025, we had cash, cash equivalents, restricted cash and marketable securities totaling $988.6 million compared to $931.3 million as of December 31, 2024. We have historically funded our operations primarily through proceeds from sales of our capital stock and debt financings. In July 2025, we entered into a senior secured credit

facility that provides up to $500.0 million. See Note 8 “Long Term Debt” to the consolidated financial statements included in this Annual Report for additional details. We began receiving revenue from sales of Rezdiffra following the receipt of accelerated FDA approval in March 2024 and CMA from the EC in August 2025.

Until we are able to generate sufficient revenue from Rezdiffra and any other future approved products, we anticipate that we will continue to incur losses. While our rate of cash usage will likely increase in the future, in particular to support our product development and clinical trial efforts, our commercialization efforts and geographic expansion activities and our business development goals, we believe our available cash resources are sufficient to fund our operations past one year from the issuance of the financial statements contained herein. Our future long-term liquidity requirements will be substantial and will depend on many factors, including our ability to effectively commercialize Rezdiffra, our decisions regarding future geographic expansion, the conduct of any future preclinical studies and clinical trials, our entry into any strategic transactions, our ability to maintain compliance with the liquidity covenant in the Financing Agreement and potential milestone payments payable pursuant to our license agreements. To meet future long-term liquidity requirements, we may need to raise additional capital to fund our operations through equity or debt financings, collaborations, partnerships or other strategic transactions. Additional capital, if needed, may not be available on terms acceptable to us, or at all. If adequate funds are not available, or if the terms of potential funding sources are unfavorable, this could have a material adverse effect on our business, results of operations and financial condition. We have the ability to delay certain commercial activities, geographic expansion activities and certain research activities and related clinical expenses, if necessary, due to liquidity concerns until a date when those concerns are relieved.

At-the-Market Sales Agreement

In May 2024, we entered into a Sales Agreement (the “Sales Agreement”) with Cowen and Company, LLC, an affiliate of TD Securities (USA) LLC (“Cowen”), replacing and superseding our prior sales agreement. We are authorized to issue and sell up to $300.0 million of shares of our common stock under the Sales Agreement. Sales of our common stock, if any, under the Sales Agreement will be made by any method that is deemed to be an “at the market” offering as defined in Rule 415(a)(4) of the Securities Act of 1933, as amended. We have no obligation to sell any common stock and may at any time suspend offers under the Sales Agreement or terminate the Sales Agreement pursuant to its terms.

We did not make any sales under the Sales Agreement during the year ended December 31, 2025. As of December 31, 2025, $300.0 million remained available for sale under the Sales Agreement and our related prospectus supplement.

Credit Facilities

Hercules Loan Facility

In May 2022 we entered into the $250.0 million Hercules Loan Facility. Interest on the Hercules Loan Facility was the greater of (i) the prime rate plus 2.45% and (ii) 8.25%. The Hercules Loan Facility included an end-of-term charge of 5.35% of the aggregate principal amount, which was accounted for in the loan discount.

On July 17, 2025, we used the proceeds received from the Financing Agreement to repay all outstanding obligations under the Hercules Loan Facility, totaling $121.7 million, and upon such repayment, terminated the Hercules Loan Facility. The amount we repaid included $115.0 million of outstanding indebtedness plus accrued and unpaid interest as of the repayment date and exit fees. As a result of the termination, all credit commitments under the Hercules Loan Facility were terminated and all security interests and guarantees in connection with the Hercules Loan Facility were released. The repayment resulted in a $2.8 million loss on extinguishment of debt, primarily due to the write off of unamortized debt issuance costs.

Blue Owl Credit Facility

On July 17, 2025 (the “Closing Date”), we entered into the Financing Agreement with the Lenders and the Administrative Agent. Under the Financing Agreement, the Lenders have committed up to $500.0 million in senior secured credit facilities, consisting of (a) the Initial Term Loan in an aggregate principal amount equal to $350.0 million and (b) Delayed Draw Term Loans in an aggregate principal amount not to exceed $150.0 million. In addition, the Financing Agreement includes uncommitted Incremental Term Loans in an aggregate principal amount not to exceed $250.0 million, subject to the satisfaction of certain terms and conditions set forth in the Financing Agreement. The Initial Term Loan was funded on the Closing Date. Delayed Draw Term Loans are available at our election from time to time until December 31, 2027. Incremental Term Loans are available at our and the Lenders’ mutual consent from time to time. The proceeds from the Financing Agreement are expected to primarily support our business development activities.

Any outstanding principal on the Term Loans will bear interest at a rate per annum on the basis of a 360-day year equal to the sum of (i) the three-month forward-looking term secured overnight financing rate administered by the Federal Reserve Bank of New York (subject to a 1.0% per annum floor) plus (ii) 4.75%. Accrued interest is payable (i) quarterly following the funding of the Initial Term Loan on the Closing Date, (ii) on any date of prepayment or repayment of the Term Loans and (iii) at maturity. The outstanding balance of the Term Loans, if not repaid sooner, shall be due and payable in full on July 17, 2030.

We may prepay the Term Loans at any time (in whole or in part) and may be required to make mandatory prepayments upon the occurrence of certain customary prepayment events. In certain instances and during certain time periods, these prepayments will be subject to customary prepayment fees. If the Term Loans are prepaid on or prior to the one-year anniversary of the original issuance date, we must pay a make-whole amount equal to the greater of (i) 3.00% of the Term Loans being prepaid at such time and (ii) the present value of all remaining interest payments on the amount repaid through the one-year anniversary of the original issuance of such Term Loans, calculated using a discount rate. Thereafter, the amount of any such prepayment fee may vary, but the maximum amount that may be due with any such prepayment would be an amount equal to 3.00% of the Term Loans being prepaid at such time, with such prepayment fee stepping down on each anniversary of the original issuance of such Term Loans.

The Financing Agreement contains affirmative covenants and negative covenants applicable to us and our subsidiaries that are customary for financings of this type. We and the Guarantors (as defined below) are also required to maintain a minimum unrestricted cash balance of $100.0 million at all times. The Financing Agreement also includes representations, warranties, indemnities and events of default that are customary for financings of this type, including an event of default relating to us experiencing a change of control. Upon the occurrence of an event of default, the Lenders may, among other things, accelerate our obligations under the Financing Agreement. Our obligations under the Financing Agreement are and will be guaranteed by certain of our existing and future direct and indirect subsidiaries, subject to certain exceptions (such subsidiaries, collectively, the "Guarantors").

On July 17, 2025, concurrently with the entry into the Financing Agreement, we, the Guarantors and the Administrative Agent entered into a Pledge and Security Agreement. As security for our obligations under the Financing Agreement, we and the Guarantors granted to the Administrative Agent, for the benefit of the Lenders and secured parties, a continuing first priority security interest in substantially all of our and the Guarantors' assets (including all equity interests owned or hereafter acquired by us and the Guarantors), subject to certain customary exceptions. On September 4, 2025, the parties amended the Financing Agreement to add certain of our subsidiaries as Guarantors.

As of December 31, 2025, the outstanding principal under the Financing Agreement was $350.0 million. The interest rate as of December 31, 2025 was 8.75%. As of December 31, 2025, we were in compliance with all loan covenants and provisions.

2024 Public Offering

In March 2024, we entered into an Underwriting Agreement with Goldman Sachs & Co. LLC, Jefferies LLC, Cowen and Company, LLC, Evercore Group L.L.C. and Piper Sandler & Co, as representatives of the several underwriters named therein (the "2024 Underwriters"), pursuant to which we sold to the 2024 Underwriters in an underwritten public offering (the "2024 Offering"): (i) 750,000 shares of common stock at a public offering price of $260.00 per share, (ii) pre-funded warrants (the "2024 Pre-Funded Warrants") to purchase 1,557,692 shares of common stock at a public offering price of $259.9999 per 2024 Pre-Funded Warrant, which represents the per share public offering price for the common stock less a $0.0001 per share exercise price for each such Pre-Funded Warrant, and (iii) a 30-day option for the 2024 Underwriters to purchase up to 346,153 additional shares of common stock at the public offering price of $260.00 per share (the "Underwriters' Option"). The 2024 Offering closed on March 21, 2024.

The net proceeds of the 2024 Offering after deducting the underwriting discount and commissions and other estimated offering expenses payable by us, were approximately $659.9 million.

The 2024 Pre-Funded Warrants are exercisable at any time after the date of issuance. A holder of 2024 Pre-Funded Warrants may not exercise the warrant if the holder, together with its affiliates, would beneficially own more than 9.99% of the number of shares of common stock outstanding immediately after giving effect to such exercise. A holder of 2024 Pre-Funded Warrants may increase or decrease this percentage, but not in excess of 19.99%, by providing at least 61 days prior notice to us.

2023 Public Offering

On September 28, 2023, we entered into an Underwriting Agreement with Goldman Sachs & Co. LLC, as representative of the several underwriters named therein, pursuant to which we sold to the underwriters in an underwritten public offering (the "2023 Offering"): (i) 1,248,098 shares of common stock at a public offering price of $151.69 per share, and (ii) pre-funded warrants (the "2023 Pre-Funded Warrants") to purchase 2,048,098 shares of common stock at a public offering price of $151.6899 per Pre-Funded Warrant, which represents the per share public offering price for the common stock less a $0.0001 per share exercise price for each such Pre-Funded Warrant. The 2023 Offering closed on October 3, 2023.

The gross proceeds of the 2023 Offering was $500.0 million, and we received net proceeds, after deducting the underwriting discount and commissions and other estimated offering expenses payable by us, of approximately $472.0 million.

The 2023 Pre-Funded Warrants are exercisable at any time after the date of issuance. A holder of 2023 Pre-Funded Warrants may not exercise the warrant if the holder, together with its affiliates, would beneficially own more than 9.99% of the number of shares of common stock outstanding immediately after giving effect to such exercise. A holder of 2023 Pre-Funded Warrants may increase or decrease this percentage, but not in excess of 19.99%, by providing at least 61 days prior notice to us.

Cash Flows

The following table summarizes our net cash flow activity (in thousands):

	Year Ended December 31,		
	2025	2024	2023
Net cash used in operating activities	$ (189,553)	$ (455,572)	$ (324,230)
Net cash provided by (used in) investing activities	$ 32,320	$ (274,386)	$ (502,520)
Net cash provided by financing activities	$ 255,984	$ 735,062	$ 595,116

Operating Activities

Net cash used in operating activities was $189.6 million for the year ended December 31, 2025. The use of cash resulted primarily from our loss from operations, driven by commercialization efforts and business development transactions, partially offset by cash receipts from sales of Rezdiffra, as adjusted for non-cash charges for stock-based compensation, and changes in our working capital accounts.

Net cash used in operating activities was $455.6 million, for the year ended December 31, 2024.The use of cash resulted primarily from our loss from operations, as adjusted for non-cash charges for stock-based compensation, and changes in our working capital accounts.

Investing Activities

Net cash provided by investing activities was $32.3 million for the year ended December 31, 2025 and consisted primarily of $1,083.3 million from sales and maturities of marketable securities from our investment portfolio, partially offset by $1,047.5 million of purchases of marketable securities for our investment portfolio.

Net cash used in investing activities was $274.4 million for the year ended December 31, 2024 and consisted primarily of $1,131.2 million of purchases of marketable securities for our investment portfolio, partially offset by $863.3 million of sales and maturities of marketable securities.

Financing Activities

Net cash provided by financing activities was $256.0 million for the year ended December 31, 2025 and consisted primarily of $350.0 million in proceeds from the Initial Term Loan under the Financing Agreement, in addition to $38.1 million from proceeds from the exercise of common stock options, partially offset by a repayment of $121.7 million under the Hercules Loan Facility and $10.4 million of debt issuance costs.

Net cash provided by financing activities was $735.1 million for the year ended December 31, 2024 and consisted primarily of $659.9 million in proceeds from the 2024 Offering, in addition to $76.9 million from proceeds from the exercise of common stock options.

Contractual Obligations and Commercial Commitments

In 2019, we entered into an operating lease for office space in certain premises located in West Conshohocken, Pennsylvania (the "Office Lease"), which was further amended by four amendments entered into from 2019 to May 2023. In August 2023, we entered into the Fifth Amendment to the Office Lease (the "Fifth Lease Amendment") pursuant to which the term of the Office Lease was extended through November 2026. As a result of the Fifth Lease Amendment, an incremental $1.6 million right-of-use asset and lease liability were recorded during the year ended December 31, 2023. In 2024, we entered into the Sixth Seventh, Eighth, and Ninth Amendments to the Office Lease, leasing additional office space available in the same premises under the Office Lease, which resulted in an incremental $1.3 million right-of-use asset and lease liability recorded.

In April 2025, we entered into an operating lease for additional office space in West Conshohocken, Pennsylvania. The lease commenced in May 2025 and resulted in a $4.0 million right-of-use asset and lease liability.

In September 2025, we entered into an operating lease for office space in Waltham, Massachusetts. The commencement date did not occur as of December 31, 2025 and therefore the new lease had no impact on the financial statements.

