UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-K

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

For the fiscal year ended December 31, 2022

or

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

For the transition period from to
Commission File Number: 001-35068

ACELRX PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**41-2193603**
(State or other jurisdiction of incorporation or organization)	**(IRS Employer Identification No.)**

25821 Industrial Boulevard, Suite 400
Hayward, CA 94545
(650) 216-3500

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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

Title of Each Class	Trading Symbol(s)	Name of Each Exchange on Which Registered
Common Stock, $0.001 par value	**ACRX**	**The Nasdaq Global Market**

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

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

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

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

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

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

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

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

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

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

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

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

The aggregate market value of the voting stock held by non-affiliates of the registrant on June 30, 2022 (the last business day of the registrant's most recently completed second fiscal quarter), based upon the last sale price reported on the Nasdaq Global Market on that date, was approximately $35,604,258. The calculation excludes 79,603 shares of the registrant's common stock held by current executive officers and directors that the registrant has concluded are affiliates of the registrant. Exclusion of such shares should not be construed to indicate that any such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the registrant or that such person is controlled by or under common control with the registrant.

As of March 20, 2023, the number of outstanding shares of the registrant's common stock was 10,918,452.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's notice of annual meeting of stockholders and proxy statement to be filed pursuant to Regulation 14A within 120 days after Registrant's fiscal year end of December 31, 2022 (the "2023 Proxy Statement"), are incorporated by reference into Part III of this report.

Unless the context indicates otherwise, the terms "AcelRx," "AcelRx Pharmaceuticals," "we," "us" and "our" refer to AcelRx Pharmaceuticals, Inc., and its consolidated subsidiaries. "Niyad" is a trademark, and "ACELRX," "DSUVIA", "DZUVEO" and "Zalviso" are registered trademarks, all owned by AcelRx Pharmaceuticals, Inc. This report also contains trademarks and trade names that are the property of their respective owners.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or Annual Report, contains statements that discuss future events or expectations, projections of results of operations or financial condition, trends in our business, business prospects and strategies and other "forward-looking" information. In some cases, you can identify "forward-looking statements" by the following words: "may," "will," "could," "would," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "predict," "project," "potential," "continue," "ongoing" or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. These forward-looking statements are not guarantees of future performance or development and involve known and unknown risks, uncertainties and other factors that are in some cases beyond our control. These forward-looking statements may relate to, among other things, our expectations regarding the scope, progress, expansion, and costs of researching, developing and commercializing our product candidates; our opportunity to benefit from various regulatory incentives; expectations for our financial results, revenue, operating expenses and other financial measures in future periods; and the adequacy of our sources of liquidity to satisfy our working capital needs, capital expenditures, and other liquidity requirements. These are only some of the factors that may affect the forward-looking statements contained in this Annual Report. For a discussion identifying additional important factors that could cause actual results to vary materially from those anticipated in the forward-looking statements, see "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Risk Factors" in this Annual Report. You should review these risk factors for a more complete understanding of the risks associated with an investment in our securities. However, we operate in a competitive and rapidly changing environment and new risks and uncertainties emerge, are identified or become apparent from time to time. It is not possible for us to predict all risks and uncertainties that could have an impact on the forward-looking statements contained in this Annual Report. You should be aware that the forward-looking statements contained in this Annual Report are based on our current views and assumptions. We undertake no obligation to revise or update any forward-looking statements made in this Annual Report to reflect events or circumstances after the date hereof or to reflect new information or the occurrence of unanticipated events, except as required by law.

Summary of Principal Risk Factors

Our business is subject to numerous risks, as more fully described in this section below this summary. You should read these risks before you invest in our common stock. We may be unable, for many reasons, including those that are beyond our control, to implement our business strategy. In particular, our risks include:

- Our Emergency Use Authorization, or EUA, Application for Niyad™ is premised on the declared COVID-19 health emergency.
- We may fail to realize the benefits expected from our acquisition of Lowell Therapeutics, Inc., or Lowell, which could adversely affect our stock price.
- We have signed an agreement with Vertical Pharmaceuticals, LLC, a wholly owned subsidiary of Alora Pharmaceuticals, LLC, or together Alora, to divest our sufentanil sublingual products (DSUVIA and DZUVEO) with the right to receive sales-based milestone and other payments. Upon closing, whether we receive royalties from DSUVIA is dependent on the ability of Alora to successfully commercialize DSUVIA. If Alora, we, or a potential partner, are unable to successfully commercialize DSUVIA, our business, financial condition, and results of operations will be materially harmed.
- Delays in clinical trials are common and have many causes, and any delay could result in increased costs to us and jeopardize or delay our ability to obtain regulatory approval and commence product sales.
- Our drug discovery and development efforts might not generate successful product candidates.
- If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.
- If we experience delays or difficulties in enrolling patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.
- If serious adverse effects or unexpected characteristics of our product candidates are identified during development, we may need to abandon or limit our development of some or all of our product candidates.
- We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.
- The process for obtaining approval of a Premarket Approval, or PMA, or New Drug Application, or NDA, is time consuming, subject to unanticipated delays and costs, and requires the commitment of substantial resources.
- Our expectations for U.S. Food and Drug Administration, or FDA, approvability of our product candidates may be inaccurate.
- We may experience difficulties in retaining our existing employees and managing our operations.
- If we, or current and potential partners, are unable to compete effectively, our products may not reach their commercial potential.
- Coverage and adequate reimbursement may not be available for our product candidates, if approved, in the United States and in Europe, which could make it difficult for us, or our partners, to sell our products profitably.
- The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.
- If we or our partners are unable to establish and maintain relationships with group purchasing organizations any future revenues or future profitability could be jeopardized.
- Existing and future legislation may increase the difficulty and cost for us to commercialize our products and affect the prices we may obtain.
- We have incurred significant losses since our inception and anticipate that we will continue to incur losses in the future.
- We require additional capital and may be unable to raise such capital, which would force us to delay, reduce or eliminate our commercialization efforts and product development programs and could cause us to be unable to continue to operate as a going concern and cease operations.
- To fund our operations, and capital requirements, we may sell additional equity securities, which may result in dilution to our stockholders, or debt securities, which may impose restrictions on our business.
- We have not yet generated significant product revenue and may never be profitable.
- Future sales of DSUVIA to the Department of Defense, or DoD, are not predictable, may occur on an irregular basis and may not meet our expectations due to various United States government-related factors that are beyond our control.
- The terms of our loan agreement with Oxford Finance, LLC, or Oxford, may restrict our current and future operations.
- We might be unable to service our existing debt due to a lack of cash flow and might be subject to default.
- We rely on third party manufacturers and suppliers for our product candidates in the United States and Europe.
- We rely on limited sources of supply for the active pharmaceutical ingredients for nafamostat-based product candidates and any disruptions in the chain of supply may cause a delay in developing our product candidates.

- Manufacture of sufentanil sublingual tablets requires specialized equipment and expertise.
- Manufacturing issues may arise that could delay or increase costs related to product development and regulatory approval.
- We rely on third parties to conduct, supervise and monitor our clinical trials.
- Our relationships with clinical investigators, health care professionals, consultants, commercial partners, third-party payers, hospitals, and other customers are subject to applicable anti-kickback, fraud and abuse and other healthcare laws, which could expose us to significant penalties.
- Significant disruptions of our information technology systems or data security incidents could result in significant financial, legal, regulatory, business and reputational harm to us.
- Business interruptions could delay our operations and sales efforts.
- Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.
- We may acquire companies, product candidates or products or engage in strategic transactions.
- We face potential product liability claims and, if such claims are successful, we may incur substantial liability.
- Our employees, agents and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.
- If we cannot defend our issued patents from third party claims or if our pending patent applications fail to issue, our business could be adversely affected.
- Litigation involving patents, patent applications and other proprietary rights is expensive and time consuming.
- It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection.
- We may be unable to adequately prevent disclosure of trade secrets and other proprietary information.
- Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and applications will be due to be paid to the United States Patent and Trademark Office and various foreign governmental patent agencies in several stages over the lifetime of the patents and/or applications.
- We may not be able to enforce our intellectual property rights throughout the world.
- We have not yet registered our trademarks in all our potential markets, and failure to secure those registrations could adversely affect our business.
- The market price of our common stock has historically been and may continue to be highly volatile.
- Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.
- Our reverse stock split may not be successful.
- We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.
- Provisions in our amended and restated certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders or remove our current management.
- Litigation may substantially increase our costs and harm our business.
- Our involvement in securities-related class action and related derivative litigation could divert our resources and management's attention and harm our business.
- Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.
- Our effective tax rate may fluctuate, we may be adversely affected by changes in tax laws and regulations, and we may incur obligations in tax jurisdictions in excess of accrued amounts.
- Macroeconomic uncertainties, including inflationary pressures, supply chain disruptions, labor shortages, significant volatility in global markets, recession risks, and the COVID-19 pandemic have in the past and may continue to adversely affect our business, future results of operations, and financial condition, the effects of which remain uncertain.
- We have identified a material weakness in our internal control over financial reporting. This material weakness could continue to adversely affect our results of operations and financial condition accurately. In the future, we may identify additional material weaknesses or otherwise fail to maintain an effective system of internal control over financial reporting or adequate disclosure controls and procedures, which may result in material errors in our financial statements or cause us to fail to meet our period reporting obligations.

ACELRX PHARMACEUTICALS, INC.

2022 ANNUAL REPORT ON FORM 10-K

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PART I

Item 1. Business

Overview

We are a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for use in medically supervised settings.

Our Portfolio

Our portfolio consists of nafamostat product candidates and pre-filled syringe product candidates. We have signed an agreement with Alora to divest our sufentanil sublingual products (DSUVIA and DZUVEO) with the right to receive sales-based milestone and other payments, which we expect to close in April 2023. We do not have plans to further develop any sufentanil sublingual product candidates.

Nafamostat Product Candidates

Product/Product Candidate	Description	Target Use	Status
Niyad™	Lyophilized vial containing nafamostat for injection	Regional anticoagulant for injection into the extracorporeal circuit	Submitted an investigational device exemption, or IDE, and received Breakthrough Device Designation from the FDA. Preliminary EUA submitted.
LTX-608	Lyophilized vial containing nafamostat for injection	IV infusion as an anti-viral treatment for COVID-19	IND to be submitted following toxicology evaluation to enable Phase 2 study
LTX-608	Lyophilized vial containing nafamostat for injection	IV infusion for disseminated intravascular coagulation, or DIC	IND to be submitted following toxicology evaluation to enable Phase 2 study
LTX-608	Lyophilized vial containing nafamostat for injection	IV infusion for acute respiratory distress syndrome, or ARDS	IND to be submitted following toxicology evaluation to enable Phase 2 study
LTX-608	Lyophilized vial containing nafamostat for injection	IV infusion for acute pancreatitis	IND to be submitted following toxicology evaluation to enable Phase 2 study

On January 7, 2022, we acquired Lowell Therapeutics, Inc., or Lowell, a privately held company, pursuant to the Agreement and Plan of Merger, dated as of November 14, 2021, or the Merger Agreement, in a transaction for consideration of approximately $32.5 million plus net cash acquired and certain other adjustments, and which includes up to approximately $26.0 million of contingent consideration payable in cash or stock at AcelRx's option, upon the achievement of regulatory and sales-based milestones, or the Merger Agreement. In connection with the Merger Agreement we acquired Niyad and LTX-608 (lyophilized vials of nafamostat for injection into the extracorporeal circuit or direct IV infusion to the patient, respectively), an in-process research and development, or IPR&D, asset. For additional information regarding the Merger Agreement, see Note 4, "Asset Acquisition" to the consolidated financial statements in this Annual Report on Form 10-K for additional information.

Niyad™

Niyad is being developed to become the first and only FDA-approved regional anticoagulant for injection into the extracorporeal circuit, such as the dialysis circuit during continuous renal replacement therapy, or CRRT, for acute kidney injury, or AKI, patients in the hospital, and for chronic kidney disease patients undergoing intermittent hemodialysis, or IHD, in dialysis centers. Niyad is expected to be used during renal replacement therapy for AKI patients in the hospital and for end-stage renal disease, or ESRD, patients receiving dialysis in outpatient clinics. Niyad is being studied under an Investigational Device Exemption, or IDE, and has received Breakthrough Device Designation from the FDA and an ICD-10 procedural code from the U.S. Centers for Medicare & Medicaid Services. While not approved for commercial use in the United States, the active drug component of Niyad, nafamostat, has been approved in Japan and South Korea as a regional anticoagulant for the dialysis circuit, disseminated intravascular coagulation and acute pancreatitis. Niyad has the potential for six years of data exclusivity upon FDA approval of the device. Niyad is a lyophilized formulation of nafamostat, a broad-spectrum, synthetic serine protease inhibitor, which has a half-life of 8 minutes, with anticoagulant, anti-inflammatory and potential anti-viral activities.