In May 2022, we entered into the $250.0 million Hercules Loan Facility. On July 17, 2025, we entered into the Financing Agreement and used the proceeds to repay all outstanding obligations under the Hercules Loan Facility, totaling $121.7 million, and upon such repayment, terminated the Hercules Loan Facility. The amount we repaid included $115.0 million of outstanding indebtedness plus accrued and unpaid interest as of the repayment date and exit fees. The Initial Term Loan of $350.0 million under the Financing Agreement was funded on July 17, 2025. Accrued interest under the Financing Agreement is payable quarterly, on any date of prepayment or repayment of the term loans outstanding thereunder and at maturity. We are not required to repay any principal amounts outstanding under the Financing Agreement until maturity in July 2030, subject to certain prepayment events set forth in the Financing Agreement. See Note 8 "Long Term Debt" to the consolidated financial statements included in this Annual Report for additional information regarding the Financing Agreement.

Pursuant to the Roche Agreement, Roche granted us a sole and exclusive license to develop, use, sell, offer for sale and import any Licensed Product (as defined in the Roche Agreement). We received FDA approval for Rezdiffra in March 2024 and EC approval for Rezdiffra in August 2025. A tiered single-digit royalty is payable to Roche on net sales of Rezdiffra, subject to certain reductions.

In July 2025, we entered into the CSPC License Agreement with CSPC for MGL-2086 (formerly known as SYH2086), an oral small molecule GLP-1 receptor agonist. Pursuant to the CSPC License Agreement, CSPC has granted us an exclusive global license to develop, manufacture, and commercialize MGL-2086. The transaction closed in September 2025. We paid CSPC an upfront payment of $120.0 million in October 2025. CSPC is eligible to receive up to $2.0 billion in development, regulatory and commercial milestone payments, as well as royalties on net sales ranging from mid-single digits to low-double digits.

In December 2025, we entered into an exclusive global license agreement with Pfizer (the "Pfizer License Agreement") to develop, manufacture and commercialize ervogastat, a Phase 2 oral DGAT-2 inhibitor, and two additional early-stage MASH assets. We paid Pfizer an upfront payment of $50.0 million in December 2025. In addition, Pfizer is eligible to receive up to $70.0 million in development and regulatory milestone payments related to ervogastat and low-double digit royalties on net sales of ervogastat. Pfizer is eligible to receive additional development, regulatory and commercial milestone payments and royalty payments on net sales of the two licensed early stage assets.

In February 2026, we entered into the Ribocure License Agreement granting us exclusive global rights to develop, manufacture and commercialize six siRNA programs. Pursuant to the Ribocure License Agreement, we will pay Ribocure an upfront payment of $60.0 million. In addition, Ribocure is eligible to receive up to $4.4 billion in development, regulatory and commercial milestone payments across all programs, as well as royalties on net sales ranging from mid-single digits to low-double digits.

We have entered into customary contractual agreements in support of the Phase 3 clinical trials and in connection with manufacturing Rezdiffra. As of December 31, 2025, we had approximately $268.3 million of obligations under these agreements related to active pharmaceutical ingredient, which is expected to be paid through 2029.

Recent Accounting Pronouncements

Refer to Note 2 "Summary of Significant Accounting Policies" in the accompanying notes to the consolidated financial statements for a discussion of recent accounting pronouncements.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Interest Rate Risk

Financing Agreement

As of December 31, 2025, our primary exposure to interest rate risk was associated with our variable rate borrowings under the Financing Agreement. Any outstanding principal on the Term Loans will bear interest at a rate per annum on the basis of a 360-day year equal to the sum of (i) the three-month forward-looking term secured overnight financing rate administered by the Federal Reserve Bank of New York (subject to a 1.0% per annum floor) plus (ii) 4.75%. See Note 8 "Long Term Debt" to the consolidated financial statements included in this Annual Report. Interest rates are sensitive to a variety of factors, including changes in fiscal and monetary policies, geopolitical events, changes in global economic conditions and other factors beyond our control. As of December 31, 2025, the interest rate associated with the $350.0 million of borrowings outstanding under the Financing Agreement was 8.75%. For the year ended December 31, 2025, the effect of a hypothetical 100 basis point increase or decrease in the interest rate would have changed our interest expense under the Financing Agreement by approximately $1.6 million.

Investment Portfolio

We are exposed to market risk with respect to our cash, cash equivalents and marketable securities. We regularly review our investments and monitor the financial markets. We invest in high-quality financial instruments, primarily money market funds, U.S. government and agency securities, government-sponsored bond obligations and certain other corporate debt securities, with the effective duration of the portfolio less than 12 months and no security with an effective duration in excess of 24 months, which we believe are subject to limited credit risk. We currently do not hedge interest rate exposure. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, we believe that an immediate 10% change in interest rates would not have a material effect on the fair market value of our portfolio. We do not believe that we have any material exposure to interest rate risk or changes in credit ratings arising from our investments.

Foreign Exchange Exposure

As we expand our operations into Europe, we are exposed to risks related to changes in foreign currency exchange rates, primarily between the U.S. dollar, euro and Swiss franc. The majority of our expenses are generally denominated in the currencies in which they are incurred, which is primarily the U.S. dollar. As we endeavor to expand our presence in international markets, to the extent we are required to enter into agreements denominated in a currency other than the U.S. dollar, results of operations and cash flows may increasingly be subject to fluctuations due to changes in foreign currency exchange rates and may be adversely affected in the future due to changes in foreign currency exchange rates. To date, we have not entered into any hedging arrangements with respect to foreign currency risk. As our international operations grow, we will continue to reassess our approach to manage our risk relating to fluctuations in currency rates.

Capital Market Risk

Although we receive product revenues from sales of Rezdiffra, we may in the future depend on funds raised through other sources. One potential source of funding is through equity offerings. Our ability to raise funds in this manner depends upon, among other things, capital market forces affecting our stock price.

Effects of Inflation

Inflation generally may affect us by increasing our cost of labor, clinical trial costs and manufacturing costs. We do not believe inflation, including as a result of recent changes in tariff policy, has had a material effect on our business, financial condition or results of operations during the years ended December 31, 2025, 2024 or 2023. Should global inflation increase in the future, we expect increases in clinical trial, selling, labor and other operating costs. If our costs were to become subject to significant inflationary pressures, we may not be able to fully offset such higher costs through price increases of our product. Our inability or failure to do so could adversely affect our business, financial condition and results of operations.

Item 8. Financial Statements and Supplementary Data.

The information required by this Item 8 is included in our Financial Statements and Supplementary Data set forth in Item 15 of Part IV of this Annual Report.

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

None.

Item 9A. Controls and Procedures.

Disclosure Controls and Procedures

We maintain disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act")) that are designed to provide reasonable assurance 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, and that such information is accumulated and communicated to our management, including our chief executive officer and chief financial officer, as appropriate, to allow timely decisions regarding required disclosure.

Under the supervision of our principal executive officer and principal financial officer, we evaluated the effectiveness of our disclosure controls and procedures as of the end of the period covered by this Annual Report. Based on that evaluation, our principal executive officer and principal financial officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2025.

Limitations on the Effectiveness of Controls and Procedures

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable, not absolute, assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs. The design of any disclosure controls and procedures also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions.

Management's Report On Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) for our company. 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 GAAP. This process includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of our assets; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with GAAP, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our financial statements. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management, including our principal executive officer and our principal financial officer, assessed the effectiveness of our internal control over financial reporting as of December 31, 2025. In making this assessment, our management used the criteria set forth in the "Internal Control—Integrated Framework" issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework). Based on its assessment under that framework, our management concluded that our internal control over financial reporting was effective as of December 31, 2025.

PricewaterhouseCoopers LLP, an independent registered public accounting firm, has audited the effectiveness of our internal control over financial reporting as of December 31, 2025, as stated in its report, which is included herein.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) for the quarter ended December 31, 2025 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

Director and Executive Officer 10b5-1 Plans

During our fiscal quarter ended December 31, 2025, none of our directors or officers adopted or terminated a "Rule 10b5-1 trading plan" or a "non-Rule 10b5-1 trading arrangement," as each is defined in Item 408 of Regulation S-K.

Executive Severance Agreements

On February 18, 2026, we entered into new severance and change of control agreements with certain of our employees, including certain of our named executive officers, pursuant to which certain severance provisions were modified to align with prevailing market practices for similarly situated companies. We entered into agreements (each, a "Severance Agreement") with Mardi Dier, our Executive Vice President and Chief Financial Officer, Carole Huntsman, our Executive Vice President and Chief Commercial Officer, Shannon Kelley, our Executive Vice President and Chief Legal Officer, and David Soergel, our Executive Vice President and Chief Medical Officer.

Pursuant to each Severance Agreement, in the event that such officer's employment is terminated by us other than for "Cause" (as defined in the applicable agreement) or if the officer resigns for "Good Reason" (as defined in the applicable agreement) during the one-year period following a Change of Control (as defined in the applicable agreement), such officer will be entitled to (i) a lump sum payment equal to 18 months of such officer's then-current base salary, (ii) a separation bonus in an amount equal to 150% of the target annual bonus to which such officer would have been entitled in the year in which the qualifying separation occurs and (iii) subject to the requirements of COBRA, continuation of medical and dental benefits at our cost (except for named executive officer's applicable contribution portion and co-pay) for up to 18 months following a qualifying separation. The other terms and conditions of the Severance Agreements are substantially the same as has been previously disclosed.

The foregoing summary of the Severance Agreements does not purport to be complete and is qualified in its entirety by reference to the full text of each Severance Agreement, copies of which are filed as exhibits to this Annual Report.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Incorporated by reference from the information in our Proxy Statement for our 2026 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this Annual Report relates.

Item 11. Executive Compensation.

Incorporated by reference from the information in our Proxy Statement for our 2026 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this Annual Report relates.

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

Incorporated by reference from the information in our Proxy Statement for our 2026 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this Annual Report relates.

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

Incorporated by reference from the information in our Proxy Statement for our 2026 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this Annual Report relates.

Item 14. Principal Accountant Fees and Services.

Incorporated by reference from the information in our Proxy Statement for our 2026 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this Annual Report relates.

PART IV

Item 15. **EXHIBITS AND FINANCIAL STATEMENT SCHEDULES**

Item 15(a) The following documents are filed as part of, or incorporated by reference into, this Annual Report:

Item 15(a)(1) and (2) The Consolidated Financial Statements beginning on page F-1 are filed as part of this Annual Report. Other financial statement schedules have been omitted because the information required to be presented in them is not applicable or is shown in the financial statements or related notes.

Item 15(a)(3) We have filed, or incorporated into this Annual Report by reference, the exhibits listed on the accompanying Exhibit Index.

Item 15(b) See Item 15(a)(3) above.

Item 15(c) See Item 15(a)(2) above.

Exhibit Number	Exhibit Description	Filed Herewith	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
3.1	Restated Certificate of Incorporation of the Registrant.		Form 10-K (Exhibit 3.1)	3/31/2017	001-33277
3.2	Certificate of Amendment to Restated Certificate of Incorporation of the Registrant, as filed on June 16, 2023 with the Secretary of State of the State of Delaware.		Form 8-K (Exhibit 3.1)	6/20/2023	001-33277
3.3	Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock.		Form 8-K (Exhibit 3.1)	6/21/2017	001-33277
3.4	Certificate of Designation of Preferences, Rights and Limitations of Series B Convertible Preferred Stock.		Form 8-K (Exhibit 3.1)	12/23/2022	001-33277
3.5	Bylaws of the Registrant, as amended April 13, 2016.		Form 8-K (Exhibit 3.1)	4/14/2016	001-33277
4.1	Form of Warrant Agreement, dated May 9, 2022, between the Registrant and Hercules Capital, Inc. and affiliates.		Form 10-Q (Exhibit 4.1)	08/04/2022	001-33277
4.2†	Form of Tranche 2 Warrant Agreement, dated February 3, 2023, by and among the Registrant and Hercules Capital, Inc. and affiliates.		Form 8-K (Exhibit 4.1)	2/9/2023	001-33277
4.3	Form of Pre-Funded Warrant of the Registrant.		Form 8-K (Exhibit 4.1)	10/2/2023	001-33277
4.4	Description of Securities of the Registrant.		Form 10-K (Exhibit 4.3)	2/23/2023	001-33277
Equity Agreements					
10.1	Securities Purchase Agreement, dated June 20, 2017, by and among the Registrant and the investors party thereto, including the Registration Rights Agreement attached as Exhibit B thereto.		Form 8-K (Exhibit 10.1)	6/21/2017	001-33277
10.2	Amendment No. 2, dated December 22, 2022, to Securities Purchase Agreement, dated June 20, 2017, by and among the Registrant and the investors listed on the signature pages thereto.		Form 8-K (Exhibit 10.2)	12/23/2022	001-33277
10.3	Sales Agreement, dated May 7, 2024, by and between the Registrant and TD Securities (USA) LLC.		Form 8-K (Exhibit 1.1)	5/7/2024	001-33277
10.4	Securities Purchase Agreement, dated December 21, 2022, by and among the Registrant and the institutional investors listed on the signature pages thereto.		Form 8-K (Exhibit 10.1)	12/23/2022	001-33277
10.6	Registration Rights Agreement, dated August 7, 2023, by and among the Registrant, 667, L.P. and Baker Brothers Life Sciences, L.P.		Form 10-Q (Exhibit 10.2)	8/8/2023	001-33277