The FDA has provided guidance for a single registrational study and endpoints for Niyad. The study will be a prospective, randomized, placebo-controlled study at up to 10 clinical sites of 160 adult patients who cannot tolerate heparin or are at risk for bleeding. The primary endpoint will be the mean post-filter activated clotting time over the first 24 hours versus placebo. We believe that decades of nafamostat studies on anticoagulation of the extracorporeal circuit can help guide and support our Niyad development efforts. An EUA submission for Niyad is currently planned for the second quarter of 2023.

LTX-608

LTX-608 is our proprietary nafamostat formulation for direct IV infusion being explored as an investigational product for: (a) antiviral treatment of COVID, (b) acute respiratory distress syndrome, or ARDS, (c) disseminated intravascular coagulation, or DIC, and (d) acute pancreatitis. Our initial focus for LTX-608 will be on its development for the treatment of ARDS and DIC, an indication for which nafamostat is approved in Japan and South Korea. Third-party studies are actively being conducted outside the U.S. where initial results demonstrate that nafamostat shortens time to clinical improvement, increasing the recovery rate and lowering the mortality rate when combined with standard of care, or SOC, compared to SOC alone in the category of the sickest COVID patients. Nafamostat has the potential for five years of data exclusivity as a new chemical entity, or NCE, upon the first FDA approval of a new drug application that is independent from any exclusivity arising from issuance of our pending patent applications. We currently have a pending patent application for Niyad with claims drawn to priming of the extracorporeal circuit and blood flow when using nafamostat, and multiple LTX-608 pending patent applications that include claims drawn to use of nafamostat in DIC, as an antiviral agent (e.g., COVID treatment), in ARDS and in other conditions.

Pre-filled Syringe Product Candidates

Product/Product Candidate	Description	Target Use	Status
Fedsyra™	Ephedrine pre-filled syringe, containing 10 ml of a solution of 3 mg/ml ephedrine for injection	Clinically important hypotension occurring in the setting of anesthesia	Product candidate licensed from Aguettant; preparing New Drug Application, or NDA, for submission to FDA. Approved in the European Union; owned and marketed by Aguettant.
Phenylephrine	Phenylephrine pre-filled syringe containing 10 ml of a solution of 50 mcg/ml phenylephrine for injection	Clinically important hypotension resulting primarily from vasodilation in the setting of anesthesia	Product candidate licensed from Aguettant; preparing NDA for submission to FDA. Approved in the European Union; owned and marketed by Aguettant.

Ephedrine (Fedsyra) and Phenylephrine

On July 14, 2021, we entered into a License and Commercialization Agreement, or the PFS Agreement, with Aguettant pursuant to which we obtained the exclusive right to develop and, subject to FDA approval, commercialize in the United States an ephedrine pre-filled syringe, or PFS, containing 10 ml of a solution of 3 mg/ml ephedrine hydrochloride for injection, and (ii) a phenylephrine PFS containing 10 ml of a solution of 50 mcg/ml phenylephrine for injection. Aguettant will supply us with the products for use in commercialization and, if they are approved in the U.S., Aguettant is entitled to receive up to $24 million in sales-based milestone payments. In connection with our and Aguettant's agreement to enter into the Amended DZUVEO Agreement and the Amended and Restated Supply Agreement (please refer to the section headed "— Our Portfolio — Sufentanil Sublingual Products" below for further details), we will enter into an amendment to the PFS Agreement with Aguettant pursuant to which, effective on the later of the closing of the transaction contemplated under the DSUVIA Agreement (as defined below in the section headed "— Our Portfolio — Sufentanil Sublingual Products") and April 1, 2023, (a) Aguettant will pay us a complementary payment in the amount of €1.5 million, and (b) the maximum amount in sales-based milestone payments that Aguettant is entitled to receive will reduce to $21 million. Refer to Note 6, "In-License Agreement", Note 7, "Out-license Agreements—DZUVEO" and Note 20, "Subsequent Events" to the consolidated financial statements in this Annual Report on Form 10-K for additional information.

Our current expectation based on our communication with the FDA is that Fedsyra, the ephedrine PFS product candidate, will be approvable by the FDA without additional manufacturing changes or clinical development. We have not yet received all the available data to support the planned NDA submission for the phenylephrine PFS product candidate. If we determine that additional development work will be needed for U.S. approval of either of the PFS product candidates, we would incur additional expense and be delayed in obtaining any revenue from that product. We expect we will be able to submit the NDA for Fedsyra in the second quarter of 2023 and the NDA for the phenylephrine PFS in 2024.

These PFS product candidates are innovative ready-to-use formulations of active ingredients that are currently approved in the United States. in concentrated formulations that must be diluted prior to administration to patients, and more recently in ready-to-use vial formulations. Hospitals currently purchase ready-to-use, pre-filled syringe presentations of these active ingredients from compounding facilities that have not obtained FDA approval for the products, or manually dilute the products in-house. Our product candidates have been developed in a ready-to-use strength and pre-filled into syringes that can be immediately administered to patients, eliminating the need for calculations and additional dilution and filling steps. Aguettant pre-filled syringes are focused on delivering commonly used medicines safely and efficiently. Perioperative medication errors continue, and pre-filled syringes are preferred for improving safety while containing costs. We believe that, if approved, our pre-filled syringe products may offer significant benefits to hospitals and surgery centers and avoid potential disadvantages of the currently available compounded products.

Sufentanil Sublingual Products

DSUVIA®

DSUVIA® (known as DZUVEO® in Europe) is focused on the treatment of acute pain, and utilizes sufentanil, delivered via a non-invasive route of sublingual administration, exclusively for use in medically supervised settings. In November 2018, the U.S. Food and Drug Administration, or FDA, approved DSUVIA for use in adults in a certified medically supervised healthcare setting, such as hospitals, surgical centers and emergency departments, for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. The commercial launch of DSUVIA in the United States occurred in the first quarter of 2019. In June 2018, the European Commission granted marketing approval of DZUVEO for the management of acute moderate to severe pain in adults in medically monitored settings. DSUVIA is a 30 mcg single-strength solid dosage form of sufentanil administered sublingually via a single-dose applicator by healthcare professionals. Sufentanil is an opioid analgesic currently also approved for IV and epidural anesthesia and analgesia. The sufentanil pharmacokinetic profile when delivered sublingually avoids the high peak plasma levels and short duration of action observed with IV administration. Recent published studies have demonstrated that when administering DSUVIA there was an overall greater than 50% reduction in morphine milligram equivalents, or MME, administered, with an 80% reduction in MMEs administered post-op in the institution versus the control group.

DSUVIA was approved with a REMS which restricts distribution to certified medically supervised healthcare settings in order to prevent respiratory depression resulting from accidental exposure. DSUVIA is only distributed to facilities certified in the DSUVIA REMS program following attestation by an authorized representative to comply with appropriate dispensing and use restrictions of DSUVIA. To become certified, a healthcare setting is required to train their healthcare professionals on the proper use of DSUVIA and have the ability to manage respiratory depression. DSUVIA is not available in retail pharmacies or for outpatient use.

On July 14, 2021, we entered into a License and Commercialization Agreement, or the DZUVEO Agreement, with Aguettant pursuant to which Aguettant obtained the exclusive right to develop and commercialize DZUVEO in the European Union, Norway, Iceland, Liechtenstein, Andorra, Vatican City, Monaco, Switzerland and the United Kingdom, or the DZUVEO Territory, for the management of acute moderate to severe pain in adults in medically monitored settings. We supply Aguettant with primary packaged product and Aguettant then completes secondary packaging of the finished product. Pursuant to the DSUVIA Agreement (as defined below), as a condition of the transaction contemplated thereunder, we and Aguettant will enter into an amendment to the DZUVEO Agreement, or the Amended DZUVEO Agreement, and an amendment and restatement to the supply agreement with respect to the manufacture and supply of DZUVEO, or the Amended and Restated Supply Agreement, in each case, in a form reasonably acceptable to Alora. The rights and obligations under the Amended DZUVEO Agreement and the Amended and Restated Supply Agreement will be assumed by Alora, as part of the DSUVIA asset divestment agreement. Refer to Note 7, “Out-License Agreements—DZUVEO” and Note 20, “Subsequent Events” to the consolidated financial statements in this Annual Report on Form 10-K for additional information.

On March 12, 2023, we entered into an asset purchase agreement, or the DSUVIA Agreement, with Alora pursuant to which Alora will acquire certain assets and assume certain liabilities relating to DSUVIA or DZUVEO, or any other single-dose pharmaceutical product for use in medically supervised settings containing a sublingual tablet that includes sufentanil as the sole active ingredient, as a 30 mcg tablet or other dosage form or strength as reasonably necessary for lifecycle management, or the Product. The Product expressly excludes Zalviso, any other multi-dose administration system containing sufentanil sublingual tablets (whether as the sole active ingredient or in combination with other active ingredients), and any single-dose formulation of sufentanil for use outside of a medically supervised setting. Subject to closing of the transaction contemplated under the DSUVIA Agreement, we will be entitled to receive quarterly payments in an amount equal to 15% of net Product sales to all customers excluding net sales to the Department of Defense and sales by or on behalf of Aguettant, and quarterly payments in an amount equal to 75% of net Product sales to the Department of Defense. Subject to closing of the transaction contemplated under the DSUVIA Agreement, we will also be entitled to receive sales milestones up to $116.5 million based on the achievement of Alora attaining certain levels of annual sales and 20% of any consideration, other than royalty payments, received by Alora and its affiliates in connection with a grant to any third party of a license related to any Product, or by Alora and its affiliates and equityholders in connection with a sale or transfer to any third party of an ownership interest in any assets acquired by Alora under the DSUVIA Agreement. We expect the transaction to close in April 2023 and we expect to support the transition to Alora under a Transition Services Agreement signed at or prior to the closing of the transaction contemplated under the DSUVIA Agreement. In addition, at or prior to the closing, we and Alora will enter into an intellectual property agreement pursuant to which Alora will grant fully-paid, royalty-free and perpetual licenses to us under certain specified intellectual property rights acquired by Alora under the DSUVIA Agreement for, among other things, the development, manufacture, commercialization and exploitation of certain products, including Zalviso. Refer to Note 20, “Subsequent Events” to the consolidated financial statements in this Annual Report on Form 10-K for additional information.

The Market Opportunity for Nafamostat Products

The current market landscape for anticoagulants used during CRRT includes heparin, a systemic anticoagulant used for anticoagulation of the patient and the circuit, and citrate, a regional anticoagulant used for anticoagulation of the circuit only and authorized under an Emergency Use Authorization, or EUA, in the United States. No anticoagulant is used in CRRT in 29% of cases, the default decision when physicians are concerned with the safety of heparin or citrate. According to our market research, when not using an anticoagulant for CRRT, frequent filter clogging was the most common issue, with 20-25% stating increased transfusions were needed. The citrate anticoagulant alternative has not received full FDA approval, and we believe that Niyad may be beneficial in certain patient populations where current products may be contraindicated. Our market research indicated physicians did not use current products because of a number of concerns, including hypocalcemia, citrate lock, calcium shortages, and nursing time required to administer and monitor citrate, among other concerns.

Niyad is designed to provide short half-life titratable, regional anticoagulation with potential benefits over existing products. For example, in a 1991 clinical study undertaken by Ohtake Y, et. al. to elucidate the relationship between various anticoagulants and the incidences of bleeding complication during continuous hemofiltration, or CHF, and continuous hemodiafiltration, or CHDF, the incidence of bleeding during CHF and/or CDHF with heparin was 66.7% as compared to 4.3% with nafamostat.

We believe Niyad's peak sales potential exceeds $200 million annually in the United States for its use in CRRT and IHD, based on an estimated addressable population of 500,000 patients undergoing CRRT of $575 million, and an estimated addressable population of 350,000 patients undergoing IHD of $3.5 billion. Exposure of blood to the dialysis filter causes clotting, which is a major limitation to care during CRRT, as it leads to inefficient dialysis, causes blood loss and depletes limited resources. Circuit clotting is the most frequent cause of therapy interruption in circuit dialysis.

The second indication for our nafamostat product development candidate, LTX-608, on which we are focused is development for the treatment of ARDS and DIC, an indication for which nafamostat is approved in Japan and South Korea. We have pending patent applications directed to the use of nafamostat in DIC, as an antiviral agent (e.g., COVID treatment), in ARDS and other conditions. Our estimate of the number of annual ARDS patients annually is approximately 125,000 and over 250,000 incidents of DIC annually. Depending upon the benefit demonstrated in clinical studies, we believe the peak sales potential could range from nearly $700 million to up to $1.4 billion.