Debt Agreements					
10.7†#	Financing Agreement by and among the Registrant, certain subsidiaries of the Registrant, certain funds managed by Blue Owl Capital Corporation and LSI Financing LLC, dated as of July 17, 2025 (as amended by the First Amendment thereto, dated as of September 4, 2025).		Form 10-Q (Exhibit 10.1)	11/04/2025	001-33277
10.8†	Second Amendment Agreement, dated as of December 30, 2025, among the Registrant, certain subsidiaries of the Registrant, certain funds managed by Blue Owl Capital Corporation and LSI Financing LLC	X			
Agreements with Respect to Collaborations, Licenses, Research and Development					
10.9†#	Research, Development and Commercialization Agreement, dated December 18, 2008, by and between Hoffmann-La Roche, Inc., F. Hoffmann-La Roche Ltd and the Registrant.		Form 10-Q (Exhibit 10.5)	11/14/2016	001-33277
10.10#	First Amendment to the Research, Development, and Commercialization Agreement, dated as of January 29, 2026, by and between the Registrant and Roche.		Form 8-K (Exhibit 10.1)	1/30/2026	001-33277
Equity Compensation Plans					
10.11*	Amended 2015 Stock Plan.		Form 8-K (Exhibit 10.1)	6/27/2024	001-33277
10.12*	Form of Incentive Stock Option Agreement under Amended 2015 Stock Plan.		Form 10-K (Exhibit 10.10)	3/31/2017	001-33277
10.13*	Form of Nonqualified Stock Option Agreement under Amended 2015 Stock Plan.		Form 10-K (Exhibit 10.11)	3/31/2017	001-33277
10.14*	Form of Nonqualified Stock Option Agreement for Directors under Amended 2015 Stock Plan (pre-2023).		Form 10-K (Exhibit 10.13)	3/31/2017	001-33277
10.15*	Form of RSU Agreement for Directors under Amended 2015 Stock Plan.		Form 10-Q (Exhibit 10.3)	8/8/2023	001-33277
10.16*	Form of RSU Agreement for Executive Officers (2023) under Amended 2015 Stock Plan.		Form 10-Q (Exhibit 10.4)	8/8/2023	001-33277
10.17*	Form of RSU Agreement for Employees under Amended 2015 Stock Plan.		Form 10-Q (Exhibit 10.5)	8/8/2023	001-33277
10.18*†	2023 Inducement Plan.		Form S-8 (Exhibit 99.1)	9/11/2023	333-27445
10.19*†	Form of Stock Option Agreement under 2023 Inducement Plan.		Form S-8 (Exhibit 99.2)	9/11/2023	333-27445
10.20*†	Form of Restricted Stock Unit Agreement under 2023 Inducement Plan.		Form S-8 (Exhibit 99.3)	9/11/2023	333-27445
10.21	2025 Inducement Plan.		Form S-8 (Exhibit 99.1)	6/20/2025	333-288200
10.22	Form of Stock Option Agreement under 2025 Inducement Plan.		Form S-8 (Exhibit 99.2)	6/20/2025	333-288200
10.23	Form of Restricted Stock Unit Agreement under 2025 Inducement Plan (Non-Section 16 Officers).		Form S-8 (Exhibit 99.3)	6/20/2025	333-288200
10.24	Form of Restricted Stock Unit Agreement under 2023 Inducement Plan (Section 16 Officers).		Form S-8 (Exhibit 99.4)	6/20/2025	333-288200
10.25	Form of Performance-Based Restricted Stock Unit Agreement under 2025 Inducement Plan.		Form S-8 (Exhibit 99.5)	6/20/2025	333-288200
Agreements with Executive Officers and Directors					
10.26*	Form of Indemnification Agreement between the Registrant and certain directors and executive officers.		Form 10-K (Exhibit 10.20)	2/28/2024	001-33277
10.27*	Letter Agreement, dated April 13, 2016, by and between the Registrant and Rebecca Taub, M.D.		Form 8-K (Exhibit 10.4)	7/22/2016	001-33277

10.28*†	Letter Agreement, dated April 16, 2025, by and between the Registrant and Rebecca Taub, M.D.		Form 10-Q (Exhibit 10.1)	8/5/2025	001-33277
10.29*†	Letter Agreement (including agreements attached as exhibits thereto), dated September 7, 2023, by and between the Registrant and William J. Sibold.		Form 8-K (Exhibit 10.1)	9/13/2023	001-33277
10.30*†	Letter Agreement (including agreements attached as exhibits thereto), dated November 5, 2023, by and between the Registrant and Carole Huntsman.		Form 10-Q (Exhibit 10.1)	5/7/2024	001-33277
10.31*†	Severance and Change of Control Agreement, dated as of February 18, 2026, by and between the Registrant and Carole Huntsman.	X			
10.32*†	Letter Agreement (including agreements attached as exhibits thereto), dated February 25, 2024, by and between the Registrant and Mardi Dier.		Form 10-Q (Exhibit 10.2)	5/7/2024	001-33277
10.33*†	Severance and Change of Control Agreement, dated as of February 18, 2026, by and between the Registrant and Mardi Dier.	X			
10.34*†	Letter Agreement, dated January 3, 2024, by and between the Registrant and Shannon Kelley, as amended and supplemented by the Letter Agreement, dated August 2, 2024, by and between Madrigal Pharmaceuticals, Inc. and Shannon Kelley.		Form 10-Q (Exhibit 10.1)	10/31/2024	001-33277
10.35*†	Severance and Change of Control Agreement, dated as of February 18, 2026, by and between the Registrant and Shannon Kelley.	X			
10.36*†	Letter Agreement (including agreements attached as exhibits thereto), dated February 12, 2025, by and between the Registrant and David Soergel.		Form 10-Q (Exhibit 10.2)	8/5/2025	001-33277
10.37*†	Severance and Change of Control Agreement, dated as of February 18, 2026, by and between the Registrant and David Soergel.	X			
10.38*	Non-Employee Director Compensation Policy.	X			
Lease					
10.39#	Office Lease (with respect to corporate headquarters facility located in West Conshohocken, Pennsylvania) and amendments thereto.		Form 10-K (Exhibit 10.25)	2/26/2025	001-33277
10.40#	First Amendment to Office Lease.		Form 10-K (Exhibit 10.26)	2/26/2025	001-33277
10.41#	Second Amendment to Office Lease.		Form 10-K (Exhibit 10.27)	2/26/2025	001-33277
10.42#	Third Amendment to Office Lease.		Form 10-K (Exhibit 10.28)	2/26/2025	001-33277
10.43#	Fourth Amendment to Office Lease.		Form 10-K (Exhibit 10.29)	2/26/2025	001-33277
10.44#	Fifth Amendment to Office Lease.		Form 10-K (Exhibit 10.30)	2/26/2025	001-33277
10.45#	Sixth Amendment to Office Lease.		Form 10-K (Exhibit 10.31)	2/26/2025	001-33277
10.46#	Seventh Amendment to Office Lease.		Form 10-K (Exhibit 10.32)	2/26/2025	001-33277
10.47#	Eighth Amendment to Office Lease.		Form 10-K (Exhibit 10.33)	2/26/2025	001-33277
10.48#	Ninth Amendment to Office Lease.		Form 10-K (Exhibit 10.34)	2/26/2025	001-33277
10.49#	Lease Agreement, dated as of April 24, 2025, by and between the Registrant and KPG FF Owner, L.P.		Form 10-Q (Exhibit 10.3)	8/5/2025	001-33277
Commercial Supply Agreement					
10.50†#	Commercial Supply Agreement, dated as of August 21, 2023, by and between Gregory Pharmaceutical Holdings, Inc. (d/b/a UPM Pharmaceuticals) and the Registrant.		Form 10-K (Exhibit 10.35)	2/26/2025	001-33277
10.51†#	Resmetirom Commercial Supply Agreement, dated as of December 23, 2024, by and between Evonik Corporation and the Registrant.		Form 10-K (Exhibit 10.36)	2/26/2025	001-33277
10.52†#	Commercial Supply Agreement, dated as of December 18, 2024, by and between Corden Pharma GmbH and the Registrant (including amendments thereto).	X			
19.1	Insider Trading Policy.	X			

21.1	List of Subsidiaries.	X			
23.1	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm.	X			
31.1	Certification of Principal Executive Officer required by Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X			
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X			
32.1**	Certifications of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X			
97.1	Incentive Compensation Recovery Policy.		Form 10-K (Exhibit 97.1)	2/28/2024	001-33277
97.2	Supplemental Compensation Recovery Policy.		Form 10-Q (Exhibit 10.3)	5/7/2024	001-33277
101.INS	Inline XBRL Instance Document.	X			
101.SCH	Inline XBRL Taxonomy Extension Schema Document.	X			
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.	X			
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.	X			
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.	X			
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.	X			
104	Inline XBRL for the cover page of this Annual Report on Form 10-K, included in the Exhibit 101 Inline XBRL Document Set.	X			

---

* Indicates a management contract, compensatory plan or arrangement.

** The certifications attached as Exhibit 32.1 that accompany this Annual Report on Form 10-K are not deemed filed with the SEC and are not to be incorporated by reference into any filing of the registrant under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K, regardless of any general incorporation language contained in any filing.

† Certain portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

Exhibits and schedules omitted pursuant to Item 601(a)(5) of Regulation S-K.

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, as amended, the registrant has duly caused this Report to be signed on its behalf by the undersigned thereunto duly authorized.

MADRIGAL PHARMACEUTICALS INC.

Date: February 19, 2026

By: /s/ WILLIAM J. SIBOLD
William J. Sibold
President and Chief Executive Officer
(Principal Executive Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each individual whose signature appears below hereby constitutes and appoints William J. Sibold and Mardi Dier and each or either of them, acting individually, as his or her true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Report, and to file the same, with all exhibits thereto and other documents in connection therewith, with the SEC, granting unto said attorney-in-fact and agent, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully for all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or any of them, or their or his or her substitutes, may lawfully do or cause to be done or by virtue hereof.

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

Signatures	Title	Date
/s/ WILLIAM J. SIBOLD William J. Sibold	President and Chief Executive Officer, Director (Principal Executive Officer)	February 19, 2026
/s/ MARDI C. DIER Mardi C. Dier	Executive Vice President and Chief Financial Officer (Principal Financial Officer)	February 19, 2026
/s/ RITA THAKKAR Rita Thakkar	Senior Vice President and Chief Accounting Officer (Principal Accounting Officer)	February 19, 2026
/s/ JULIAN C. BAKER Julian C. Baker	Chair of the Board	February 19, 2026
/s/ REBECCA TAUB, M.D. Rebecca Taub, M.D.	Director	February 19, 2026
/s/ PAUL A. FRIEDMAN, M.D. Paul A. Friedman, M.D.	Director	February 19, 2026
/s/ RAYMOND CHEONG, M.D., PH.D. Raymond Cheong, M.D., Ph.D.	Director	February 19, 2026
/s/ RICHARD S. LEVY, M.D. Richard S. Levy, M.D.	Director	February 19, 2026

Signatures	Title	Date
/s/ JAMES M. DALY James M. Daly	Director	February 19, 2026
/s/ JACQUALYN FOUSE, Ph.D. Jacqualyn Fouse, Ph.D.	Director	February 19, 2026
/s/ DANIEL BRENNAN Daniel Brennan	Director	February 19, 2026

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

	Page
Report of Independent Registered Public Accounting Firm (PCAOB ID 238)	F-2
Consolidated Financial Statements:	
Consolidated Balance Sheets	F-4
Consolidated Statements of Operations	F-5
Consolidated Statements of Comprehensive Loss	F-6
Consolidated Statements of Stockholders' Equity	F-7
Consolidated Statements of Cash Flows	F-8
Notes to Consolidated Financial Statements	F-9

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

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of Madrigal Pharmaceuticals, Inc. and its subsidiaries (the "Company") as of December 31, 2025 and 2024, and the related consolidated statements of operations, of comprehensive loss, of stockholders' equity and of cash flows for each of the three years in the period ended December 31, 2025, including the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2025, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2025 and 2024, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2025 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2025, based on criteria established in Internal Control - Integrated Framework (2013) issued by the COSO.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report On Internal Control Over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on the Company's consolidated financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (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 audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

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 (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of 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.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that (i) relates to accounts or disclosures that are material to the consolidated financial statements and (ii) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters 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.

Recognition of Product Revenue, Net

As described in Note 2 to the consolidated financial statements, the Company recognizes revenue at a point in time when the customer obtains control of promised goods or services in an amount that reflects the consideration to which the Company expects to be entitled in exchange for those goods or services. Revenue is recorded net of variable consideration, which includes prompt pay discounts, returns, chargebacks, rebates, and co-payment assistance. Total product revenue, net, recognized during the year ended December 31, 2025 was $958.4 million.

The principal consideration for our determination that performing procedures relating to the recognition of product revenue, net is a critical audit matter is a high degree of auditor effort in performing procedures related to the Company's revenue recognition.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included testing the effectiveness of controls relating to the revenue recognition process. These procedures also included, among others, (i) testing revenue recognized for a sample of revenue transactions by obtaining and inspecting source documents, such as customer contracts, purchase orders, invoices, proof of delivery and subsequent cash receipts, where applicable; (ii) testing the Company's reconciliation of gross revenue recognized from product sales to third-party information, and (iii) testing, on a sample basis, variable consideration transactions by obtaining and inspecting source documents such as rebate claims received from indirect customers and corresponding payments, and evaluating for consistency with the contractual terms and the Company's policies.

/s/ PricewaterhouseCoopers LLP
Philadelphia, Pennsylvania
February 19, 2026

We have served as the Company's auditor since 2016.

MADRIGAL PHARMACEUTICALS, INC.

Consolidated Balance Sheets

(in thousands, except share and per share amounts)

	December 31, 2025	December 31, 2024
Assets		
Current assets:		
Cash and cash equivalents	$ 198,693	$ 100,019
Restricted cash	5,090	5,000
Marketable securities	784,866	826,232
Trade receivables, net	134,476	53,822
Inventory	74,841	34,068
Prepaid expenses and other current assets	47,804	13,786
Total current assets	1,245,770	1,032,927
Property and equipment, net	1,499	2,190
Intangible assets, net	7,381	4,729
Right-of-use asset	4,939	2,401
Total assets	$ 1,259,589	$ 1,042,247
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 48,878	$ 43,599
Accrued liabilities	260,392	124,695
Lease liabilities	1,018	983
Total current liabilities	310,288	169,277
Long term liabilities:		
Loan payable, net of discount	339,881	117,569
Lease liabilities	6,731	1,018
Total long term liabilities	346,612	118,587
Total liabilities	656,900	287,864
Stockholders' equity:		
Preferred stock, par value $0.0001 per share authorized: 5,000,000 shares at December 31, 2025 and December 31, 2024; 2,369,797 shares issued and outstanding at December 31, 2025 and December 31, 2024	—	—
Common stock, par value $0.0001 per share authorized: 200,000,000 at December 31, 2025 and December 31, 2024; 22,842,073 and 22,004,679 shares issued and outstanding at December 31, 2025 and December 31, 2024, respectively	2	2
Additional paid-in-capital	2,692,280	2,556,095
Accumulated other comprehensive income	873	468
Accumulated deficit	(2,090,466)	(1,802,182)
Total stockholders' equity	602,689	754,383
Total liabilities and stockholders' equity	$ 1,259,589	$ 1,042,247

See accompanying notes to consolidated financial statements.

MADRIGAL PHARMACEUTICALS, INC.

Consolidated Statements of Operations

(in thousands, except share and per share amounts)

	Year Ended December 31,		
	2025	**2024**	**2023**
Revenues:			
Product revenue, net	$ 958,403	$ 180,133	$ —
Operating expenses:			
Cost of sales	56,148	6,233	—
Research and development	388,525	236,718	272,350
Selling, general and administrative	813,827	435,057	108,146
Total operating expenses	1,258,500	678,008	380,496
Loss from operations	(300,097)	(497,875)	(380,496)
Interest income	37,364	46,654	19,578
Interest expense	(22,309)	(14,671)	(12,712)
Loss on extinguishment of debt	(2,779)	—	—
Other expense, net	(463)	—	—
Net loss	$ (288,284)	$ (465,892)	$ (373,630)
Net loss per common share:			
Basic and diluted net loss per common share	$ (12.85)	$ (21.90)	$ (19.99)
Basic and diluted weighted average number of common shares outstanding	22,434,310	21,272,962	18,687,774

See accompanying notes to consolidated financial statements.

MADRIGAL PHARMACEUTICALS, INC.

Consolidated Statements of Comprehensive Loss

(in thousands, except share and per share amounts)

	Year Ended December 31,		
	2025	2024	2023
Net loss	$ (288,284)	$ (465,892)	$ (373,630)
Other comprehensive income:			
Net unrealized gain on available-for-sale securities	392	—	500
Foreign currency translation gain	13	—	—
Total other comprehensive income	405	—	500
Comprehensive loss	$ (287,879)	$ (465,892)	$ (373,130)

See accompanying notes to consolidated financial statements.

MADRIGAL PHARMACEUTICALS, INC.

Consolidated Statements of Stockholders' Equity

(in thousands, except share and per share amounts)

	Preferred stock		Common stock		Additional paid-in Capital	Accumulated other comprehensive income (loss)	Accumulated deficit	Total stockholders' equity
	Shares	Amount	Shares	Amount				
Balance at December 31, 2022	2,369,797	$ —	18,102,523	$ 2	$ 1,160,079	$ (32)	$ (962,660)	$ 197,389
Issuance of common shares in equity offerings, excluding to related parties, net of transaction costs	—	—	1,346,199	—	260,187	—	—	260,187
Sale of warrants and common shares to related parties and exercise of common stock options, net of transaction costs	—	—	426,705	—	270,292	—	—	270,292
Stock-based compensation expense related to equity-classified awards	—	—	—	—	49,735	—	—	49,735
Unrealized gain on marketable securities	—	—	—	—	—	500	—	500
Hercules warrant	—	—	—	—	860	—	—	860
Net loss	—	—	—	—	—	—	(373,630)	(373,630)
Balance at December 31, 2023	2,369,797	$ —	19,875,427	$ 2	$ 1,741,153	$ 468	$ (1,336,290)	$ 405,333
Issuance of common shares in equity offerings, excluding to related parties, net of transaction costs	—	—	1,096,153	—	397,487	—	—	397,487
Sale of warrants and common shares to related parties and exercise of common stock options, net of transaction costs	—	—	1,033,099	—	337,575	—	—	337,575
Stock-based compensation expense related to equity-classified awards	—	—	—	—	79,880	—	—	79,880
Net loss	—	—	—	—	—	—	(465,892)	(465,892)
Balance at December 31, 2024	2,369,797	$ —	22,004,679	$ 2	$ 2,556,095	$ 468	$ (1,802,182)	$ 754,383
Issuance of common stock under equity plans	—	—	837,394	—	38,055	—	—	38,055
Stock-based compensation expense related to equity-classified awards	—	—	—	—	98,130	—	—	98,130
Other comprehensive income	—	—	—	—	—	405	—	405
Net loss	—	—	—	—	—	—	(288,284)	(288,284)
Balance at December 31, 2025	2,369,797	$ —	22,842,073	$ 2	$ 2,692,280	$ 873	$ (2,090,466)	$ 602,689

See accompanying notes to consolidated financial statements.

MADRIGAL PHARMACEUTICALS, INC.

Consolidated Statements of Cash Flows

(in thousands, except share and per share amounts)

	Year Ended December 31,		
	2025	**2024**	**2023**
Cash flows from operating activities:			
Net loss	$ (288,284)	$ (465,892)	$ (373,630)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation expense	98,130	79,880	49,735
Depreciation and amortization expense	1,506	1,096	527
Amortization of debt issuance costs and discount	1,604	2,089	2,414
Amortization and interest accretion related to operating leases	3,210	(400)	—
Loss on extinguishment of debt	2,779	—	—
Changes in operating assets and liabilities:			
Trade receivables, net	(80,654)	(53,822)	—
Inventory	(36,978)	(34,068)	—
Prepaid expenses and other current assets	(34,018)	(10,636)	(555)
Accounts payable	5,279	15,558	4,210
Accrued liabilities	131,902	34,715	(1,481)
Accrued interest, net of interest received on maturity of investments	5,971	(24,092)	(5,450)
Net cash used in operating activities	(189,553)	(455,572)	(324,230)
Cash flows from investing activities:			
Purchases of marketable securities	(1,047,510)	(1,131,207)	(834,439)
Sales and maturities of marketable securities	1,083,297	863,283	333,398
Acquisition of intangible asset	(3,000)	(5,000)	—
Purchases of property and equipment, net of disposals	(467)	(1,462)	(1,479)
Net cash provided by (used in) investing activities	32,320	(274,386)	(502,520)
Cash flows from financing activities:			
Proceeds from issuances of stock, excluding related parties, net of transaction costs	—	397,487	260,187
Proceeds from related parties - warrants, exercise of common stock options, net of transaction costs	38,055	337,575	270,292
Proceeds from issuance of debt	350,000	—	65,000
Payment of debt issuance costs	(10,407)	—	(363)
Repayment of debt	(121,664)	—	—
Net cash provided by financing activities	255,984	735,062	595,116
Effect of exchange rate changes on cash, cash equivalents and restricted cash	13	—	—
Net increase (decrease) in cash, cash equivalents, and restricted cash	98,764	5,104	(231,634)
Cash, cash equivalents, and restricted cash at beginning of period	105,019	99,915	331,549
Cash, cash equivalents, and restricted cash at end of period	$ 203,783	$ 105,019	$ 99,915
Supplemental disclosure of cash flow information:			
Obtaining a right-of-use asset in exchange for a lease liability	$ 3,982	$ 1,330	$ 1,628

See accompanying notes to consolidated financial statements.

1. Organization, Business and Basis of Presentation

Organization and Business

Madrigal Pharmaceuticals, Inc. (the "Company" or "Madrigal") is a biopharmaceutical company focused on delivering novel therapeutics for metabolic dysfunction-associated steatohepatitis ("MASH"), a serious liver disease with high unmet medical need that can lead to cirrhosis, liver failure, liver cancer, need for liver transplantation and premature mortality. MASH was previously known as nonalcoholic steatohepatitis ("NASH"). MASH is the leading cause of liver transplantation in women, the second leading cause of all liver transplantation in the United States and the fastest-growing indication for liver transplantation in Europe. The Company's medication, Rezdiffra (resmetirom), is a once-daily, oral, liver-directed thyroid hormone receptor beta ("THR-β") agonist designed to target key underlying causes of MASH. In March 2024, Rezdiffra became the first therapy approved by the U.S. Food and Drug Administration ("FDA") for patients with MASH and was commercially available in the United States beginning in April 2024. Following receipt of conditional marketing authorization ("CMA") from the European Commission ("EC"), the Company launched Rezdiffra in Germany in September 2025. Rezdiffra was the first medication approved by both the FDA and EC for the treatment of adults with noncirrhotic MASH with moderate to advanced liver fibrosis (F2 to F3 fibrosis). The Company is also evaluating Rezdiffra in patients with compensated MASH cirrhosis (consistent with F4c fibrosis) in its MAESTRO-NASH OUTCOMES trial, that, if successful, could expand the eligible patient population for Rezdiffra. In addition, the Company plans to evaluate its pipeline candidates with the goal of delivering best-in-disease therapies for the treatment of MASH.

Basis of Presentation

The accompanying consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the United States of America ("U.S. GAAP") and include accounts of the Company and its wholly-owned subsidiaries. Certain prior period amounts have been reclassified to align with current period presentation.

2. Summary of Significant Accounting Policies

Principle of Consolidation

The consolidated financial statements include the financial statements of the Company and its wholly owned subsidiaries. All significant intercompany balances and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect certain reported amounts of assets and liabilities, and the reported amounts of revenues and expenses during the reporting periods. The Company bases its estimates on historical experience and various other assumptions that management believes to be reasonable under the circumstances. Changes in estimates are recorded in the period in which they become known. Actual results could differ from those estimates.

Revenue Recognition

The Company recognizes revenue in accordance with ASC Topic 606 - Revenue from Contracts with Customers ("ASC 606"). Revenue is recognized at a point in time when the customer obtains control of promised goods or services in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligation(s) in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligation(s) in the contract; and (v) recognize revenue when (or as) the Company satisfies its performance obligation(s).

Product Revenue, Net

On March 14, 2024, the Company announced that the FDA granted accelerated approval of Rezdiffra (resmetirom) in conjunction with diet and exercise for the treatment of adults with noncirrhotic MASH with moderate to

advanced liver fibrosis (consistent with stages F2 to F3 fibrosis). The Company enters into agreements with specialty pharmacies and specialty distributors (each a "Customer" and collectively the "Customers") to sell Rezdiffra in the U.S.. Revenues from product sales are recognized when the Customer obtains control of the Company's product, which occurs at a point in time, typically upon delivery to the Customer.

Revenue is recorded net of variable consideration, which includes prompt pay discounts, returns, chargebacks, rebates and co-payment assistance. The variable consideration is estimated based on contractual terms as well as management assumptions and historical data. The amount of variable consideration is calculated by using the expected value method, which is the sum of probability-weighted amounts in a range of possible outcomes, or the most likely amount method, which is the single most likely amount in a range of possible outcomes. Estimates are reviewed quarterly and adjusted as necessary.

Accruals are established for gross to net deductions and actual amounts incurred are offset against applicable accruals. The Company reflects these accruals as either a reduction in the related account receivable from the customer or as a current liability, depending on the means by which the deduction is settled. Sales deductions are based on management's estimates that involve a substantial degree of judgment.

Prompt Pay: Customers receive a prompt pay discount for payments made within a contractually agreed number of days before the due date. The discounts are accounted for as a reduction of the transaction price and recorded as a contra receivable.