The Market Opportunity for Pre-Filled Syringe Products

Our product candidates are innovative ready-to-use formulations of molecules that are currently approved in a concentrated formulation that must be diluted prior to administration to patients, and more recently in ready-to-use vial formulations. Hospitals currently purchase non-FDA approved ready-to-use, pre-filled syringe products from compounding facilities, or manually dilute the products in-house. Our product candidates have been developed in a ready-to-use strength and pre-filled into syringes that can be immediately administered to patients, potentially eliminating the need for on-the-spot calculations and additional dilution and filling steps. We therefore believe that, if approved, our products could offer significant benefits to hospitals and surgery centers over the current compounded products. We believe our two pre-filled syringe product candidates could have a peak sales potential of over $100 million.

The Market Opportunity for Sufentanil Sublingual Products

Upon closing of the transaction under the DSUVIA Agreement, Alora will be responsible for commercializing DSUVIA and targeting the appropriate strategy for maximizing sales. Based on commissioned research we conducted in 2016, we estimate that there are over 90 million patients in the United States who are treated in various medically supervised settings for their moderate-to-severe acute pain which is significant enough to warrant the use of an opioid. We believe these patients may be eligible for treatment with DSUVIA. The target patient population for DSUVIA are those patients in a certified medically supervised healthcare setting, such as hospitals, surgical centers, and emergency departments, for less than 24 hours. Our current estimate of patients in moderate-to-severe acute pain in medically supervised settings, by setting, is as follows:

Emergency services (includes pre-hospital and Emergency Department treatment)	52 million
Outpatient surgery	11 million
Hospital/surgery center/office-based procedures	20 million
Inpatient surgery/inpatient conditions	10 million

There can be no assurance that our estimates regarding the number of patients treated in the various settings will be accurate.

Outside of the medically supervised setting, the Department of Defense remains a large opportunity for DSUVIA that is difficult to quantify. With the divestment of DSUVIA, we will retain the responsibility for driving the demand within the Department of Defense and will also receive quarterly payments in an amount equal to 75% of net product sales to the Department of Defense.

Our Strategy

Our strategy is focused on developing, obtaining approval, and commercializing our product candidates, Niyad and the pre-filled syringes. We plan to divest DSUVIA to Alora in April 2023, who will continue to commercialize the product and pay us sales-based milestone and other payments. We believe this will maximize the value of DSUVIA as Alora has more available resources to invest on the commercialization and as a result can execute a more robust commercial plan to support DSUVIA sales expansion, while we further reduce our operating costs. We have no plans on further developing or commercializing any of our other sufentanil sublingual products that were previously our product candidates. We are focused on achieving an Emergency Use Authorization, or EUA, for Niyad in 2023, and if successful, we expect to begin commercialization, while also initiating the clinical study for full regulatory approval.

Sales and Marketing

On March 12, 2023 we executed the DSUVIA Agreement. As a result, we also plan to eliminate our sales and marketing infrastructure, with the exception of certain key personnel that are preparing pre-launch activities for Niyad and the pre-filled syringes, as well as continuing to drive DSUVIA demand with the Department of Defense. We are currently evaluating the market opportunity as well as the strategy for a potential launch of Niyad with either internal resources, or with a potential commercial partner. The pre-filled syringe product candidates will not require a significant sales force as we expect this will mainly be sold through contracting with hospital networks, wholesalers and group purchasing organizations.

Intellectual Property

We have actively pursued patent protection in the United States and internationally for our commercial products DSUVIA, DZUVEO and Zalviso. We also seek patent protection in the United States and internationally for our product candidates Niyad and LTX-608. Our policy is to pursue, maintain and defend patent rights developed internally or acquired externally and to protect the technology, inventions and improvements that are commercially important to the development of our business. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents granted to us in the future will be commercially useful in protecting our technology. We also rely on trade secrets to protect our commercial products and product candidates. Our commercial success also depends in part on our non-infringement of the patents or proprietary rights of third parties. For a more comprehensive discussion of the risks related to our intellectual property, please see “Risk Factors—Risks Related to Our Intellectual Property” appearing elsewhere in this Form 10-K.

Our success will depend significantly on our ability to:

- obtain and maintain patent and other proprietary protection for our commercial products and our product candidates Fedsyra, phenylephrine, Niyad, LTX-608 and Zalviso;
- defend our patents;
- preserve the confidentiality of our trade secrets; and
- operate our business without infringing or misappropriating patents and other third-party proprietary rights.

We have established and continue to build proprietary positions for our product candidates Fedsyra, phenylephrine, Niyad, LTX-608 and Zalviso in the United States and abroad.

As mentioned above, at or prior to the closing of the DSUVIA Agreement, Alora will grant fully-paid, royalty-free and perpetual licenses to us under certain specified intellectual property rights acquired by Alora under the DSUVIA Agreement for, among other things, the development, manufacture, commercialization and exploitation of certain products, including Zalviso. As of December 31, 2022, we were the owner of record of 28 issued U.S. patents, which together provide coverage for sufentanil sublingual tablets, and the device components of Zalviso and DSUVIA. We have listed 18 of these U.S. patents in the Orange Book for DSUVIA. These patents have expiry dates extending to at least 2027. We also hold ten issued European patents, each validated and maintained in at least eight countries in Europe, seven patents in Japan, eight in China and seven in Korea, and a number of other international patents have expiry dates extending to at least 2027 excluding any potential patent term adjustments or extensions in those countries. We are also pursuing a number of U.S. and foreign patent applications. The patent applications that we have filed and have not yet been granted may fail to result in issued patents in the United States or in foreign countries. Even if the patents do successfully issue, third parties may challenge the patents.

We continue to seek to obtain and expand our patent protection for both compositions of matter and delivery devices, as well as methods of treatment related to our commercial products and our product candidates Niyad and LTX-608.

We have recently filed for additional patent coverage in the United States and Europe. If issued, and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, we expect that these patents will extend into 2040, excluding any additional term for potential patent term adjustments or patent term extensions in the United States. We note that the patent laws of foreign countries differ from those in United States, and the degree of protection afforded by foreign patents may be different from the protection offered by U.S. patents.

Further, we seek trademark protection in the United States and internationally where available and when appropriate.

Competition

Nafamostat Products

Niyad is the first nafamostat product candidate we are developing to be used as a regional anticoagulant for injection into the extracorporeal circuit. There are currently no products approved by the FDA for use as an anticoagulant in the extracorporeal circuit. Niyad would be the first and only product approved for this indication, if approved. The current standards of care being used today are heparin and citrate. Heparin is a systemic anticoagulant and cannot be used in patients at risk of bleeding. Citrate is complex to administer and requires significant human resource time and attention given the nature of the product, and cannot be used in patients with liver failure, which is approximately 43% of acute kidney injury patients. Based on our market research of the CRRT market, heparin is used approximately 43% of the time, while citrate is used approximately 28% of the time. The remaining 29% of the time there is no anticoagulant used which is partly driven by the safety concerns with heparin or citrate. We believe the primary opportunity for Niyad is within the 57% of the market that uses either citrate or no anticoagulant.

The second indication for our nafamostat product development candidate, LTX-608, on which we are focused is for the treatment of ARDS and DIC, an indication for which nafamostat is approved in Japan and South Korea. We have pending patent applications directed to the use of nafamostat in DIC, as an antiviral agent (e.g., COVID treatment), in ARDS and other conditions.

Pre-filled Syringe Products

Hospitals currently purchase non-FDA approved ready-to-use, pre-filled syringe products from compounding facilities, or manually dilute the products in-house. Our product candidates have been developed in a ready-to-use strength and pre-filled into syringes that can be immediately administered to patients, potentially eliminating the need for calculations and additional dilution and filling steps. We therefore believe that, if approved, our products may offer significant benefits to hospitals and surgery centers over the current compounded products. In addition, our pre-filled syringe product candidates will also compete with existing generic versions of concentrated vial forms of product, ready-to-use diluted vial forms of product, and for Fedsyra, a recently FDA-approved pre-filled syringe with a different formulation and concentration than our product candidate.

Sufentanil Sublingual Products

Our industry is highly competitive and subject to rapid and significant technological change. Our potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical and generic drug companies, and medical technology companies. We believe the key competitive factors that will affect the development and commercial success of our products are the safety, efficacy and tolerability profile, the patient and healthcare professional satisfaction with using our products in relation to available alternatives and the reliability, convenience of dosing, price and reimbursement of our products. Over the past year, we have monitored changes in the pharmaceutical industry in response to opioid use in the United States. Pharmaceutical companies engaged in the distribution and sale of opioids, in particular for the treatment of chronic pain, are refocusing their efforts in order to support responsible opioid use. While our products are designed for the treatment of moderate-to-severe acute pain for use in medically supervised settings, rather than for the treatment of chronic pain or for outpatient use, these industry changes could impact the commercial success of DSUVIA.

DSUVIA competes with a number of existing and future pharmaceuticals and drug delivery devices developed, manufactured and marketed by others. In particular, DSUVIA may compete with a wide variety of products and product candidates including (i) injectable opioid products, such as morphine, fentanyl, hydromorphone and meperidine; (ii) oral opioids such as oxycodone and hydrocodone; (iii) generic injectable local anesthetics, such as bupivacaine or branded formulations thereof; (iv) non-steroidal anti-inflammatory drugs, or NSAIDS, including ketorolac in intranasal or generic IV form, and IV meloxicam; and (v) transmucosal fentanyl products.

Pharmaceutical and Device Manufacturing and Supply

Upon closing of our announced divestment of DSUVIA, Alora will assume responsibility for all manufacturing and supply chain activities for DSUVIA. Accordingly, they will assume all contract manufacturing agreements, and certain owned equipment related to the production of DSUVIA.

For Niyad, we rely on contract manufacturers to produce our development batches, and if approved by the FDA, and/or an EUA is received from the FDA, we will rely on contract manufacturers for commercial supply of Niyad. We are in discussions to have a primary source of supply of Niyad, as well as a back-up manufacturer of Niyad to ensure there is not a single source of supply. We currently have a single contract manufacturer that is producing the nafamostat API for Niyad, and a separate contract manufacturer producing the finished product used for development.

Aguettant will be our sole sourced manufacturer of our commercial supply of pre-filled syringe products. Aguettant currently has their own manufacturing facilities, where they produce pre-filled syringes for the European market. We will purchase the pre-filled syringes from Aguettant under our existing supply agreement if and when the FDA approves the pre-filled syringe products for marketing.

Government Regulation

Government authorities in the United States at the federal, state and local level, and in other countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing, export and import of pharmaceutical and medical device products, which must be approved by the FDA before they may legally be marketed in the United States.

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The process of obtaining regulatory approvals and complying with applicable laws and regulations requires the expenditure of substantial time and financial resources. Failure to comply at any time during the product development and approval process, or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, Warning Letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug product may be marketed in the United States generally involves the following:

- completion of non-clinical laboratory tests, animal trials and formulation studies according to Good Laboratory and Manufacturing Practices regulations;
- submission to the FDA of an investigational new drug, or IND, application which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to Good Clinical Practices, or GCP, to establish the clinical safety and efficacy of the proposed drug product for its intended use;
- submission to the FDA of an NDA for a new drug product;

- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug product and the drug substance(s) are produced to assess compliance with cGMP;

- payment of application, annual program fees; and

- FDA review and approval of the NDA.

The testing and approval process requires substantial time, effort and financial resources and we cannot be certain that approval for our product candidates will be granted on a timely basis, if at all.

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

- *Phase 1.* The product is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

- *Phase 2.* Involves trials in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted conditions and to determine dosage tolerance and optimal dosage and schedule.

- *Phase 3.* Clinical trials are undertaken to further evaluate dosage, clinical safety and efficacy 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 and provide an adequate basis for product labeling.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events. 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 Institutional Review Board, or 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 or biological product has been associated with unexpected serious harm to patients.

Concurrent with clinical trials, companies usually complete additional animal trials and must also develop additional information about the chemistry and physical characteristics of the product and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP and QSR for medical device 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 the identity, strength, quality and purity of the final product. 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.

The results of product development, preclinical trials and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on our drug products, proposed labeling and other relevant information, will be submitted to the FDA as part of an NDA for a new drug product, requesting approval to market the product in the United States. The submission of an NDA is subject to the payment of a substantial user fee; a waiver of such fee may be obtained under certain limited circumstances. During its review of an NDA, the FDA may inspect our manufacturers for GMP and QSR compliance, and our pivotal clinical trial sites for GCP compliance.

In addition, under the Pediatric Research Equity Act, an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers.

The approval process is lengthy and difficult, and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical data or other data and information. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the 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. The FDA issues a Complete Response Letter at the conclusion of its review if the NDA is not yet deemed ready for approval. A Complete Response Letter generally outlines the deficiencies in the submission and may require substantial additional testing or information for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included.

If a product candidate does receive regulatory approval, the approval may be limited to specific conditions and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. A REMS, which can include a medication guide, patient package insert, a communication plan, elements to assure safe use and implementation system, must include a timetable for assessment of the REMS. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. In addition, the FDA may require post-approval testing which involves clinical trials designed to further assess a drug product's safety and effectiveness after the NDA.