Returns: The Company records allowances for product returns as a reduction of revenue at the time product sales are recorded. Product returns are estimated based on forecasted sales and historical and industry data. Returns are permitted in accordance with the return goods policy defined within each customer agreement. A returns reserve is recorded as an accrued liability.

Chargebacks: The Company estimates obligations resulting from contractual commitments with the government and other entities to sell products to qualified healthcare providers at prices lower than the list prices charged to the customer who directly purchases from the Company. The customer charges the Company for the difference between what it pays to the Company for the product and the selling price to the qualified healthcare providers, with the difference recorded as a contra receivable.

Co-Payment Assistance: Co-payment assistance programs are offered to eligible end-users as price concessions and are recorded as accrued liabilities and a reduction of the transaction price. The Company uses a third-party to administer the co-payment program for pharmacy benefit claims.

Rebates: The Company's rebates include amounts paid to Medicaid, Medicare, certain other payors and other rebate programs. Reserves for rebates are recorded in the same period the related product revenue is recognized, resulting in a reduction of product revenues and a current liability that is included in accrued expenses on the consolidated balance sheet. The Company's estimate for rebates is based on statutory or contractual discount rates, expected utilization or an estimated number of patients on treatment, as applicable.

Trade Receivables, Net

The Company's trade receivables relate to amounts due from Customers related to product sales and are recorded net of prompt pay discounts and chargebacks. The Company assesses collectibility of overdue receivables and those determined to be uncollectible are written-off. As of December 31, 2025, there were no receivables written off.

Cash and Cash Equivalents

The Company considers all highly liquid debt instruments with an original maturity of three months or less to be cash equivalents. The carrying amount reported in the Company's consolidated balance sheets for cash and cash equivalents approximates its fair value.

Marketable Securities

Marketable securities consist of available-for-sale debt securities that are presented as current assets in the Company's consolidated balance sheets.

The Company adjusts the cost of available-for-sale debt securities for amortization of premiums and accretion of discounts to maturity. The Company includes such amortization and accretion as a component of interest income, net. Realized gains and losses and declines in value, if any, that the Company judges to be the result of impairment or as a result of recognizing an allowance for credit losses on available-for-sale securities are reported as a component of interest income. To determine whether an impairment exists, the Company considers whether it intends to sell the debt security and, if the Company does not intend to sell the debt security, it considers available evidence to assess whether it is more

likely than not that it will be required to sell the security before the recovery of its amortized cost basis. During the years ended December 31, 2025, 2024 and 2023, the Company determined it did not have any securities that were other-than-temporarily impaired.

Marketable securities are stated at fair value, including accrued interest, with their unrealized gains and losses included as a component of accumulated other comprehensive income or loss, which is a separate component of stockholders' equity. The fair value of these securities is based on quoted prices and observable inputs on a recurring basis. Realized gains and losses are determined on the specific identification method. During the years ended December 31, 2025, 2024 and 2023, realized gains and losses on marketable securities were not material to the consolidated financial statements.

Fair Value of Financial Instruments

The carrying amounts of the Company's financial instruments, which include cash equivalents, and marketable securities, approximate their fair values. The fair value of the Company's financial instruments reflects the amounts that would be received upon sale of an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. The fair value hierarchy has the following three levels:

Level 1—quoted prices in active markets for identical assets and liabilities.

Level 2—observable inputs other than Level 1 inputs. Examples of Level 2 inputs include quoted prices in active markets for similar assets or liabilities and quoted prices for identical assets or liabilities in markets that are not active.

Level 3—unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability.

Financial assets and liabilities are classified in their entirety within the fair value hierarchy based on the lowest level of input that is significant to the fair value measurement. The Company measures the fair value of its marketable securities by taking into consideration valuations obtained from third-party pricing sources. The pricing services utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of and broker-dealer quotes on the same or similar securities, issuer credit spreads, benchmark securities and other observable inputs.

As of December 31, 2025 and 2024, the Company's financial assets valued based on Level 1 inputs consisted of cash and cash equivalents in a money market fund, its financial assets valued based on Level 2 inputs consisted of high-grade corporate and government agency bonds and commercial paper, and it had no financial assets valued based on Level 3 inputs. During the years ended December 31, 2025, 2024 and 2023, the Company did not have any transfers of financials assets between Levels 1 and 2. As of December 31, 2025 and 2024, the Company did not have any financial liabilities that were recorded at fair value on a recurring basis on the balance sheet.

Inventory

Inventory, which consists of work in process and finished goods, is stated at the lower of cost or estimated net realizable value, using actual cost, based on a first-in, first-out method. The balance sheet classification of inventory as current or non-current is determined by whether it will be consumed within the Company's normal operating cycle. The Company analyzes its inventory levels quarterly and writes down inventory subject to expiry or in excess of expected requirements, or that has a cost basis in excess of its expected net realizable value. These write downs are charged to cost of sales in the accompanying Consolidated Statements of Operations. The Company capitalizes inventory costs when future commercial sale in the ordinary course of business is probable.

The Company considered regulatory approval of its product candidate to be uncertain and product manufactured prior to regulatory approval could not have been sold unless regulatory approval was obtained. As such, the manufacturing costs incurred prior to regulatory approval were not capitalized as inventory, but rather were expensed as incurred as research and development expenses. The Company began capitalizing inventory in March 2024 after FDA approval was granted.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development costs are comprised of costs incurred in performing research and development activities, including internal costs (including cash compensation and stock-based compensation), costs for consultants, milestone payments under licensing agreements, and other costs associated with the Company's preclinical and clinical programs. In particular, the Company has conducted safety studies in animals, optimized and implemented the manufacturing of its drug, and conducted clinical trials, all of which are

considered research and development expenditures. Management uses significant judgment in estimating the amount of research and development costs recognized in each reporting period. Management analyzes and estimates the progress of its clinical trials, completion of milestone events per underlying agreements, invoices received and contracted costs when estimating the research and development costs to accrue in each reporting period. Actual results could differ from the Company's estimates.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist primarily of salaries, benefits and stock-based compensation expenses for employees, management costs, costs associated with obtaining and maintaining our patent portfolio, commercial and marketing activities, advertising, professional fees for accounting, auditing, consulting and legal services, and allocated overhead expenses.

Advertising costs are expensed as incurred. During the years ended December 31, 2025 and 2024, advertising costs were approximately $145.1 million and $52.7 million. The Company did not have any commercial products during the year ended December 31, 2023 and therefore no related advertising costs.

Leases

The Company determines if an arrangement is a lease at contract inception. All leases are classified as operating leases. Lease assets represent the right to use an underlying asset for the lease term and lease liabilities represent an obligation to make lease payments arising from the leasing arrangement. Operating lease assets and liabilities are recognized at commencement date based on the present value of lease payments over the lease term. When an implicit rate is not readily determinable, an incremental borrowing rate is estimated based on information available at commencement. Lease expense is recognized on a straight-line basis over the lease term. Short-term leases of 12 months or less at commencement date are expensed as incurred.

Patents

Costs to secure and defend patents are expensed as incurred and are classified as selling, general and administrative expense in the Company's statements of operations. Patent expenses were approximately $0.7 million, $0.7 million and $0.9 million for the years ended December 31, 2025, 2024 and 2023, respectively.

Intangible Assets, Net

Intangible assets with finite lives are amortized to cost of sales over their estimated useful lives using the straight-line method. Intangible assets are tested for recoverability whenever events or changes in circumstances indicate that the carrying amounts may not be recoverable.

Stock-Based Compensation

The Company recognizes stock-based compensation expense based on the grant date fair value of stock options, restricted stock units, and other stock-based compensation awards granted to employees, officers, directors, and consultants. Awards that vest as the recipient provides service are expensed on a straight-line basis over the requisite service period.

The Company uses the Black-Scholes option pricing model to determine the grant date fair value of stock options as management believes it is the most appropriate valuation method for its option grants. The Black-Scholes model requires inputs for risk-free interest rate, dividend yield, volatility and expected lives of the options. The expected lives for options granted represent the period of time that options granted are expected to be outstanding. The Company uses the simplified method for determining the expected lives of options. Expected volatility is based upon an industry estimate, the Company's historical trading activity, or a blended rate of the two. The risk-free rate for periods within the expected life of the option is based on the U.S. Treasury yield curve in effect at the time of the grant. The Company estimates the forfeiture rate based on historical data. This analysis is re-evaluated at least annually and the forfeiture rate is adjusted as necessary.

For other stock-based compensation awards granted to employees and directors that vest based on market conditions, such as the trading price of the Company's common stock achieving or exceeding certain price targets, the Company uses a Monte Carlo simulation model to estimate the grant date fair value and recognize stock compensation expense over the derived service period. The Monte Carlo simulation model requires key inputs for risk-free interest rate, dividend yield, volatility, and expected life.

The assumptions used in computing the fair value of equity awards reflect the Company's best estimates but involve uncertainties related to market and other conditions. Changes in any of these assumptions may materially affect the fair value of awards granted and the amount of stock-based compensation recognized.

Income Taxes

The Company accounts for income taxes in accordance with ASC 740, "Income Taxes", which prescribes the use of the liability method where deferred tax asset and liability account balances are determined based on differences between financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. The Company provides a valuation allowance, if necessary, to reduce deferred tax assets to their estimated realizable value if it is more likely than not that a portion or all of the deferred tax assets will not be realized based on the weight of available positive and negative evidence. The Company currently maintains a 100% valuation allowance on its deferred tax assets.

The Company recognizes the financial statement effects of a tax position when it is more likely than not (a likelihood of greater than 50%) that the position will be sustained upon examination by the relevant taxing authority, based on the technical merits of the position. Uncertain tax positions are recorded based upon certain recognition and measurement criteria. The Company re-evaluates uncertain tax positions at each reporting date and considers all available information, including, but not limited to, changes in tax laws or regulations, developments in case law, changes in the expected timing or outcome of audits, settlements with taxing authorities, and changes in facts or circumstances related to a particular tax position. Adjustments to recognized tax positions are recorded in the period in which new information becomes available. Interest and penalties related to unrecognized tax benefits are recognized as a component of income tax expense in the Consolidated Statements of Operations.

Comprehensive Income (Loss)

Comprehensive income (loss) is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. The difference between the Company's net income (loss) and comprehensive income (loss) includes changes in unrealized gains and losses on marketable securities and foreign currency translation adjustments.

Basic and Diluted Loss Per Common Share

Basic net loss per share is computed using the weighted average number of common shares outstanding during the period. Diluted net loss per common share is computed using the weighted average number of common shares outstanding and the weighted average dilutive potential common shares outstanding using the treasury stock method. However, for the years ended December 31, 2025, 2024 and 2023, diluted net loss per share is the same as basic net loss per share because the inclusion of weighted average shares of common stock issuable upon the exercise of stock options and warrants or vesting of restricted stock units, and common stock issuable upon the conversion of preferred stock would be anti-dilutive.

The following table summarizes outstanding securities not included in the computation of diluted net loss per common share as their inclusion would be anti-dilutive:

	As of December 31,		
	2025	2024	2023
Common stock options	979,861	1,528,143	2,355,779
Restricted stock units	798,422	499,559	376,117
Performance-based restricted stock units	256,488	235,520	150,000
Convertible preferred stock	2,369,797	2,369,797	2,369,797
Warrants	19,454	19,454	19,454
Pre-funded warrants	3,605,790	3,605,790	2,048,098

Recent Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board ("FASB") or other standard setting bodies and adopted by the Company as of the specified effective date. Except as noted below, the Company believes that the impact of recently issued standards that are not yet effective will not have a material impact on its condensed consolidated financial statements and disclosures.

In December 2023, the FASB issued ASU 2023-09, Income Taxes (Topic 740): Improvements to Income Tax Disclosures, which enhances the disclosures required for income taxes in the Company's annual consolidated financial statements. The amendments are effective for annual periods beginning after December 15, 2024. The Company adopted ASU 2023-09 prospectively, and the adoption impacted the Company's income tax disclosures only and did not have an impact on its consolidated financial statements.

In November 2024, the FASB issued ASU 2024-03, Disaggregation of Income Statement Expenses ("DISE"), which applies to all public entities and requires disclosures about specific types of expenses included in the expense captions presented on the face of the income statement as well as disclosures about selling expenses. Public entities must adopt the new standard prospectively for fiscal years beginning after December 15, 2026, and interim reporting periods beginning after December 15, 2027. Early adoption and retrospective application are permitted. The Company is currently evaluating the impact of ASU 2024-03 on its consolidated financial statements.

In September 2025, the FASB issued ASU 2025-06, Intangibles - Goodwill and Other - Internal-Use Software (Subtopic 350-40): Targeted Improvements to the Accounting for Internal-Use Software ("ASU 2025-06"), which clarifies and aligns existing guidance related to accounting for certain costs incurred in connection with internal-use software, including updated guidance regarding agile and iterative software development methodologies. The standard applies to all entities that incur costs to develop internal-use software. ASU 2025-06 is effective for annual periods beginning after December 15, 2027, and interim periods within those annual periods. Early adoption is permitted. The Company is currently evaluating the impact of ASU 2025-06 on its consolidated financial statements.

3. Liquidity and Uncertainties

The Company is subject to risks common to development stage companies and early commercial companies in the biopharmaceutical industry including, but not limited to, uncertainty of product development and commercialization, dependence on key personnel, uncertainty of market acceptance of products and product reimbursement, product liability, uncertain protection of proprietary technology, potential inability to raise additional financing necessary for development and commercialization, and compliance with applicable regulations.

The Company has incurred losses since inception, including $288.3 million for the year ended December 31, 2025, resulting in an accumulated deficit of $2,090.5 million and $1,802.2 million as of December 31, 2025 and 2024, respectively. The Company has historically funded its operations primarily through proceeds from sales of the Company's capital stock and debt financings. In July 2025, the Company entered into a senior secured credit facility that provides up to $500.0 million. See Note 8 "Long Term Debt" for additional details. In addition, following FDA and EC approval, the Company receives revenue from sales of Rezdiffra. Management expects to incur losses until the Company is able to generate sufficient revenue from Rezdiffra and any other approved products. The Company believes that its cash, cash equivalents and marketable securities at December 31, 2025 will be sufficient to fund operations past one year from the issuance of these financial statements. The Company's future long-term liquidity requirements will be substantial and will depend on many factors, including the Company's ability to effectively commercialize Rezdiffra, the Company's decisions regarding future geographic expansion, the conduct of any future preclinical studies and clinical trials, the Company entering into any strategic transactions, the Company's ability to maintain compliance with the liquidity covenant in the Financing Agreement (as defined in Note 8) and potential milestone payments payable pursuant to its license agreements. To meet its future capital needs, the Company may need to raise additional capital through debt or equity financings, collaborations, partnerships or other strategic transactions. However, there can be no assurance that the Company will be able to complete any such transactions on acceptable terms or otherwise. The inability of the Company to obtain sufficient funds on acceptable terms when needed, if at all, could have a material adverse effect on the Company's business, results of operations and financial condition. The Company has the ability to delay certain commercial activities, geographic expansion activities and certain research activities and related clinical expenses if necessary due to liquidity concerns until a date when those concerns are relieved.

4. Product Revenue, Net

The following table summarizes balances and activity for gross to net reserves (in thousands):

	Chargebacks, Discounts for Prompt Pay and Other Allowances	Rebates, Customer Fees/Credits, Co-Pay Assistance, and Other	Totals
Balance at December 31, 2023	$ —	$ —	$ —
Provision related to sales in the current year	8,045	35,115	43,160
Adjustments related to prior year sales	—	—	—
Payments and customer credits issued	(3,857)	(13,412)	(17,269)
Balance at December 31, 2024	$ 4,188	$ 21,703	$ 25,891
Provision related to sales in the current year	36,640	208,462	245,102
Adjustments related to prior year sales	(1,573)	(4,655)	(6,228)
Payments and customer credits issued	(30,417)	(135,006)	(165,423)
Balance at December 31, 2025	$ 8,838	$ 90,504	$ 99,342

Concentrations of Credit Risk and Significant Customers

The Company generates revenue from a small number of large, reputable customers. The following customers accounted for over 10% of total gross product revenue during the year ended December 31, 2025 and the year ended December 31, 2024. Rezdiffra was first made commercially available in April 2024, and therefore there were no sales and no corresponding customer concentrations in 2023.

	Year ended December 31,		
	2025	2024	2023
Customer A	34 %	39 %	— %
Customer B	22 %	21 %	— %
Customer C	15 %	14 %	— %
Customer D	12 %	12 %	— %

5. Cash, Cash Equivalents, Restricted Cash, and Marketable Securities

The Company held restricted cash of $5.1 million and $5.0 million as of December 31, 2025 and 2024, respectively, predominately as collateral to its corporate credit card program. The Company did not have any restricted cash as of December 31, 2023.

A summary of cash, cash equivalents, restricted cash and available-for-sale marketable securities held by the Company as of December 31, 2025 and 2024 is as follows (in thousands):

	December 31, 2025			
	Cost	Unrealized gains	Unrealized losses	Fair value
Cash and cash equivalents:				
Cash (Level 1)	$ 109,708	$ —	$ —	$ 109,708
Money market funds (Level 1)	50,211	—	—	50,211
U.S. government and government-sponsored entity (GSE) securities (Level 1)	9,129	—	—	9,129
Corporate debt securities with original maturities of 3 months or less (Level 2)	34,735	—	—	34,735
Total cash and cash equivalents	203,783	—	—	203,783
Marketable securities:				
Corporate debt securities with original maturities of 1 year or less (Level 2)	372,096	178	(16)	372,258
U.S. government and GSE securities with original maturities of 1 year or less (Level 2)	298,007	460	(1)	298,466
U.S. government and GSE securities with original maturities of 1 to 2 years (Level 2)	91,936	211	—	92,147
Corporate debt securities with original maturities of 1 to 2 years (Level 2)	21,968	30	(3)	21,995
Total cash, cash equivalents, restricted cash, and marketable securities	$ 987,790	$ 879	$ (20)	$ 988,649

	December 31, 2024			
	Cost	Unrealized gains	Unrealized losses	Fair value
Cash and cash equivalents:				
Cash (Level 1)	$ 24,495	$ —	$ —	$ 24,495
Money market funds (Level 1)	65,302	—	—	65,302
U.S. government and GSE securities (Level 1)	12,711	—	—	12,711
Corporate debt securities with original maturities of 3 months or less (Level 2)	2,511	—	—	2,511
Total cash and cash equivalents	105,019	—	—	105,019
Marketable securities:				
Corporate debt securities with original maturities of 1 year or less (Level 2)	367,950	190	(64)	368,076
U.S. government and GSE securities with original maturities of 1 year or less (Level 2)	382,793	279	(62)	383,010
U.S. government and GSE securities with original maturities of 1 to 2 years (Level 2)	71,739	156	(25)	71,870
Corporate debt securities with original maturities of 1 to 2 years (Level 2)	3,282	—	(6)	3,276
Total cash, cash equivalents, restricted cash, and marketable securities	$ 930,783	$ 625	$ (157)	$ 931,251

6. Inventory

The following table summarizes the Company's inventory balances as of December 31, 2025 and 2024 (in thousands):

	December 31, 2025	December 31, 2024
Raw materials	$ —	$ —
Work in process	67,633	29,533
Finished goods	7,208	4,535
Total	$ 74,841	$ 34,068

There was no provision for excess inventory recorded during the years ended December 31, 2025, 2024 or 2023.

7. Accrued Liabilities

Accrued liabilities as of December 31, 2025 and 2024 consisted of the following (in thousands):

	December 31, 2025	December 31, 2024
Gross to net accrued expenses	$ 90,504	$ 21,703
Clinical study, manufacturing and drug supply	26,907	43,890
Compensation and benefits	69,211	34,209
Selling, general and administrative	40,026	18,257
Other	33,744	6,636
Total accrued liabilities	$ 260,392	$ 124,695

8. Long Term Debt

Hercules Loan Facility

In May 2022, the Company entered into a $250.0 million senior secured loan facility (as amended from time to time, the "Hercules Loan Facility") with several banks and other financial institutions or entities party thereto (collectively, the "Hercules Lenders"), and Hercules Capital, Inc. ("Hercules"), in its capacity as administrative agent and collateral agent for itself and the Hercules Lenders. Interest on the Hercules Loan Facility was the greater of (i) the prime rate plus 2.45% and (ii) 8.25%. The Hercules Loan Facility included an end-of-term charge of 5.35% of the aggregate principal amount, which was accounted for in the loan discount. In connection with the first tranche drawn at closing, the Company issued Hercules a warrant to purchase 14,899 shares of Company common stock, which had a Black-Scholes value of $0.6 million. In addition, the Company issued to Hercules and its affiliates warrants to purchase an aggregate of 4,555 shares of common stock, which had a Black-Scholes value of $0.9 million, following the closing of the second tranche.

On July 17, 2025, the Company used the proceeds of the Initial Term Loan under the Financing Agreement (each as defined below) to repay all outstanding obligations under the Hercules Loan Facility, totaling $121.7 million, and upon such repayment, terminated the Hercules Loan Facility. The amount repaid by the Company included $115.0 million of outstanding indebtedness plus accrued and unpaid interest as of the repayment date and exit fees. As a result of the termination, all credit commitments under the Hercules Loan Facility were terminated and all security interests and guarantees executed in connection with the Hercules Loan Facility were released. The repayment resulted in a $2.8 million loss on extinguishment of debt, primarily due to the write off of unamortized debt issuance costs.

Blue Owl Credit Facility

On July 17, 2025 (the "Closing Date"), the Company entered into a Financing Agreement (as amended from time to time, the "Financing Agreement") with certain funds managed by Blue Owl Capital Corporation, as the lenders (the "Lenders"), and LSI Financing LLC, as the administrative agent for the Lenders (the "Administrative Agent"). Under the Financing Agreement, the Lenders have committed up to $500.0 million in senior secured credit facilities, consisting of (a) an initial term loan in an aggregate principal amount equal to $350.0 million (the "Initial Term Loan") and (b) delayed draw term loan commitments in an aggregate principal amount not to exceed $150.0 million (the loans thereunder, if any, the "Delayed Draw Term Loans"). In addition, the Financing Agreement includes an uncommitted incremental facility in an aggregate principal amount not to exceed $250.0 million (the loans thereunder, if any, the "Incremental Term Loans", together with the Initial Term Loan and any Delayed Draw Term Loans, collectively the "Term Loans"), subject to the satisfaction of certain terms and conditions set forth in the Financing Agreement. The Initial Term Loan was funded on the Closing Date. Delayed Draw Term Loans are available at the Company's election from time to time after the Closing Date until December 31, 2027. Incremental Term Loans are available at the Company's and the Lenders' mutual consent from time to time after the Closing Date.

Any outstanding principal on the Term Loans will bear interest at a rate per annum on the basis of a 360-day year equal to the sum of (i) the three-month forward-looking term secured overnight financing rate administered by the Federal Reserve Bank of New York (subject to 1.0% per annum floor) plus (ii) 4.75%. Accrued interest is payable quarterly following the funding of the Initial Term Loan on the Closing Date, on any date of prepayment or repayment of the Term Loans and at maturity. The outstanding balance of the Term Loans, if not repaid sooner, shall be due and payable in full on the maturity date thereof. The stated maturity date of the Term Loans is July 17, 2030.

The Company may prepay the Term Loans at any time (in whole or in part) and may be required to make mandatory prepayments upon the occurrence of certain customary prepayment events. In certain instances and during certain time periods, these prepayments will be subject to customary prepayment fees. If the Term Loans are prepaid on or prior to the one-year anniversary of the original issuance, the Company must pay a make-whole amount equal to the greater of (i) 3.00% of the Term Loans being prepaid at such time and (ii) the present value of all remaining interest payments on the amount repaid through the one-year anniversary of the original issuance of such Term Loans, calculated using a discount rate. Thereafter, the amount of any such prepayment fee may vary, but the maximum amount that may be due with any such prepayment would be an amount equal to 3.00% of the Term Loans being prepaid at such time, with such prepayment fee stepping down on each anniversary of the original issuance of such Term Loans.

The Financing Agreement contains affirmative covenants and negative covenants applicable to the Company and its subsidiaries that are customary for financings of this type. The Company and the Guarantors (as defined below) are also required to maintain a minimum unrestricted cash balance of $100.0 million at all times. The Financing Agreement also includes representations, warranties, indemnities and events of default that are customary for financings of this type, including an event of default relating to a change of control of the Company. Upon the occurrence of an event of default,

the Lenders may, among other things, accelerate the Company's obligations under the Financing Agreement. The obligations of the Company under the Financing Agreement are and will be guaranteed by certain of the Company's existing and future direct and indirect subsidiaries, subject to certain exceptions (such subsidiaries, collectively, the "Guarantors").

On July 17, 2025, concurrently with the entry into the Financing Agreement, the Company and the Administrative Agent entered into a Pledge and Security Agreement. As security for the obligations of the Company and the Guarantors, each of the Company and the Guarantors are required to grant to the Administrative Agent, for the benefit of the Lenders and secured parties, a continuing first priority security interest in substantially all of the assets of the Company and the Guarantors (including all equity interests owned or hereafter acquired by the Company and the Guarantors), subject to certain customary exceptions. On September 4, 2025, the parties amended the Financing Agreement to add certain of the Company's subsidiaries as Guarantors.

As of December 31, 2025, the outstanding principal under the Financing Agreement was $350.0 million. The interest rate as of December 31, 2025 was 8.75%. As of December 31, 2025, the Company was in compliance with all loan covenants and provisions.

Future minimum payments, including interest and principal, under the loans payable outstanding as of December 31, 2025 are as follows (in thousands):

Period Ending December 31:	Amount
2026	$ 29,886
2027	29,886
2028	29,968
2029	29,886
2030	366,212
	$ 485,838
Less amount representing interest	(135,838)
Less unamortized discount	(10,119)
Loans payable, net of discount	$ 339,881

9. Stockholders' Equity

Common Stock

Each common stockholder is entitled to one vote for each share of common stock held. The common stock will vote together with all other classes and series of stock of the Company as a single class on all actions to be taken by the Company's stockholders. Each share of common stock is entitled to receive dividends, as and when declared by the Company's Board of Directors (the "Board"). The Company has never declared cash dividends on its common stock and does not expect to do so in the foreseeable future.