Post-Approval Requirements

Any drug products for which we receive FDA approval are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated clinical safety and efficacy information, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements. Phase 4 clinical trials are conducted after approval to gain additional experience from the treatment of patients in the intended therapeutic indication or when otherwise requested by the FDA in the form of post marketing requirements or commitments. Failure to promptly conduct any required Phase 4 clinical trials could result in withdrawal of NDA approval. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market. Drug products may be promoted only for the approved indications and in accordance with the provisions of the approved label. Further, manufacturers of drug products must continue to comply with cGMP requirements, which are extensive and require considerable time, resources and ongoing investment to ensure compliance. In addition, changes to the manufacturing process generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

Drug product manufacturers and other entities involved in the manufacturing and distribution of approved drug products 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. The cGMP requirements apply to all stages of the manufacturing process, including the production, processing, packaging, labeling, storage and shipment of the drug product. Manufacturers must establish validated systems to ensure that products meet specifications and regulatory standards, and test each product batch or lot prior to its release.

The FDA may withdraw a product approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. Further, the failure to maintain compliance with regulatory requirements may result in administrative or judicial actions, such as fines, Warning Letters, holds on clinical trials, product recalls or seizures, product detention or refusal to permit the import or export of products, refusal to approve pending applications or supplements, restrictions on marketing or manufacturing, injunctions or civil or criminal penalties.

Medical Devices

Niyad, our nafamostat product in development for use as a regional anticoagulant for injection into the extracorporeal circuit, is regulated by the FDA as a medical device since it achieves its primary intended purposes outside the body. Niyad is being studied under an Investigational Device Exemption, or IDE, and has received Breakthrough Device Designation from the FDA. Under the FDCA, medical devices are classified into one of three classes—Class I, Class II or Class III—depending on the degree of risk associated with each medical device and the extent of control needed to provide reasonable assurances with respect to safety and effectiveness. Niyad is a Class III device as it is novel and not eligible to demonstrate substantial equivalence to a predicate device under the 510(k) process. Class III devices are subject to the PMA application process, which is generally more costly and time consuming than the 510(k) process. Through the PMA application process, the applicant must submit data and information demonstrating reasonable assurance of the safety and effectiveness of the device for its intended use to the FDA's satisfaction. Accordingly, a PMA application typically includes, but is not limited to, extensive technical information regarding device design and development, nonclinical study and clinical trial data, manufacturing information and labeling. The PMA application must provide valid scientific evidence that demonstrates to the FDA's satisfaction a reasonable assurance of the safety and effectiveness of the device for its intended use.

In the United States, a device that presents a "significant risk" to human health, as defined by the FDA, must be the subject of an IDE application to the FDA that has to be approved by the FDA prior to the commencement of human clinical trials. The IDE application must be supported by appropriate data, such as animal and laboratory testing results, showing that it is safe to test the device in humans and that the testing protocol is scientifically sound. All clinical trials must be conducted in accordance with the FDA's IDE regulations that govern investigational device labeling, prohibition of promotion, recordkeeping, and reporting and monitoring responsibilities of study sponsors and study investigators. Clinical trials must further comply with the FDA's good clinical practice regulations for IRB approval and for informed consent and other human subject protections. Required records and reports are subject to inspection by the FDA. The commencement or completion of any clinical trial may be delayed or halted, by the FDA or an IRB.

Following receipt of a PMA application, the FDA conducts an administrative review to determine whether the application is sufficiently complete to permit a substantive review. If it is not, the agency will refuse to file the PMA. The FDA, by statute and by regulation, has 180 days to review a filed PMA application, although the review of an application more often occurs over a significantly longer period of time. During this review period, the FDA may request additional information or clarification of information already provided, and the FDA may issue a major deficiency letter to the applicant, requesting the applicant's response to deficiencies communicated by the FDA. Before approving or denying a PMA, an FDA advisory committee may review the PMA at a public meeting and provide the FDA with the committee's recommendation on whether the FDA should approve the submission, approve it with specific conditions, or not approve it. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Prior to approval of a PMA, the FDA may conduct inspections of the clinical trial data and clinical trial sites, as well as inspections of the manufacturing facility and processes. Overall, the FDA's review of a PMA application generally takes between one and three years, but may take significantly longer. The FDA can delay, limit or deny approval of a PMA application for many reasons.

If the FDA evaluation of a PMA is favorable, the FDA will issue either an approval letter, or an approvable letter, the latter of which usually contains a number of conditions that must be met in order to secure final approval of the PMA. When and if those conditions have been fulfilled to the satisfaction of the FDA, the agency will issue a PMA approval letter authorizing commercial marketing of the device, subject to the conditions of approval and the limitations established in the approval letter. If the FDA's evaluation of a PMA application or manufacturing facilities is not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. The FDA also may determine that additional tests or clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the trials are conducted and data is submitted in an amendment to the PMA, or the PMA is withdrawn and resubmitted when the data are available.

In approving a PMA application, as a condition of approval, the FDA may also require some form of post-approval study or post-market surveillance, whereby the applicant conducts a follow-up study or follows certain patient groups for a number of years and makes periodic reports to the FDA on the clinical status of those patients when necessary to protect the public health or to provide additional or longer-term safety and effectiveness data for the device. The FDA may also approve a PMA application with other post-approval conditions intended to ensure the safety and effectiveness of the device, such as, among other things, restrictions on labeling, promotion, sale, distribution and use.

The Breakthrough Devices Program is a voluntary program intended to expedite the review, development, assessment and review of certain medical devices that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human diseases or conditions for which no approved or cleared treatment exists or that offer significant advantages over existing approved or cleared alternatives. All submissions for devices designated as breakthrough devices will receive priority review, meaning that the review of the submission is placed at the top of the appropriate review queue and receives additional review resources, as needed. Although breakthrough designation or access to any other expedited program may expedite the development or approval process, it does not change the standards for approval. Breakthrough designation may also be withdrawn by the FDA if it believes that the designation is no longer supported by data from our clinical development program. Additionally, breakthrough designation does not ensure that we will ultimately obtain FDA approval.

Pervasive and Continuing Regulation

After a device is placed on the market, numerous regulatory requirements continue to apply. These include:

- the FDA's QSR, which requires manufacturers, including their suppliers, to follow stringent design, testing, control, documentation and other quality assurance procedures during all aspects of the manufacturing process;

- labeling regulations and FDA prohibitions against the promotion of products for uncleared, unapproved or off-label uses;

- medical device reporting regulations, which require that manufacturers report to the FDA if their device may have caused or contributed to a death or serious injury or malfunctioned in a way that would likely cause or contribute to a death or serious injury if the malfunction were to recur;

- medical device recalls, which require that manufacturers report to the FDA any recall of a medical device, provided the recall was initiated to either reduce a risk to health posed by the device, or to remedy a violation of the FDCA caused by the device that may present a risk to health; and

- post-market surveillance regulations, which apply when necessary to protect the public health or to provide additional safety and effectiveness data for the device.

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 to the extent we choose to sell any products outside of the United States.

Controlled Substances Regulations

Sufentanil, a Schedule II controlled substance, is the API in DSUVIA and Zalviso. Controlled substances are governed by the DEA. Similarly, sufentanil is regulated as a controlled substance in Europe and other territories outside of the U.S. The handling of controlled substances and/or drug product by us, our contract manufacturers, analytical laboratories, packagers and distributors, are regulated by the Controlled Substances Act and regulations thereunder. Ephedrine is a scheduled listed chemical product under the Combat Methamphetamine Epidemic Act of 2005. Under this law, DEA applies strict controls and quotas on importation of ephedrine containing drug products.

The Drug Supply Chain Security Act of 2013, or DSCSA, imposes obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing. Among the requirements are that manufacturers must provide certain information regarding the drug product to individuals and entities to which product ownership is transferred, label drug product with a product identifier, and keep certain records regarding the drug product. Further, manufacturers have drug product investigation, quarantine, disposition, and notification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death.

Unforeseen delays to the drug substance and drug product manufacture and supply chain may occur due to delays, errors or other unforeseen problems with the permitting and quota process. Also, any one of our suppliers, contract manufacturers, laboratories, packagers and/or distributors could be the subject of DEA violations and enforcement could lead to delays or even loss of DEA license by the contractors.

Federal and State Fraud and Abuse and Data Privacy and Security and Transparency Laws and Regulations

In addition to FDA restrictions on marketing of pharmaceutical and medical device products, federal and state healthcare laws restrict certain business practices in the pharmaceutical and medical device industries. These laws include, but are not limited to, anti-kickback, false claims, data privacy and security, and transparency statutes and regulations.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity from knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for, purchasing, leasing, ordering or arranging for the purchasing, leasing or ordering of any item or service reimbursable under Medicare, Medicaid or other federal healthcare program. The term "remuneration" has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payment, ownership interests and providing anything at less than its fair market value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers and/or formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exceptions and safe harbors are drawn narrowly, and practices involving remuneration that may be alleged to be intended to induce purchasing, leasing or ordering may be subject to scrutiny if they do not qualify for an exception or safe harbor. The failure to satisfy all of the requirements of an applicable exception or safe harbor do not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances.

Additionally, the intent standard under the federal Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, collectively, the Affordable Care Act to a stricter standard such that a person or entity no longer needs to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation. Rather, if "one purpose" of the remuneration is to induce referrals, the federal Anti-Kickback Statute is violated. In addition, the Affordable Care Act codified case law that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute also constitutes a false or fraudulent claim for purposes of the civil False Claims Act (discussed below).

The federal civil False Claims Act and related laws prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment or approval to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. Pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Companies also have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, and thus non-reimbursable, uses.

Further, the Civil Monetary Penalties Law imposes civil penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to, among others, a federal healthcare program that the person knows or should know is for a medical or other item or service that was not provided as claimed or is false or fraudulent.

In addition, 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, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information primarily on covered entities, business associates and their covered subcontractors. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to business associates that are independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, 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 attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. International laws, such as the European Union General Data Protection Regulation, or GDPR, (EU 2016/679) and Swiss Federal Act on Data Protection, regulate the processing of personal data within the European Union and between countries in the European Union and countries outside of the European Union, including the United States. Failure to provide adequate privacy protections and maintain compliance with safe harbor mechanisms could jeopardize business transactions across borders and result in significant penalties.

Additionally, the federal Physician Payments Sunshine Act within the Affordable Care Act and its implementing regulations, require that certain manufacturers of drugs, devices, biologicals and medical supplies, for which federal healthcare program payment is available, report information related to certain payments or other transfers of value made or distributed to physicians, (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members.

Also, many states have similar healthcare statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payer. FDA and some states require the posting of information relating to clinical studies. In addition, certain states such as California require pharmaceutical companies to implement a comprehensive compliance program that includes a limit on expenditures for, or payments to, individual medical or health professionals. Moreover, several states have enacted legislation requiring pharmaceutical manufacturers to, among other things, file periodic reports with the state, make periodic public disclosures on sales and marketing activities, report information related to drug pricing, require the registration of sales representatives, and prohibit certain other sales and marketing practices.

If our operations are found to be in violation of any of the health regulatory laws described above or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil and/or administrative penalties, damages, fines, disgorgement, imprisonment, exclusion of products from reimbursement under government programs, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products will be sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Pharmaceutical Coverage, Pricing and Reimbursement

In both domestic and foreign markets, sales of any approved products will depend in part on the availability of coverage and adequate reimbursement from third-party payers. Third-party payers include government health administrative authorities, managed care providers, private health insurers and other organizations. Sales of approved products will depend substantially, both domestically and abroad, on the extent to which the costs of such products will be paid by third-party payers. These third-party payers are increasingly focused on containing healthcare costs by challenging the price and examining the cost-effectiveness of medical products and services. In addition, significant uncertainty exists as to the coverage and reimbursement status of newly approved healthcare products. Such payers may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the FDA-approved drugs for a particular indication. Third-party payers and hospitals may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such products. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact utilization. Because each third-party payer individually approves coverage and reimbursement levels, obtaining coverage and adequate reimbursement is a time-consuming, costly and sometimes unpredictable process. We or our providers may be required to provide scientific and clinical support for the use of any product to each third-party payer and hospital separately with no assurance that approval would be obtained, and we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. This process could delay the market acceptance of any product and could have a negative effect on our future revenues and operating results. We cannot be certain that any approved product will be considered medically necessary or cost-effective. Because coverage and reimbursement determinations are made on a payer-by-payer basis, obtaining acceptable coverage and reimbursement from one payer does not guarantee that we will obtain similar acceptable coverage or reimbursement from another payer. If we or our partners are unable to obtain and maintain coverage of, and adequate reimbursement and payment levels for, the products from third-party payers, physicians may limit how much or under what circumstances they will prescribe or administer them. This in turn could affect our or our partners' ability to successfully commercialize products and impact our profitability, results of operations, financial condition and future success. Third-party payers, government healthcare programs, wholesalers, group purchasing organizations, and hospitals frequently require that companies negotiate agreements that provide discounts or rebates from list prices. We expect increasing pressure to offer larger discounts or discounts to a greater number of these organizations to maintain acceptable reimbursement levels for and access to our products. Net prices for drugs may be reduced by these mandatory discounts or rebates required by government healthcare programs, private payers, wholesalers, group purchasing organizations, hospitals, and by any future relaxation of laws that presently restrict imports of drugs from policy and payment limitations in setting their own reimbursement policies. In addition, if competitors reduce the prices of their products, or otherwise demonstrate that they are better or more cost effective than our products, this may result in a greater level of reimbursement for their products relative to our products, which would reduce sales of our products and harm our results of operations.

There have been, and there will continue to be, legislative and regulatory proposals to change the healthcare system in ways that could impact our ability to commercialize our products profitably. We anticipate that the federal and state legislatures and the private sector will continue to consider and may adopt and implement healthcare policies, such as the Affordable Care Act, intended to curb rising healthcare costs. These cost containment measures may include: controls on government-funded reimbursement for drugs; new or increased requirements to pay prescription drug rebates to government health care programs; controls on healthcare providers; challenges to or limits on the pricing of drugs, including pricing controls, or limits or prohibitions on reimbursement for specific products through other means; requirements to try less expensive products or generics before a more expensive branded product; and public funding for cost effectiveness research, which may be used by government and private third-party payers to make coverage and payment decisions.

In addition, in many foreign countries, particularly the countries of the European Union, the pricing of prescription drugs is subject to government control. In some non-U.S. jurisdictions, 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. A member state may approve a specific price for the medicinal product, or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. We may face competition for our products from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. In addition, there may be importation of foreign products that compete with our own products, which could negatively impact our profitability.

Healthcare Reform

In the United States and foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the United States federal and state level that seek to reduce healthcare costs. Government payment for some of the costs of prescription drugs may increase demand for our products for which we receive marketing approval. However, any negotiated prices for our future products will likely be lower than the prices we might otherwise obtain from non-governmental payers. Moreover, private payers often follow federal healthcare coverage policy and payment limitations in setting their own payment rates.

Furthermore, political, economic and regulatory influences are subjecting the healthcare industry in the United States to fundamental change. Initiatives to reduce the federal deficit and to reform healthcare delivery are increasing cost-containment efforts. We anticipate that Congress, state legislatures and the private sector will continue to review and assess alternative benefits, controls on healthcare spending through limitations on the growth of private health insurance premiums and Medicare and Medicaid spending, the creation of large insurance purchasing groups, price controls on pharmaceuticals and other fundamental changes to the healthcare delivery system. Any proposed or actual changes could limit or eliminate our spending on development projects and affect our ultimate profitability.

In the United States, the Affordable Care Act was enacted in an effort to, among other things, broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, impose new taxes and fees on the health industry and impose additional health policy reforms. There have been judicial, executive branch and Congressional challenges to certain aspects of the Affordable Care Act. For example, on June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. In addition, there have been a number of health reform initiatives by the Biden administration that have impacted the Affordable Care Act. For example, President Biden signed the Inflation Reduction Act of 2022, or the IRA, into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in Affordable Care Act marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program. It is possible that there will be additional health reform measures. It is possible that the Affordable Care Act will be subject to judicial or Congressional challenges in the future. It is unclear how such challenges, and the healthcare reform measures of the Biden administration will impact the Affordable Care Act. In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. Aggregate reductions of Medicare payments to providers of 2% per fiscal year went into effect on April 1, 2013 and will stay in effect through 2031 unless Congressional action is taken. The American Taxpayer Relief Act further reduced Medicare payments to several providers, including hospitals. Under current legislation the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% in the final fiscal year of this sequester. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024.

Legislative and regulatory proposals have been made to expand post-approval requirements and further restrict sales and promotional activities for pharmaceutical and medical device products. We are not sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our products, if any, may be.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we or our collaborators are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or our collaborators are not able to maintain regulatory compliance, our products may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing and reform government program reimbursement methodologies for drugs. For example, at the federal level, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue to advance these principles. In addition, the IRA, among other things (i) directs HHS to negotiate the price of certain high-expenditure, single-source drugs and biologics covered under Medicare and (ii) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. In addition, the Biden administration released an additional executive order on October 14, 2022, directing HHS to report on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, measures designed to encourage importation from other countries and bulk purchasing.

Further, there may continue to be additional proposals relating to the reform of the U.S. healthcare system, some of which could further limit the prices we are able to charge for our products, or the amounts of reimbursement available for our products once approved. If future legislation were to impose direct governmental price controls and access restrictions, it could have a significant adverse impact on our business. Managed care organizations, as well as Medicaid and other government agencies, continue to seek price discounts. Some states have implemented, and other states are considering, price controls or patient access constraints under the Medicaid program, and some states are considering price-control regimes that would apply to broader segments of their populations that are not Medicaid-eligible. Due to the volatility in the current economic and market dynamics, we are unable to predict the impact of any unforeseen or unknown legislative, regulatory, payer or policy actions, which may include cost containment and other healthcare reform measures. Such policy actions could have a material adverse impact on our profitability.

Employees and Human Capital Resources

As of December 31, 2022, we employed 19 full-time employees, approximately 80% of whom work out of our corporate offices in Hayward, CA. The rest of our employees work remotely in various locations throughout the United States and are members of our commercial team. AcelRx is committed to pay equity, regardless of gender or race/ethnicity, and conducts pay equity analyses on an annual basis.

We invest in our workforce by offering competitive salaries, wages, and benefits. We endeavor to foster a strong sense of ownership by offering all employees stock options and restricted stock units under our broad-based stock incentive program. We also offer comprehensive and locally relevant benefits for all eligible employees. We recognize and support the growth and development of our employees.

None of our employees are subject to a collective bargaining agreement. We consider our relationship with our employees to be good.

Corporate Information

We were originally incorporated as SuRx, Inc. in Delaware on July 13, 2005. We subsequently changed our name to AcelRx Pharmaceuticals, Inc. We file electronically with the U.S. Securities and Exchange Commission, or SEC, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act. We make available on our website at www.acelrx.com, free of charge, copies of these reports as soon as reasonably practicable after filing these reports with, or furnishing them to, the SEC.

Item 1A. Risk Factors

Our operations and financial results are subject to various risks and uncertainties. You should carefully consider the risks described below, together with all of the other information in this report, including our financial statements and notes thereto. If any of the following risks actually materialize, our business, financial condition, results of operations, liquidity, and future prospects could be materially harmed, the price of our common stock could decline, and you could lose part or all of your investment.

Risks Related to COVID-19 Pandemic

Our Emergency Use Authorization Application for Niyad™ is premised on the declared COVID-19 health emergency.

Our Emergency Use Authorization, or EUA, submission that is currently under review by FDA for Niyad is based upon the U.S. government's declaration of a national health emergency due to the COVID-19 pandemic. On January 30, 2023, President Joe Biden informed Congress that he will end the twin national emergencies for addressing COVID-19 on May 11, 2023. Although the FDA will maintain the discretion to keep EUAs in effect after the public health emergency has ended, the anticipation of its end may negatively impact our prospects for obtaining authorization in the first place, and even if authorized, any sales for a COVID-related indication may be limited and distract us from the goal of obtaining Premarket Approval, or PMA, for Niyad.

Risks Related to Drug Development and Commercialization

We may fail to realize the benefits expected from our acquisition of Lowell, which could adversely affect our stock price.

Our acquisition of Lowell is our largest acquisition to date. Our primary business strategy is focused on developing, obtaining approval, and commercializing our product candidates, including Niyad and LTX-608 that we acquired from Lowell. The anticipated benefits we expect from this acquisition are, necessarily, based on projections and assumptions about the combined businesses of our company and Lowell, which may not materialize as expected or which may prove to be inaccurate. The value of our common stock could be adversely affected if we are unable to realize the anticipated benefits from the acquisition on a timely basis or at all. Achieving the benefits of the acquisition of Lowell will depend, in part, on our ability to continue integrate the business, operations and products of Lowell successfully and efficiently with our business. The challenges involved in this integration include, but are not limited to, (i) difficulties entering new markets and integrating new product candidates with which we have no or limited direct prior experience; and (ii) successfully managing relationships with our combined supplier base.

Our failure to identify or accurately assess the magnitude of certain liabilities we assumed in the acquisition could result in unexpected litigation or regulatory exposure, unfavorable accounting charges, unexpected increases in taxes due, a loss of anticipated tax benefits or other adverse effects on our business, operating results or financial condition.

Whether we receive royalties from DSUVIA is dependent on the ability of Alora to successfully commercialize DSUVIA. If Alora or another potential partner, are unable to successfully commercialize DSUVIA, our business, financial condition, and results of operations will be materially harmed.

Upon closing of the DSUVIA Agreement to divest DSUVIA, Alora will continue to commercialize the product and we will receive royalties and milestone payments based on their sales. The commercial success of DSUVIA will depend heavily on numerous factors, including:

- Alora's ability to market, sell, and distribute DSUVIA;
- Alora's ability to establish and maintain commercial manufacturing relationships with our third-party service providers;
- acceptance by the medical community, including physicians, nurses, patients and pharmacy and therapeutics committees;
- acceptance of pricing and placement on payers' formularies;
- Alora's ability to effectively compete with other medications for the treatment of moderate-to-severe acute pain in medically supervised settings, including IV-opioids and any subsequently approved products;

- effective management of, and compliance with, the DSUVIA Risk Evaluation and Mitigation Strategy, or REMS, program;
- continued demonstration of an acceptable safety profile of DSUVIA; and
- Alora's ability to obtain, maintain, enforce, and defend the intellectual property rights and claims for DSUVIA.

If Alora is unable to successfully commercialize DSUVIA, our business, financial condition, and results of operations will be materially harmed.

Delays in clinical trials are common and have many causes, and any delay could result in increased costs to us and jeopardize or delay our ability to obtain regulatory approval and commence product sales.

We have experienced and may in the future experience delays in clinical trials of our product candidates. Our FDA-required clinical trials for our product candidates, could be delayed for a variety of reasons, including:

- inability to raise funding necessary to initiate or continue a trial;
- inability to pay significant FDA filing fees;
- delays in obtaining regulatory approval to commence a trial;
- delays in reaching agreement with the FDA on final trial design;
- imposition of a clinical hold by the FDA, Institutional Review Board, or IRB, or other regulatory authorities;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites;
- delays in obtaining required IRB approval at each site;
- delays in recruiting suitable patients or subjects to participate in a trial;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- clinical sites dropping out of a trial to the detriment of enrollment or being delayed in entering data to allow for clinical trial database closure;
- time required to add new clinical sites; or
- delays by our contract manufacturers to produce and deliver sufficient supply of clinical trial materials.

If any future FDA-required clinical trials are delayed for any reason, our development costs may increase, our approval process for our product candidates could be delayed, our ability to commercialize and commence sales of our product candidates could be materially harmed, which could have a material adverse effect on our business.

Our drug discovery and development efforts might not generate successful product candidates.

We plan to invest a significant portion of our efforts and financial resources in the identification or asset acquisition of our product candidates, Niyad, LTX-608 and the pre-filled syringes. Our ability to generate product revenue from these product candidates, which may not occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of Niyad, LTX-608 and the pre-filled syringes. The success of these product candidates and any other product candidates we may develop will depend on many factors, including the following:

- successful enrollment in, and completion of, clinical trials;
- demonstrating safety and efficacy;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and non-patent exclusivity for our product candidates;
- developing a sales and marketing organization or outsourcing these functions to third parties;

- launching commercial sales of the product candidates, if and when approved, whether alone or selectively in collaboration with others;
- acceptance of the product candidates, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other products;
- a continued acceptable safety profile of the products following approval;
- enforcing and defending intellectual property rights and claims; and
- other legal, regulatory, compliance, privacy, and fraud and abuse matters.

If we do not accomplish one or more of these goals in a timely manner, or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would harm our business.

If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials could occur at any stage of testing. The outcome of early clinical trials may not be predictive of the success of later clinical trials, and interim results of a particular clinical trial do not necessarily predict final results of that trial.

Moreover, clinical data is often susceptible to multiple interpretations and analyses. 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.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including that:

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate; enrollment in these clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate; and
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;

- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Product development costs will also increase if we experience delays in testing or in receiving marketing approvals. We do not know whether any clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates, could allow our competitors to bring products to market before we do, and could impair our ability to successfully commercialize our product candidates, any of which may harm our business and results of operations.

If we experience delays or difficulties in enrolling patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to identify and enroll a sufficient number of eligible patients to participate in these trials as required by the U.S. Food and Drug Administration, or the FDA, or analogous regulatory authorities outside the United States. In addition, some of our competitors may have ongoing clinical trials for product candidates that would treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. Patient enrollment is also affected by other factors, including:

- severity of the disease under investigation;
- availability and efficacy of approved medications for the disease under investigation;
- eligibility criteria for the trial in question;
- perceived risks and benefits of the product candidate under study;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of health care professionals;
- the ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll enough patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

If serious adverse effects or unexpected characteristics of our product candidates are identified during development, we may need to abandon or limit our development of some or all of our product candidates.