Preferred Stock

The Company's Series A Preferred Stock and Series B Preferred Stock (together, the "Series A and B Preferred Stock") have a par value of $0.0001 per share and are convertible into shares of the Company's common stock at a one-to-one ratio, subject to adjustment as provided in the Certificates of Designation of Preferences, Rights and Limitations of Series A Preferred Stock and Series B Preferred Stock that the Company filed with the Secretary of State of the State of Delaware on June 21, 2017 and December 22, 2022, respectively. The terms of the Series A and B Preferred Stock are set forth in such Certificates of Designation. Each share of the Series A and B Preferred Stock is convertible into shares of common stock following notice that may be given at the holder's option. Upon any liquidation, dissolution or winding-up of the Company, whether voluntary or involuntary, after the satisfaction in full of the debts of the Company and the payment of any liquidation preference owed to the holders of shares of capital stock of the Company ranking prior to the Series A and B Preferred Stock upon liquidation, the holders of the Series A and B Preferred Stock shall participate pari passu with the holders of the common stock (on an as-if-converted-to-common-stock basis) in the net assets of the Company. Shares of the Series A and B Preferred Stock will generally have no voting rights, except as required by law. Shares of the Series A and B Preferred Stock will be entitled to receive dividends before shares of any other class or series

of capital stock of the Company (other than dividends in the form of the common stock) equal to the dividend payable on each share of the common stock, on an as-converted basis.

2024 Public Offering

On March 18, 2024, the Company entered into an Underwriting Agreement with Goldman Sachs & Co. LLC, Jefferies LLC, Cowen and Company, LLC, Evercore Group L.L.C. and Piper Sandler & Co, as representatives of the several underwriters named therein (the "2024 Underwriters"), pursuant to which the Company sold to the 2024 Underwriters in an underwritten public offering (the "2024 Offering"): (i) 750,000 shares of common stock at a public offering price of $260.00 per share, (ii) pre-funded warrants (the "2024 Pre-Funded Warrants") to purchase 1,557,692 shares of common stock at a public offering price of $259.9999 per 2024 Pre-Funded Warrant, which represents the per share public offering price for the common stock less a $0.0001 per share exercise price for each such Pre-Funded Warrant, and (iii) a 30-day option for the 2024 Underwriters to purchase up to 346,153 additional shares of common stock at the public offering price of $260.00 per share (the "Underwriters' Option"). The 2024 Offering closed on March 21, 2024. The gross proceeds of the 2024 Offering was $600.0 million, and the Company received net proceeds, after deducting the underwriting discount and commissions and other estimated offering expenses payable by the Company, of approximately $574.0 million.

The Underwriters' Option was later exercised in full, and closed on April 2, 2024. The net proceeds to the Company for the exercise of the Underwriters' Option, after deducting the underwriting discounts and commissions and estimated offering expenses payable by the Company, was approximately $85.9 million.

The 2024 Pre-Funded Warrants are exercisable at any time after the date of issuance. A holder of 2024 Pre-Funded Warrants may not exercise the warrant if the holder, together with its affiliates, would beneficially own more than 9.99% of the number of shares of common stock outstanding immediately after giving effect to such exercise. A holder of 2024 Pre-Funded Warrants may increase or decrease this percentage, but not in excess of 19.99%, by providing at least 61 days prior notice to the Company.

2023 Public Offering

On September 28, 2023, the Company entered into an Underwriting Agreement with Goldman Sachs & Co. LLC, as representative of the several underwriters named therein, pursuant to which the Company sold to the underwriters in an underwritten public offering (the "2023 Offering"): (i) 1,248,098 shares of common stock at a public offering price of $151.69 per share, and (ii) pre-funded warrants (the "Pre-Funded Warrants") to purchase 2,048,098 shares of common stock at a public offering price of $151.6899 per Pre-Funded Warrant, which represents the per share public offering price for the common stock less a $0.0001 per share exercise price for each such Pre-Funded Warrant. The 2023 Offering closed on October 3, 2023.

The gross proceeds of the 2023 Offering was $500.0 million, and the Company received net proceeds, after deducting the underwriting discount and commissions and other estimated offering expenses payable by the Company, of approximately $472.0 million.

The 2023 Pre-Funded Warrants are exercisable at any time after the date of issuance. A holder of Pre-Funded Warrants may not exercise the warrant if the holder, together with its affiliates, would beneficially own more than 9.99% of the number of shares of common stock outstanding immediately after giving effect to such exercise. A holder of Pre-Funded Warrants may increase or decrease this percentage, but not in excess of 19.99%, by providing at least 61 days prior notice to the Company.

At-The-Market Issuance Sales Agreement

In May 2024, the Company entered into a Sales Agreement (the "Sales Agreement") with Cowen and Company, LLC ("Cowen"). Pursuant to the Sales Agreement, the Company is authorized to issue and sell up to $300.0 million in shares of the Company's common stock, at the Company's option, through Cowen as its sales agent. Sales of common stock through Cowen could be made by any method that is deemed an "at-the-market" offering as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, including by means of ordinary brokers' transactions at market prices, in block transactions or as otherwise agreed by the Company and Cowen. Subject to the terms and conditions of the Sales Agreement, Cowen would use commercially reasonable efforts consistent with its normal trading and sales practices to sell the common stock based upon the Company's instructions (including any price, time or size limits or other customary parameters or conditions the Company imposed). The Company sold no shares in the years ended December 31, 2025 or 2024 under the Sales Agreement.

10. Stock-based Compensation

2015 Stock Plan

The 2015 Stock Plan, as amended (the "2015 Stock Plan"), is our shareholder-approved incentive plan through which equity based grants are awarded. The 2015 Stock Plan provides for the grant of incentive stock options, non-statutory stock options, restricted stock, restricted stock units and other stock-based compensation awards to employees, officers, directors, and consultants of the Company. The administration of the 2015 Stock Plan is under the general supervision of the Compensation Committee of the Board of Directors. The terms of stock options awarded under the 2015 Stock Plan, in general, are determined by the Compensation Committee, provided the exercise price per share generally shall not be set at less than the fair market value of a share of the common stock on the date of grant and the term shall not be greater than ten years from the date the option is granted. As of December 31, 2025, 654,994 shares were available for future issuance under the 2015 Stock Plan.

2023 Inducement Plan

In September 2023, the Company adopted the 2023 Inducement Plan (the "2023 Inducement Plan"), pursuant to which the Company from time to time was permitted to make equity grants to new employees as a material inducement to their employment. The 2023 Inducement Plan was adopted without stockholder approval, pursuant to Nasdaq Listing Rule 5635(c)(4), and was administered by the Compensation Committee of the Board. The 2023 Inducement Plan provided for the granting of non-statutory stock options, restricted stock, restricted stock units, performance stock units and other stock-based compensation awards to new employees, but did not allow for the granting of incentive stock options. The terms of the stock options under the 2023 Inducement Plan, in general, were determined by the Compensation Committee, provided the exercise price per share generally would not be set at less than the fair market value of a share of the common stock on the date of grant and the term would not be greater than ten years from the date the option or award was granted. A total of 500,000 shares of the Company's common stock were reserved for issuance under the 2023 Inducement Plan. In June 2025, the Company terminated the 2023 Inducement Plan, and therefore no additional awards may be made from the 2023 Inducement Plan. Any awards outstanding under the 2023 Inducement Plan will continue to be governed by the terms thereof.

2025 Inducement Plan

In June 2025, the Company adopted the 2025 Inducement Plan (the "2025 Inducement Plan"), pursuant to which the Company may from time to time make equity grants to new employees as a material inducement to their employment. The 2025 Inducement Plan was adopted without stockholder approval, pursuant to Nasdaq Listing Rule 5635(c)(4), and is administered by the Compensation Committee of the Board. The 2025 Inducement Plan provides for the granting of non-statutory stock options, restricted stock, restricted stock units, performance stock units and other stock-based compensation awards to new employees, but does not allow for the granting of incentive stock options. The terms of the stock options under the 2025 Inducement Plan, in general, are determined by the Compensation Committee, provided the exercise price per share generally shall not be set at less than the fair market value of a share of the common stock on the date of grant and the term shall not be greater than ten years from the date the option or award is granted. A total of 100,000 shares of the Company's common stock were initially reserved for issuance under the 2025 Inducement Plan. In September 2025, the 2025 Inducement Plan was amended to increase the aggregate number of shares reserved for issuance by an additional 300,000 shares. A total of 267,451 shares were available for future issuance as of December 31, 2025.

Stock Options

The following table summarizes stock option activity during the year ended December 31, 2025:

	Shares	Weighted average exercise price	Weighted average remaining contractual life (years)	Aggregate intrinsic value (in thousands)
Outstanding at December 31, 2024	1,528,143	$ 93.57		
Options granted	145,219	340.27		
Options exercised	(681,134)	55.91		
Options cancelled	(12,367)	177.52		
Outstanding at December 31, 2025	979,861	$ 155.25	5.19	$ 418,487
Exercisable at December 31, 2025	715,046	$ 112.02	4.28	$ 336,297

The total cash received by the Company as a result of stock option exercises was $38.1 million, $76.9 million and $34.0 million for the years ended December 31, 2025, 2024, and 2023. The total intrinsic value of options exercised was $227.5 million, $167.8 million, and $70.4 million for the years ended December 31, 2025, 2024, and 2023. The weighted-average grant date fair values, based on the Black-Scholes option model, of options granted during the year ended December 31, 2025, 2024 and 2023 was $200.55, $155.42, and $149.15, respectively.

The following table summarizes the weighted average values of the assumptions used in computing the fair value of option grants during 2025, 2024, and 2023.

	2025	2024	2023
Risk-free interest rate	4.1 %	4.1 %	4.4 %
Expected dividend yield	— %	— %	— %
Expected option life	6.2 years	4.7 years	6.3 years
Expected volatility	58 %	82 %	92 %

Restricted Stock Units

The Company awards restricted stock units (“RSUs”) to employees, officers, directors and consultants to the Company. RSUs vest over a period of years and are subject to forfeiture if employment or service terminates before vesting.

The following table summarizes RSU activity, excluding performance-based RSUs, during the year ended December 31, 2025:

	Shares	Weighted average grant date fair value
Outstanding at December 31, 2024	499,559	$ 237.07
RSUs granted	491,079	357.36
RSUs vested	(151,464)	239.43
RSUs forfeited	(40,752)	291.04
Outstanding at December 31, 2025	798,422	$ 307.85

For the years ended December 31, 2025 and 2024 the total fair value of RSUs vested was $54.3 million, $28.9 million, respectively. For the year ended December 31, 2023 the fair value of RSUs vested was immaterial. For the years

ended December 31, 2025, 2024, and 2023, the weighted-average grant date fair value of RSUs granted was $357.36, $236.90, and $243.81, respectively.

Performance-Based Restricted Stock Units

The Company has granted various performance-based restricted stock units ("PSUs") to certain senior leadership. Depending on the terms of the PSUs and the outcome of the pre-established performance criteria, which may include a market and/or performance condition, a recipient may ultimately earn the target number of PSUs granted or a specified multiple thereof at the end of the vesting period.

The following table summarizes PSU activity during the year ended December 31, 2025:

	PSUs	Eligible to Earn PSUs	Weighted average grant date fair value
Outstanding PSUs at December 31, 2024	92,760	235,520	$ 257.77
PSUs granted	61,717	123,434	580.38
PSUs attained	(50,000)	(100,000)	146.37
PSUs forfeited	(1,233)	(2,466)	593.93
Outstanding at December 31, 2025	103,244	256,488	$ 500.55
Exercisable at December 31, 2025	—	—	$ —

For the years ended December 31, 2025, 2024, and 2023, the weighted average grant date fair value of PSUs granted was $580.38, $388.02, and $146.37, respectively.

Outstanding Awards

As of December 31, 2025, the Company had RSUs, PSUs and options outstanding pursuant to which an aggregate of 2,034,771 shares of its common stock may be issued pursuant to the terms of all awards granted under the 2015 Stock Plan, 2023 Inducement Plan and 2025 Inducement Plan.

Stock-Based Compensation Expense

Stock-based compensation expense during the years ended December 31, 2025, 2024 and 2023 was as follows (in thousands):

	Year Ended December 31,		
	2025	2024	2023
Stock-based compensation expense by type of award:			
Stock options	$ 21,328	$ 26,977	$ 30,613
Restricted stock units	58,610	35,136	14,974
Performance-based restricted stock units	18,192	17,767	4,148
Total stock-based compensation expense	$ 98,130	$ 79,880	$ 49,735
Effect of stock-based compensation expense by line item:			
Research and development	$ 22,147	$ 22,158	$ 20,864
Selling, general and administrative	75,983	57,722	28,871
Total stock-based compensation expense included in net loss	$ 98,130	$ 79,880	$ 49,735

Unrecognized stock-based compensation expense as of December 31, 2025 was $238.8 million with a weighted average remaining period of 2.81 years.