It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive marketing approval. Adverse events or undesirable side effects caused by, or other unexpected properties of, our product candidates could cause us, any current or future collaborators, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of one or more of our product candidates and could result in a more restrictive label, or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. If adverse effects were to arise in patients being treated with any of our product candidates, it could require us to halt, delay or interrupt clinical trials of such product candidate or adversely affect our ability to obtain requisite approvals to advance the development and commercialization of such product candidate. If our product candidates are associated with undesirable side effects or have characteristics that are unexpected, we may need to abandon their development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

We have limited financial and managerial resources. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements.

The process for obtaining approval of a PMA or NDA is time consuming, subject to unanticipated delays and costs, and requires the commitment of substantial resources.

If the FDA determines that any of the clinical work submitted, including the clinical trials, Human Factors studies and bench testing submitted for a product candidate in support of a premarket approval application (PMA) or NDA were not conducted in full compliance with the applicable protocols for these trials, studies and testing as well as with applicable regulations and standards, or if the FDA does not agree with our interpretation of the results of such trials, studies and testing, the FDA may reject the data and results. The FDA may audit some or all of our clinical trial sites to determine the integrity of our clinical data. The FDA may audit some or all of our study sites to determine the integrity of our data and may audit the data and results of bench testing. Any rejection of any of our data would negatively impact our ability to obtain marketing authorization for our product candidates and would have a material adverse effect on our business and financial condition. In addition, an NDA or PMA may not be approved, or approval may be delayed, as a result of changes in FDA policies for drug or device approval during the review period. For example, although many products have been approved by the FDA in recent years under Section 505(b)(2) of the FDCA, objections have been raised to the FDA's interpretation of Section 505(b)(2). If challenges to the FDA's interpretation of Section 505(b) (2) are successful, the FDA may be required to change its interpretation, which could delay or prevent the approval of such an NDA. Any significant delay in the acceptance, review or approval of an NDA or PMA that we have submitted would have a material adverse effect on our business and financial condition and would require us to obtain significant additional funding.

Our expectations for FDA approvability of our product candidates may be inaccurate, and we may be required to conduct additional manufacturing, nonclinical or clinical development work in order to obtain FDA approval for these products, which would add to our expenses and delay any associated revenue.

On July 14, 2021, we entered into the PFS Agreement with Aguettant pursuant to which we obtained the exclusive right to develop and, subject to FDA approval, commercialize in the United States (i) an ephedrine pre-filled syringe containing 10 ml of a solution of 3 mg/ml ephedrine hydrochloride for injection, and (ii) a phenylephrine pre-filled syringe containing 10 ml of a solution of 50 mcg/ml phenylephrine for injection. Aguettant will supply us with the products for use in commercialization, if they are approved in the U.S. In connection with our and Aguettant's agreement to enter into the Amended DZUVEO Agreement and the Amended and Restated Supply Agreement (please refer to the section headed "Part I.— Item 1. Business — Our Portfolio — Sufentanil Sublingual Products" for further details), we will enter into an amendment to the PFS Agreement with Aguettant pursuant to which, effective on the later of the closing of the transaction contemplated under the DSUVIA Agreement (as defined in the section headed "Part I. — Item 1. Business — Our Portfolio — Sufentanil Sublingual Products") and April 1, 2023, (a) Aguettant will pay us a complementary payment in the amount of €1.5 million, and (b) the maximum amount in sales-based milestone payments that Aguettant is entitled to receive will reduce to $21 million. Refer to Note 6, "In-License Agreement", Note 7, "Out-license Agreements—DZUVEO" and Note 20, "Subsequent Events" to the consolidated financial statements in this Annual Report on Form 10-K for additional information. Our current expectation based on our communication with the FDA is that Fedsyra™, the PFS ephedrine product candidate, will be approvable by the FDA without additional manufacturing changes or clinical development. We have not yet received all the available data to support the planned NDA submission for the PFS phenylephrine product. If we or the FDA determine that additional development work will be needed for U.S. approval of either of the PFS product candidates, we would incur additional expense and be delayed in obtaining any revenue from that product.

Nafamostat is being developed for both medical device and drug indications for use. Although nafamostat is approved for certain uses in Japan, our ability to leverage that for an expedited development and approval pathway with the FDA may be limited, and we may be required to conduct additional unanticipated nonclinical studies and clinical trials in order to seek approval in the U.S. We plan to study Niyad™ under an investigational device exemption, or IDE and although we have submitted an IDE to FDA, it remains under review. Niyad has received Breakthrough Device Designation from the FDA for regional anticoagulant for injection into the extracorporeal circuit and is expected to be used during renal replacement therapy for acute kidney injury patients in the hospital and for end-stage renal disease patients receiving dialysis in outpatient clinics. We expect that Niyad will require approval of a Premarket Approval, or PMA, application for commercialization in the U.S., and as a company we have never submitted nor received approval for a PMA.

The active drug component of Niyad, nafamostat, is also being developed for drug indications as LTX-608, for which we expect to submit Investigational New Drug applications once IND-enabling studies have been completed. We may be delayed in the submission of our planned INDs if there are unexpected findings in our nonclinical studies.

A key part of our business strategy is to establish collaborative relationships to commercialize and fund development and approval of our products, particularly outside of the United States. We may not succeed in establishing and maintaining collaborative relationships, which may significantly limit our ability to develop and commercialize our products successfully, if at all.

We will need to establish and maintain successful collaborative relationships to obtain international sales, marketing and distribution capabilities for our products. The process of establishing and maintaining collaborative relationships is difficult, time-consuming and involves significant uncertainty. For example:

- our partners may seek to renegotiate or terminate their relationships with us due to unsatisfactory clinical or regulatory results, manufacturing issues, a change in business strategy, a change of control or other reasons;
- our contracts for collaborative arrangements are or may be terminable at will on written notice and may otherwise expire or terminate, and we may not have alternatives available to achieve the potential for our products in those territories or markets;
- our partners may choose to pursue alternative technologies, including those of our competitors;
- we may have disputes with a partner that could lead to litigation or arbitration, including in connection with any contractual breach notice including force majeure tied to the COVID-19 pandemic;
- we have limited control over the decisions of our partners, and they may change the priority of our programs in a manner that would result in termination of the agreement or add significant delays to the partnered program;
- our ability to generate future payments and royalties from our partners depends upon the abilities of our partners to establish the safety and efficacy of our drugs and devices, maintain regulatory approvals and our ability to successfully manufacture and achieve market acceptance of our products;
- we or our partners may fail to properly initiate, maintain or defend our intellectual property rights, where applicable, or a party may use our proprietary information in such a way as to invite litigation that could jeopardize or potentially invalidate our proprietary information or expose us to potential liability;
- our partners may not devote sufficient capital or resources towards our products; and
- our partners may not comply with applicable government regulatory requirements necessary to successfully market and sell our products.

If any collaborator fails to fulfill its responsibilities in a timely manner, or at all, any research, clinical development, manufacturing or commercialization efforts pursuant to that collaboration could be delayed or terminated, or it may be necessary for us to assume responsibility for expenses or activities that would otherwise have been the responsibility of our collaborator. If we are unable to establish and maintain collaborative relationships on acceptable terms we may have to undertake development and commercialization activities at our own expense.

We may experience difficulties in retaining our existing employees and managing our operations.

We need to retain and maintain our existing managerial, operational, regulatory, developmental, finance and other personnel and resources in order to develop our product candidates and manage our operations. Our current infrastructure may be inadequate to support our strategy and any future workforce reduction, such as the reduction that eliminated approximately 40% of our workforce in May 2022 and subsequent related workforce reductions, may be disruptive to our operations, may negatively affect our productivity, and may constrain our commercialization activities. For example, a further workforce reduction could yield unanticipated consequences, such as attrition beyond planned staff reductions, negatively impacting employee morale and our corporate culture, or increased difficulties in our day-to-day operations, and prevent us from developing our product candidates as rapidly as planned. If we encounter such unanticipated consequences, we may have difficulty retaining and attracting personnel. In addition, the implementation of any additional workforce or expense reduction programs may divert the efforts of our management team and other key employees, which could adversely affect our business. Furthermore, we may not realize, in full or in part, the anticipated benefits, savings and improvements in our cost structure from our cost reduction plan, due to unforeseen difficulties, delays or unexpected costs. If we are unable to realize the expected operational efficiencies and cost savings from the cost reduction plan, our operating results and financial condition would be adversely affected.

If we, or current and potential partners, are unable to compete effectively, our products may not reach their commercial potential.

The U.S. biotechnology and pharmaceutical industries are characterized by intense competition and cost pressure. Our Niyad product candidate, if approved in the U.S., may compete with currently available anticoagulants such as heparin and citrate. The PFS product candidates, if approved in the U.S., may compete with other ready-to-use formulations of ephedrine and phenylephrine. The nafamostat product candidates, if approved in the U.S., may compete with heparin and citrate.

Key competitive factors affecting the commercial success of our approved products are likely to be efficacy, safety profile, reliability, convenience of dosing, price and reimbursement. Many of our competitors and potential competitors have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of drug candidates, obtaining FDA and other regulatory approval of products, and the commercialization of those products. Accordingly, our competitors may be more successful than we are in obtaining FDA approval for drugs and devices and achieving widespread market acceptance. Our competitors' drugs, devices or drug delivery systems may be more effective, have fewer adverse effects, be less expensive to develop and manufacture, or be more effectively marketed and sold than any product we may seek to commercialize. This may render our products obsolete or non-competitive. We anticipate that we will face intense and increasing competition as new drugs and devices enter the market, additional technologies become available, and competitors establish collaborative or licensing relationships, which may adversely affect our competitive position. These and other competitive risks may materially adversely affect our ability to attain or sustain profitable operations.

Coverage and adequate reimbursement may not be available for our product candidates, if approved, in the United States and in Europe, which could make it difficult for us, or our partners, to sell our products profitably.

Our and our partners' ability to commercialize our product candidates in the future, if approved, in the United States will depend, in part, on the extent to which coverage and adequate reimbursement will be available from government payer programs at the federal and state levels, authorities, including Medicare and Medicaid, private health insurers, managed care plans and other third-party payers.

No uniform policy requirement for coverage and reimbursement for drug products exists among third-party payers in the United States or Europe. Therefore, coverage and reimbursement can differ significantly from payer to payer. As a result, the coverage determination process is often a time-consuming and costly process that will require us or our partners to provide scientific and clinical support for the use of the approved products to each payer separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such products. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact utilization. Our or our partners' inability to promptly obtain and sufficiently maintain coverage and adequate reimbursement rates from third party payers could significantly harm our operating results, our ability to raise capital needed to commercialize our approved drugs and our overall financial condition.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payers have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products. There have been a number of legislative and regulatory proposals to change the healthcare system in the United States and in some foreign jurisdictions that could affect our or our partners' ability to sell the products profitably. These legislative and/or regulatory changes may negatively impact the reimbursement for our products, following approval. The availability of numerous generic pain medications may also substantially reduce the likelihood of reimbursement for approved products in Europe and elsewhere. The application of user fees to generic drug products may expedite the approval of additional pain medication generic drugs. We would expect that DSUVIA will experience pricing pressures in connection with the product sale due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. If we or our partners fail to successfully secure and maintain reimbursement coverage for our products or are significantly delayed in doing so, there may be difficulty achieving market acceptance of our products and our business will be harmed.

Furthermore, market acceptance and sales of our products will depend on reimbursement policies and may be affected by future healthcare reform measures. Government authorities and third-party payers, such as private health insurers, hospitals and health maintenance organizations, decide which drugs and devices they will pay for and establish reimbursement levels. We cannot be sure that reimbursement will be available for DSUVIA or our product candidates, if approved, in the United States or in Europe. Also, reimbursement amounts may reduce the demand for, or the price of, our products. For example, additional studies in Europe may be needed to ensure premium reimbursement in certain countries. If reimbursement is not available, or is available only to limited levels, we, or our partners, may not be able to successfully commercialize DSUVIA or our product candidates, if approved, in the United States or in Europe.