11. Leases

In 2019, the Company entered into an operating lease for office space located in West Conshohocken, Pennsylvania (the "Office Lease"), which was further amended by four amendments entered into from 2019 to May 2023. In August 2023, the Company entered into the Fifth Amendment to the Office Lease (the "Fifth Lease Amendment"). The Fifth Lease Amendment extended the term of the Office Lease through November 2026. As a result of the Fifth Lease Amendment, an incremental $1.6 million right-of-use asset and lease liabilities were recorded during the year ended December 31, 2023. In 2024, the Company entered into the Sixth, Seventh, Eighth, and Ninth Amendments to the Office Lease, leasing additional office space available in the same premises under the Office Lease, which resulted in an incremental $1.3 million right-of-use asset and lease liability recorded.

In April 2025, the Company entered into an operating lease for additional office space in West Conshohocken, Pennsylvania. The lease commenced in May 2025 and resulted in a $4.0 million right-of-use asset and lease liability.

In September 2025, the Company entered into an operating lease for office space in Waltham, Massachusetts. The commencement date did not occur as of December 31, 2025 and therefore the new lease had no impact on the financial statements.

Future minimum payments under the Company's operating leases related to the ROU asset and lease liability as of December 31, 2025 was as follows (in thousands):

	Operating Leases
2026	$ 1,242
2027	2,065
2028	2,102
2029	2,140
2030	2,178
Thereafter	555
Total minimum payments	$ 10,282
Less: imputed interest	(2,533)
Present value of lease liabilities	$ 7,749

As of December 31, 2025, the weighted average remaining operating lease term was 3.6 years and the weighted average discount rate used to determine the operating lease liabilities was 10.04%. Cash paid related to lease liabilities was $1.4 million for the year ended December 31, 2025 and $1.1 million for the years ended December 31, 2024 and 2023, respectively. Operating lease costs were $1.9 million, $0.9 million and $1.1 million for the years ended December 31, 2025, 2024 and 2023, respectively. Rent, short term and variable lease costs were immaterial during the years ended December 31, 2025, 2024 and 2023.

12. Commitments and Contingencies

Licenses and Other Commitments

The Company has entered into customary contractual arrangements and letters of intent in preparation for and in support of operations in the normal course of business. As of December 31, 2025, the Company had approximately $268.3 million of obligations under these agreements related to active pharmaceutical ingredient, which is expected to be paid through 2029.

Roche Agreement

The Company has a Research, Development and Commercialization Agreement (as amended, the "Roche Agreement") with Hoffmann-La Roche ("Roche") which grants the Company a sole and exclusive license to develop, use, sell, offer for sale and import any Licensed Product (as defined in the Roche Agreement). In January 2026, the Company entered into an amendment to the Roche Agreement to provide the Company the full and exclusive right and discretion to control all patent term adjustments and patent term extensions applicable to Rezdiffra, including patents owned by Roche and jointly owned between the parties. In consideration of the foregoing, the royalty payable to Roche based on net sales of

Rezdiffra will not be reduced until the expiration of certain patent term extensions that have been, or could have been, filed.

The Roche Agreement required certain milestone payments to Roche. In March 2024, upon receiving FDA approval of Rezdiffra, a milestone was achieved and $5.0 million was paid to Roche. In August 2025, upon receiving conditional marketing authorization from the EC, a milestone was achieved and $3.0 million was paid to Roche. Furthermore, a tiered single-digit royalty is payable on net sales of resmetirom or a product developed from resmetirom, subject to certain reductions. The Company began incurring royalty expense following its commercial launch of Rezdiffra in April 2024.

CSPC License (MGL-2086)

In July 2025, the Company entered into an exclusive global license agreement (the "CSPC License Agreement") with CSPC Pharmaceutical Group Limited ("CSPC") for MGL-2086 (formerly known as SYH2086), an oral small molecule GLP-1 receptor agonist. Pursuant to the CSPC License Agreement, CSPC has granted the Company an exclusive global license to develop, manufacture, and commercialize MGL-2086. The transaction closed in September 2025. The Company paid CSPC an upfront payment of $120.0 million in October 2025. CSPC is eligible to receive up to $2.0 billion in development, regulatory and commercial milestone payments, as well as royalties on net sales ranging from mid-single digits to low-double digits.

Pfizer License (ervogastat)

In December 2025, the Company entered into an exclusive global license agreement with Pfizer (the "Pfizer License Agreement") to develop, manufacture and commercialize ervogastat, a Phase 2 oral DGAT-2 inhibitor, and two additional early-stage MASH assets. The Company paid Pfizer an upfront payment of $50.0 million in December 2025. In addition, Pfizer is eligible to receive up to $70.0 million in development and regulatory milestone payments related to ervogastat and low-double digit royalties on net sales of ervogastat. Pfizer is eligible to receive additional development, regulatory and commercial milestone payments and royalty payments on net sales of the two licensed early stage assets.

Ribocure License (siRNA programs)

In February 2026, the Company entered into an exclusive global license agreement (the "Ribocure License Agreement") with Suzhou Ribo Life Science Co. Ltd. and Ribocure Pharmaceuticals AB (together, "Ribocure") granting the Company exclusive global rights to develop, manufacture and commercialize six siRNA programs. Pursuant to the Ribocure License Agreement, the Company will pay Ribocure an upfront payment of $60.0 million. In addition, Ribocure is eligible to receive up to $4.4 billion in development, regulatory and commercial milestone payments across all programs, as well as royalties on net sales ranging from mid-single digits to low-double digits.

13. Income Taxes

The Company is subject to U.S. federal, state, and foreign income taxes. For the years ended December 31, 2025, 2024, and 2023, the components of loss before provision for income taxes consisted of $158.5 million, $465.9 million, and $373.6 million, respectively, for the United States and $129.8 million for foreign in 2025. The Company did not have any foreign operations in 2024 or 2023.

As of December 31, 2025, the Company had federal net operating loss ("NOL") carryforwards of approximately $1,179.0 million available to reduce future taxable income, of which $40.4 million will expire between 2031 and 2037. In addition, the Company had foreign NOL carryforwards of approximately $130.8 million available to reduce future taxable income, which will begin to expire in 2033. The Company also had state NOL carryforwards of approximately $979.5 million available to reduce future taxable income, which expire between 2031 and 2043. In addition, the Company had unused federal and state research and development tax credit carryforwards of approximately $81.6 million.

Under Section 382 of the Internal Revenue Code ("IRC"), the utilization of NOL carryforwards may be limited in the event of certain cumulative changes in ownership over a three-year period. Such an ownership change could limit the Company's ability to utilize its NOL carryforwards and could be triggered by future issuances or sales of securities by the Company or its stockholders. The Company has determined that an ownership change occurred during the year ended December 31, 2017. As a result, the Company's NOL carryforwards are estimated to be subject to an annual limitation; however, none of the NOLs are expected to expire before becoming available to reduce future taxable income.

In assessing the realizability of deferred tax assets, management considers whether it is more likely than not that some portion of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which those temporary differences become deductible.

As there is no assurance of future taxable income, a full valuation allowance has been established to offset the deferred tax assets. The valuation allowance increased $82.2 million for the year ended December 31, 2025. Changes in the deferred tax asset will be recorded as an income tax benefit or expense on the accompanying consolidated statements of operations.

Entities are also required to evaluate, measure, recognize and disclose any uncertain income tax provisions taken on their income tax returns. The Company has analyzed its tax positions and determined that it had net liabilities for uncertain tax positions, including accrued interest and penalties, of $12.1 million as of December 31, 2025. There were no uncertain tax positions as of December 31, 2024. Of the liabilities for uncertain tax positions as of December 31, 2025, none would impact the Company's effective tax rate if recognized. The Company does not reasonably expect any material changes to the estimated liability associated with its uncertain tax positions in the next twelve months. Interest and penalties, if any, as they relate to income taxes assessed, are included in the income tax provision. There were no income tax related interest and penalties included in the income tax provision for 2025.

Unrecognized tax benefits were as follows (in thousands):

	For the years ended December 31,		
	2025	2024	2023
Balance at beginning of period	$ —	$ —	$ —
Increases related to current period tax positions	3,160	—	—
Increases related to prior period tax positions	8,898	—	—
Balance at end of period	$ 12,058	$ —	$ —

The Company files U.S. federal income tax returns and income tax returns in various state, local, and foreign jurisdictions and is routinely subject to examination by taxing authorities in those jurisdictions. Tax years beginning in 2021 remain open to examination by the Internal Revenue Service ("IRS"), state, and foreign taxing authorities. To the extent that the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon IRS, state, or foreign tax authorities' examination to the extent utilized in a future period.

Temporary differences that give rise to deferred tax assets and liabilities are as follows (in thousands):

	For the years ended December 31,		
	2025	2024	2023
Deferred tax liabilities			
Unrealized gains on investments	$ 117	$ 117	$ 117
Other deferred tax liabilities	—	100	—
Property, plant & equipment	245	—	—
Total deferred tax liabilities	$ 362	$ 217	$ 117
Deferred tax assets			
Accrued expenses	14,958	8,082	3,857
Intangibles	40,777	401	503
Gross to net accruals	3,462	167	—
Stock compensation	21,940	16,342	33,976
Property, plant & equipment	—	172	95
Net operating losses and other carryforwards	318,121	214,464	121,589
Capitalized R&D	120,932	200,199	175,145
Other deferred tax assets	2,192	—	—
R&D credit	69,029	69,201	48,074
Total deferred tax assets before valuation allowance	591,411	509,028	383,239
Valuation allowance	(591,049)	(508,811)	(383,122)
Total deferred tax assets	362	217	117
Net deferred tax assets	$ —	$ —	$ —

A reconciliation of the U.S. federal statutory tax rate to the Company's effective tax rate for the year ended December 31, 2025 is as follows (in thousands, except percent):

	For the year ended December 31, 2025	
	Amount	Percent
Tax benefit at U.S. federal statutory rate	$ (60,352)	21.0 %
State and local income taxes, net of federal income tax effect	—	—
Foreign tax effects		
Switzerland		
Statutory tax rate difference between Switzerland & United States	17,227	(6.0)
Change in valuation allowance	10,242	(3.6)
Other foreign jurisdictions	95	—
Tax credits	(11,886)	4.1
Change in valuation allowance	64,331	(22.4)
Nontaxable or nondeductible items		
Stock based compensation	(44,008)	15.3
162M limitation	9,755	(3.4)
Change in unrecognized Tax Benefits	12,058	(4.2)
Other adjustments	2,538	(0.9)
Income tax expense (benefit) and effective	$ —	— %

A reconciliation of the U.S. federal statutory tax rate to the Company's effective tax rate for the years ended December 31, 2024 and 2023 is as follows (in thousands):

	For the years ended December 31,	
	2024	2023
Tax benefit at U.S. federal statutory rate	$ (97,837)	$ (78,462)
Stock-based compensation	(9,954)	(8,287)
162M limitation	21,627	3,183
Other nondeductible expenses	835	53
State income tax benefit before valuation allowance, net of federal benefit	(19,280)	(16,246)
Increase in domestic valuation allowance	125,689	112,606
Research and development credit	(17,679)	(12,971)
Other adjustments	(3,401)	124
Income tax expense (benefit)	$ —	$ —

14. Segment Information

The Company operates as one reportable segment focused on delivering novel therapeutics for MASH. The Company's Chief Executive Officer, as the chief operating decision maker ("CODM"), leads the Company in support of four core values—focus on the patient, having an owner mindset, the relentless pursuit of innovation and commitment to collaboration. To best align the Company with these values, the CODM reviews consolidated financials, along with qualitative information, to evaluate performance, manage and allocate resources, make operating decisions, and assess planning and forecasting on a total company basis. Assets, liabilities and equity are reviewed and presented on the same level as the Company's consolidated balance sheet.

Management does not segment business operations for internal reporting or decision making purposes. As the Company has a single reporting segment, the segment accounting policies are the same as those at the Company level, as

described in Note 2 "Summary of Significant Accounting Policies." As of December 31, 2025, the Company did not have material revenue or assets outside of the United States.

The following table presents net income reported at the segment measure of profit and loss:

	Year Ended December 31,		
	2025	2024	2023
Product revenue, net	$ 958,403	$ 180,133	$ —
Cost of sales	(56,148)	(6,233)	—
Research and development - personnel and internal expense	(73,283)	(73,418)	(56,824)
Research and development - external expense	(315,242)	(163,300)	(215,526)
Selling, general and administrative	(813,827)	(435,057)	(108,146)
Other segment income[(1)]	11,813	31,983	6,866
Net loss	$ (288,284)	$ (465,892)	$ (373,630)

[(1)] Other segment income includes interest income, interest expense, loss on extinguishment of debt and other expense, net.

MADRIGAL PHARMACEUTICALS, INC.
FOUR TOWER BRIDGE
200 BARR HARBOR DRIVE, SUITE 200
WEST CONSHOHOCKEN, PENNSYLVANIA 19428