Additionally, the regulations that govern marketing approvals, pricing, coverage and reimbursement for new drugs and devices vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a product before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues able to be generated from the sale of the product in that country. For example, separate pricing and reimbursement approvals may impact the ability to market and successfully commercialize DZUVEO in the 27 member states of the European Union. Adverse pricing limitations may hinder Alora's ability to sell DSUVIA in the United States, or our ability to recoup our investment in other product candidates, even after obtaining FDA marketing approval.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

If we are found to have improperly promoted off-label uses of our products in the United States, we may become subject to significant liability. Such enforcement has become more common in the industry. The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription drug and device products. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If the FDA determines that our or our partners' public disclosures, promotional materials or training constitutes promotion of non-approved or off-label use, it could request modifications to disclosure policies, training or promotional materials or subject us or our partners to regulatory or enforcement actions, including the issuance of an untitled letter, a Warning Letter, injunction, seizure, civil fine or criminal penalties and a requirement for corrective advertising, including Dear Doctor letters. It is also possible that other federal, state or foreign enforcement authorities might take action if they consider our or our partners' promotional or training materials to constitute promotion of non-approved or off-label use, which could result in significant civil, criminal and/or administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from government-funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, increased losses and diminished profits and the curtailment or restructuring of operations, any of which could adversely affect our or our partners' ability to operate and, thus, adversely impact our business and our financial results. The FDA or other enforcement authorities could also request that we enter into a consent decree or a corporate integrity agreement or seek a permanent injunction against us under which specified promotional conduct is monitored, changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, in the United States, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

If we or our partners are unable to establish and maintain relationships with group purchasing organizations any future revenues or future profitability could be jeopardized.

Many end-users of pharmaceutical and medical device products have relationships with group purchasing organizations, or GPOs, whereby such GPOs provide such end-users access to a broad range of pharmaceutical and medical device products from multiple suppliers at competitive prices and, in certain cases, exercise considerable influence over the drug and device purchasing decisions of such end-users. Hospitals and other end-users contract with the GPO of their choice for their purchasing needs. We expect to derive revenue from end-user customers that are members of GPOs for DSUVIA and our product candidates, if approved. Establishing and maintaining strong relationships with these GPOs will require us to be a reliable supplier, remain price competitive and comply with FDA regulations. The GPOs with whom we have relationships may have relationships with manufacturers that sell competing products, and such GPOs may earn higher margins from these products or combinations of competing products or may prefer products other than ours for other reasons. If we, or our partners, are unable to establish or maintain our GPO relationships, sales of DSUVIA and our product candidates, if approved, and related revenues could be negatively impacted.

Risks Related to Regulatory Approval of Our Product Candidates and Other Legal Compliance Matters

Existing and future legislation may increase the difficulty and cost for us to commercialize our products and affect the prices we may obtain.

In the United States, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the Affordable Care Act, was enacted in an effort to, among other things, broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, impose new taxes and fees on the health industry and impose additional health policy reforms.

The Affordable Care Act continues to substantially change health care financing and delivery by both governmental and private insurers, which may increase our regulatory burdens and operating costs.

There have been executive, judicial and Congressional challenges to certain aspects of the Affordable Care Act. For example, on June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. In addition, there have been a number of health reform initiatives by the Biden administration that have impacted the Affordable Care Act . For example, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or the IRA, into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in Affordable Care Act marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program. It is possible that there will be additional health reform measures It is possible that the Affordable Care Act will be subject to judicial or Congressional challenges in the future. It is also unclear how any such challenges and the healthcare reform measures of the Biden administration will impact the Affordable Care Act. We expect that the Affordable Care Act and other healthcare reform measures that may be adopted in the future, could have a material adverse effect on our industry generally and on our ability to successfully commercialize our products. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we or our collaborators are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or our collaborators are not able to maintain regulatory compliance, our products may lose regulatory approval and we may not achieve or sustain profitability, which would adversely affect our business.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. Aggregate reductions of Medicare payments to providers of 2% per fiscal year went into effect on April 1, 2013 and due to subsequent legislative amendments to the statute will stay in effect until 2031, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic, unless Congressional action is taken. Under current legislation the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. The American Taxpayer Relief Act further reduced Medicare payments to several providers, including hospitals. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024.

In the United States, there has been increasing legislative and enforcement interest 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 and reform government program reimbursement methodologies for drugs. At the federal level, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue to advance these principles. In addition, the IRA, among other things (i) directs HHS to negotiate the price of certain high-expenditure, single-source drugs and biologics covered under Medicare and (ii) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. In addition, the Biden administration released an additional executive order on October 14, 2022, directing HHS to report on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, measures designed to encourage importation from other countries and bulk purchasing. Furthermore, even after initial price and reimbursement approvals, reductions in prices and changes in reimbursement levels can be triggered by multiple factors, including reference pricing systems and publication of discounts by third party payers or authorities in other countries. In Europe, prices can be reduced further by parallel distribution and parallel trade (i.e., arbitrage between low-priced and high-priced countries). If any of these events occur, revenue from sales of our products in Europe would be negatively affected.

Legislative and regulatory proposals have been made to expand post-approval requirements and further restrict sales and promotional activities for pharmaceutical products. We are not sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our products, if any, may be.

We expect that additional healthcare reform measures will be adopted within and outside the United States in the future, any of which could negatively impact our business. 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 drug or device products for which we have obtained or may obtain regulatory approval, our ability to set a price that we believe is fair for our products, our ability to obtain coverage and reimbursement approval for a product, our ability to generate revenues and achieve or maintain profitability, and the level of taxes that we are required to pay.

Risks Related to Our Financial Condition and Need for Additional Capital

We have incurred significant losses since our inception and anticipate that we will continue to incur losses in the future.

We have incurred significant net losses since our inception in July 2005, and as of December 31, 2022, we had an accumulated deficit of $425.8 million.

We have devoted most of our financial resources to research and development, including our non-clinical development activities and clinical trials. To date, we have financed our operations primarily through the issuance of equity securities, borrowings, payments from Grünenthal, the monetization of certain future royalties and commercial sales milestones from the European sales of Zalviso by Grünenthal, funding from the Department of Defense, or DoD, and more recently with revenues from sales of DSUVIA since the commercial launch in the first quarter of 2019 and the upfront payment under the DZUVEO Agreement with Aguettant. The size of our future net losses will depend, in part, on the rate of future expenditures and our ability to generate revenues. We expect to continue to incur substantial expenses as we support research and development activities for our product candidates. If our product candidates are not successfully developed or commercialized in the U.S., or if revenues are insufficient following marketing approval, we will not achieve profitability and our business may fail. Our success is also dependent on current and future collaborations to market our products outside of the United States, which may not materialize or prove to be successful.

We require additional capital and may be unable to raise such capital, which would force us to delay, reduce or eliminate our commercialization efforts and product development programs and could cause us to be unable to continue to operate as a going concern and cease operations.

Launch of a commercial pharmaceutical product and pharmaceutical development activities can be time consuming and costly. We expect to incur significant expenditures in connection with supporting our research and development activities for our product candidates.

Clinical trials, regulatory reviews, and the launch of a commercial product are expensive activities. In addition, commercialization costs for DSUVIA and our product candidates, if approved, in the United States may be significantly higher than estimated as a result of technical difficulties or otherwise. Revenues may be lower than expected and costs to produce such revenues may exceed those revenues. We will need to seek additional capital to continue operations. Such capital demands could be substantial. In the future, we may seek to sell additional equity securities, including under the Controlled Equity Offering^{SM} Sales Agreement, or the ATM Agreement, with Cantor Fitzgerald & Co., or Cantor, as agent, and debt securities, monetize or securitize certain assets, refinance our loan agreement, enter into product development, license or distribution agreements with third parties, or divest any of our product candidates. Such arrangements may not be available on favorable terms, if at all.

If we are unsuccessful in efforts to raise additional capital, based on our current levels of operating expenses, our current capital is not expected to be sufficient to fund our operations for the next twelve months. These conditions raise substantial doubt about our ability to continue as a going concern.

The consolidated financial statements for the year ended December 31, 2022 were prepared on the basis of a going concern, which contemplates that we will be able to realize our assets and discharge liabilities in the normal course of business. The financial statements do not include any adjustments that might be necessary if we are unable to continue as a going concern.

Future events and circumstances, including those beyond our control, may cause us to consume capital more rapidly than we currently anticipate. Furthermore, any product development, licensing, distribution or sale agreements that we enter into may require us to relinquish valuable rights. We may not be able to obtain sufficient additional funding or enter into a strategic transaction in a timely manner. If adequate funds are not available, we would be required to reduce our workforce, reduce the scope of, or cease, the development and subsequent potential commercial launch of our product candidates in advance of the date on which we exhaust our cash resources to ensure that we have sufficient capital to meet our obligations and continue on a path designed to preserve stockholder value.

Securing additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to develop our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. If we are unable to raise additional capital when required or on acceptable terms, we may be required to:

- further scale back or discontinue the development of our product candidates;
- seek corporate partners for our product candidates on terms that might be less favorable than might otherwise be available; or
- relinquish, or license on unfavorable terms, our rights to technologies, products or product candidates that we otherwise would seek to develop or commercialize ourselves.

During the past several years, domestic and international financial markets have experienced, and they may continue to experience, extreme disruption from time to time, including, among other things, high volatility, significant declines in stock prices and severely diminished liquidity and credit availability for both borrowers and investors. Such adverse capital and credit market conditions could make it more difficult to obtain additional capital on favorable terms, or at all, which could have a material adverse effect on our business and growth prospects. For example, our ability to raise additional capital may be adversely impacted by deteriorating global economic conditions and the disruptions to and volatility in the credit and financial markets in the U.S. and worldwide resulting from the evolving effects of the COVID-19 pandemic and the ongoing military conflict between Russian and Ukraine and related sanctions imposed against Russia.

To fund our operations and capital requirements, we may sell additional equity securities, which may result in dilution to our stockholders, or debt securities, which may impose restrictions on our business.

We expect that significant additional capital will be needed in the future to continue our planned operations and capital requirements. In the long-term, our existing capital resources will not be sufficient to fund our operations until such time as we may be able to generate sufficient revenues to sustain our operations. In order to raise additional funds to support our operations, we may sell additional equity securities, including under the ATM Agreement with Cantor. 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. Selling additional equity securities may result in dilution to our existing stockholders and new investors may be materially diluted by subsequent sales. Incurring additional indebtedness, including through the sale of debt securities, would result in increased fixed payment obligations and could also result in additional restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions, such as minimum cash balances, that could adversely impact our ability to conduct our business. Sales of equity or debt securities may also provide new investors with rights superior to our existing stockholders. If we are unable to expand our operations or otherwise capitalize on our business opportunities, our business, financial condition and results of operations could be materially adversely affected, and we may not be able to meet our debt service obligations.

We have not yet generated significant product revenue and may never be profitable.

Our ability to generate revenue from commercial sales and/or royalties and achieve profitability depends on our ability, alone and with collaborators, to successfully complete the development of, obtain the necessary regulatory approvals for, and commercialize our products. Although we received FDA approval of DSUVIA and began the commercial launch of DSUVIA in the United States, we may never generate enough revenues from sales of DSUVIA, or our product candidates, if approved, in the United States to become profitable. Although the EC granted marketing approval of DZUVEO in June 2018, we only recently entered into the DZUVEO Agreement with Aguettant to commercialize DZUVEO in Europe and there can be no assurance that Aguettant, or Alora pursuant to the DSUVIA Agreement, will successfully commercialize DZUVEO or DSUVIA. Although we had a collaboration agreement with Grünenthal for commercialization of Zalviso in Europe and Australia, Grünenthal was unable to achieve a level of commercial sales of Zalviso to trigger sales milestone payments that would have been payable to us. The Grünenthal Agreements have been terminated and Grünenthal's rights to market and sell Zalviso reverted back to us on May 12, 2021. The European Marketing Authorization for Zalviso was withdrawn in July 2022.

We do not anticipate generating significant near-term revenues from DSUVIA or our product candidates, if approved, in the United States. Our ability to generate future revenues from product sales depends heavily on the success in:

- maintaining regulatory approval for DSUVIA and obtaining and maintaining regulatory approval for our product candidates in the United States; and

- launching and commercializing our product candidates, if approved, in the United States by building, internally or through collaborations, an institutionally focused sales force, and launching and commercializing DZUVEO internationally through collaborations, which may require additional funding.

Because of the numerous risks and uncertainties associated with launching a commercial pharmaceutical product, pharmaceutical product development and the regulatory environment, we are unable to predict the timing or amount of increased expenses, or when, or if, we will be able to achieve or maintain profitability. Our expenses could increase beyond expectations if we are delayed in receiving regulatory approval for our product candidates in the United States, or if we are required by the FDA to complete activities in addition to those we currently anticipate or have already completed.

Even if we are able to generate revenues from DSUVIA or our product candidates, if approved, in the United States, we may not become profitable and may need to obtain additional funding to continue operations.

Future sales of DSUVIA to the DoD are not predictable, may occur on an irregular basis and may not meet our expectations due to various U.S. government-related factors that are beyond our control and into which we have little to no visibility, including the timing and extent of future U.S. military deployments. If DoD spending on DSUVIA does not meet our expectations, it could adversely affect our expected results of operations, financial condition and liquidity.

In April 2020, DSUVIA achieved Milestone C approval by the DoD, a decision that clears the path for the DoD to begin placing orders for DSUVIA to fulfill its updating requirements for all Army Sets, Kits, and Outfits, or SKOs, for deployed/deploying troops. Completion of this SKO fulfillment process is dependent on the Army's completion of their product information package including instructions on fulfillment and training which remains in process. In September 2020, we announced that DSUVIA was added to the DoD Joint Deployment Formulary, a core list of pharmaceutical products that are designated for deploying military units across all service branches. Upon closing of the transaction contemplated under the DSUVIA Agreement, Alora will be responsible for commercializing DSUVIA except that we will retain the responsibility for driving the demand within the DoD, and we will receive quarterly payments in an amount equal to 75% of net Product sales to the DoD. Refer to Note 7, "Out-License Agreements—DZUVEO" and Note 20, "Subsequent Events" to the consolidated financial statements in this Annual Report on Form 10-K for additional information. Future sales of DSUVIA by Alora to the DoD are not predictable, may occur on an irregular basis, and may not meet expectations due to various U.S. government-related factors that are beyond our control and into which we have little to no visibility, including the timing and extent of future U.S. military deployments. Even if Alora does generate revenue from such sales and we receive payments, we may never generate revenue that is significant or predictable, which could impair our value and our ability to raise capital, expand our business or continue our operations. The placement of new orders by the DoD is, among other things, contingent upon overall U.S. government policies, budget and appropriation decisions and processes which are driven by numerous factors, including geo-political events, deployment of military units, macroeconomic conditions, and the ability of the U.S. government to enact relevant legislation, such as appropriations bills and accords on the debt ceiling. The timing and size of initial stocking orders for the SKOs and other orders by the DoD are based on troop deployment schedules. If DoD spending on DSUVIA does not meet our expectations, it could have a material adverse effect on our expected results of operations, financial condition and liquidity.

The terms of our loan agreement with Oxford may restrict our current and future operations, particularly our ability to respond to changes in business or to take certain actions, including to pay dividends to our stockholders.

On May 30, 2019, we entered into the Loan Agreement with Oxford Finance LLC, or Oxford, a Delaware limited liability company, as the Lender. The Loan Agreement contains, and any future indebtedness we incur will likely contain, a number of restrictive covenants that impose operating restrictions, including restrictions on our ability to engage in acts that may be in our best long-term interests. The Loan Agreement includes covenants that, among other things, restrict our ability to (i) declare dividends or redeem or repurchase equity interests; (ii) incur additional liens; (iii) make loans and investments; (iv) incur additional indebtedness; (v) engage in mergers, acquisitions, and asset sales; (vi) transact with affiliates; (vii) undergo a change in control; (viii) add or change business locations; and (ix) engage in businesses that are not related to our existing business. The Loan Agreement also requires that we at all times maintain unrestricted cash of not less than $5.0 million.

A breach of any of these covenants could result in an event of default under the Loan Agreement. Upon the occurrence of such an event of default, a default interest rate of an additional 5% may be applied to the outstanding loan balances and all outstanding obligations under the Loan Agreement can be declared to be immediately due and payable If our indebtedness is accelerated, we cannot assure you that we will have sufficient assets to repay the indebtedness. The restrictions and covenants in the Loan Agreement and any future financing agreements may adversely affect our ability to finance future operations or capital needs or to engage in other business activities.

We might be unable to service our existing debt due to a lack of cash flow and might be subject to default.

As of December 31, 2022, we had approximately $5.4 million of outstanding debt under the Loan Agreement. The Loan Agreement has a scheduled maturity date of June 1, 2023 and is secured by a first priority security interest in substantially all of our assets, with the exception of our intellectual property and those assets sold under the Royalty Monetization, where the security interest is limited to proceeds of intellectual property if it is licensed or sold.

If we do not make the required payments when due, either at maturity, or at applicable installment payment dates, or if we breach the agreement or become insolvent, the Lender could elect to declare all amounts outstanding, together with accrued and unpaid interest, and other payments, to be immediately due and payable. Additional capital may not be available on terms acceptable to us, or at all. Even if we were able to repay the full amount in cash, any such repayment could leave us with little or no working capital for our business. If we are unable to repay those amounts, the Lender will have a first claim on our assets pledged under the Loan Agreement. If the lender should attempt to foreclose on the collateral, it is unlikely that there would be any assets remaining after repayment in full of such secured indebtedness. Any default under the Loan Agreement and resulting foreclosure would have a material adverse effect on our financial condition and our ability to continue our operations.

Risks Related to Our Reliance on Third Parties

We rely on third party manufacturers to produce commercial supplies of DSUVIA in the United States and DZUVEO for Aguettant in Europe, and will rely on third party manufacturers to produce clinical supplies of our product candidates. The failure of third-party manufacturers to provide us with adequate commercial and clinical supplies could result in a material adverse effect on our business.

Upon closing of the DSUVIA Agreement, Alora will manufacture DSUVIA and, pursuant to the Amended DZUVEO Agreement, and the Amended and Restated Supply Agreement, the rights and obligations under the Amended DZUVEO Agreement will be assumed by Alora, as part of the DSUVIA asset divestment agreement. We currently use third party manufacturers produce commercial and clinical supplies of our products and product candidates. Reliance on third party manufacturers entails many risks including:

- the inability to meet our product specifications and quality requirements consistently;

- the inability to procure raw materials in a timely fashion due to ongoing challenges in the global supply chain;
- a delay or inability to procure or expand sufficient manufacturing capacity;
- manufacturing and product quality issues related to scale-up of manufacturing;
- costs and validation of new equipment and facilities required for scale-up;
- a failure to maintain in good order our production and manufacturing equipment for our products;
- a failure to comply with cGMP and similar foreign standards;
- the inability to negotiate manufacturing or supply agreements with third parties under commercially reasonable terms;
- termination or nonrenewal of manufacturing or supply agreements with third parties in a manner or at a time that is costly or damaging to us;
- the reliance on a limited number of sources, and in some cases, single sources for product components, such that if we are unable to secure a sufficient supply of these product components, we will be unable to manufacture and sell our products in a timely fashion, in sufficient quantities or under acceptable terms;
- the lack of qualified backup suppliers for those components that are currently purchased from a sole or single source supplier;
- operations of our third-party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier, or government orders related to the COVID-19 pandemic;
- carrier disruptions or increased costs that are beyond our control; and
- the failure to deliver our products under specified storage conditions and in a timely manner.

Any of these events could lead to stock outs, inability to successfully commercialize our products, clinical trial delays, or failure to obtain regulatory approval. Some of these events could be the basis for FDA action, including injunction, recall, seizure, or total or partial suspension of production. If any of these events were to occur, our business would be materially adversely affected.

We rely on limited sources of supply for the active pharmaceutical ingredient, or API, of our nafamostat-based product candidates and any disruption in the chain of supply may cause a delay in developing our product candidates.

We currently have a single source of supply of API for our nafamostat-based product candidates. If supply from that vendor is interrupted or discontinued, there could be a significant impact on our development activities for those product candidates.

Manufacturing issues may arise that could delay or increase costs related to product development and regulatory approval.

We have relied, and will continue to rely, on contract manufacturers, component fabricators and third-party service providers to produce the necessary Niyad product for clinical and non-clinical development and eventually for commercial sales. We currently outsource manufacturing and packaging of Niyad to third parties and intend to continue to do so. These component purchases were made and will continue to be made utilizing short-term purchase agreements and we may not be able to enter into long-term agreements for commercial supply with these third-party manufacturers or may be unable to do so on acceptable terms. In addition, we may encounter production issues with our current or future contract manufacturers and other third-party service providers, including the reliability of the production equipment, quality of the components produced, their inability to meet demand or other unanticipated delays.

As we scale up manufacturing of Niyad in the future to support commercial demand, and conduct required production and stability testing, these processes may require refinement or resolution. For example, as we scale up, we may identify significant issues which could result in failure to maintain regulatory approval of Niyad, increased scrutiny by regulatory agencies, delays in clinical development and regulatory approval, increases in our operating expenses, or failure to obtain approval for our product candidates in the United States.

The facilities of any of our future manufacturers of Niyad must be approved by the FDA before commercial distribution from such manufacturers occurs. We do not fully control the manufacturing process and are completely dependent on these third-party manufacturing partners for compliance with the FDA or other foreign regulatory agency's requirements for manufacture. In addition, although our third-party manufacturers are well-established commercial manufacturers, we are dependent on their continued adherence to cGMP manufacturing and acceptable changes to their processes. If our manufacturers do not meet the FDA or other foreign regulatory agency's strict regulatory requirements, they will not be able to secure FDA or other foreign regulatory agency approval for their manufacturing facilities. If the FDA or the relevant foreign regulatory agency does not approve these facilities for the commercial manufacture of Niyad, we will need to find alternative suppliers, which would result in significant delays in obtaining regulatory agency approval. These challenges may have a material adverse impact on our business, results of operations, financial condition and prospects.

We may not be able to establish additional sources of supply for Niyad. Such suppliers are subject to FDA and other foreign regulatory agency's regulations requiring that materials be produced under cGMPs or Quality System Regulations, or QSR. Failure by any of our suppliers to comply with applicable regulations may result in delays. In addition, due to the recent strains on the global supply chain, the lead times for many components used in our production are getting longer and may impact our ability to manufacture our products in a timely manner.

We rely on third parties to conduct, supervise and monitor our clinical trials, and if those third parties perform in an unsatisfactory manner, it may harm our business.

We utilized contract research organizations, or CROs, for the conduct of the Phase 2 and 3 clinical trials of DSUVIA, as well as our Phase 3 clinical program for Zalviso. We will also utilize CROs for development of our product candidates. We will continue to rely on such CROs, as well as clinical trial sites, to ensure the proper and timely conduct of our clinical trials and document preparation. While we have agreements or will enter into such agreements governing their activities, we have limited influence over their actual performance. We have relied and plan to continue to rely upon CROs to monitor and manage data for our post-approval clinical programs for any FDA-required clinical programs for our product candidates, as well as the execution of nonclinical and clinical trials. We control only certain aspects of our CROs' activities. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities.

We, and our CROs, are required to comply with the FDA's current good clinical practices, or cGCPs, which are regulations and guidelines enforced by the FDA for all product candidates in clinical development. The FDA enforces these cGCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our marketing applications. Upon inspection, the FDA may determine that our clinical trials do not comply with cGCPs. Accordingly, if our CROs or clinical trial sites fail to comply with these regulations, we may be required to repeat clinical trials, which would delay the regulatory process.

Our CROs are not our employees, and we cannot control whether or not they devote sufficient time and resources to our ongoing clinical and nonclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials, or other drug development activities which could harm our competitive position. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may allow our potential competitors to access our proprietary technology. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates, if approved, would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

Risks Related to Our Business Operations and Industry

Our relationships with clinical investigators, health care professionals, consultants, commercial partners, third-party payers, hospitals, and other customers are subject to applicable anti-kickback, fraud and abuse and other healthcare laws, which could expose us to significant penalties.

Healthcare providers, including physicians, and others play a primary role in the recommendation and prescribing of any products for which we may obtain marketing approval. Our business operations and arrangements with investigators, healthcare professionals, consultants, commercial partners, hospitals, third-party payers and customers may expose us to broadly applicable fraud and abuse and other healthcare laws. These laws may constrain the business or financial arrangements and relationships through which we research, market, sell and distribute the products for which we obtain marketing approval. Applicable federal and state healthcare laws include, but are not limited to, the following:

- the federal healthcare Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under federal healthcare programs such as Medicare and Medicaid;

- the federal civil and criminal false claims laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false or fraudulent or from knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which, among other things, imposes criminal liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payer (e.g., public or private) and knowingly or willfully falsifying, concealing, or covering up by any trick or device a material fact or making any materially false statement in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, which impose certain obligations, including mandatory contractual terms, on covered healthcare providers, health plans and clearinghouses, and their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, as well as their covered subcontractors with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- foreign laws, regulations, standards and regulatory guidance which govern the collection, use, disclosure, retention, security and transfer of personal data, including the European Union General Data Privacy Regulation, or GDPR, which introduces strict requirements for processing personal data of individuals within the European Union;

- the federal transparency law, enacted as part of the Affordable Care Act, and its implementing regulations, which requires certain manufacturers of drugs, devices, biologicals and medical supplies to report annually to the CMS information related to payments and other transfers of value provided to physicians, (defined to include, doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;

- analogous state laws that may apply to our business practices, including but not limited to, state laws that require pharmaceutical companies to implement compliance programs and/or comply with the pharmaceutical industry's voluntary compliance guidelines; state laws that impose restrictions on pharmaceutical companies' marketing practices and require manufacturers to track and file reports relating to pricing and marketing information, which requires tracking and reporting gifts, compensation and other remuneration and items of value provided to healthcare professionals and entities, state and local laws that require the registration of pharmaceutical sales representatives, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, with differing effects; and

- the federal Foreign Corrupt Practices Act of 1977, United Kingdom Bribery Act 2010 and other similar anti-bribery laws in other jurisdictions which generally prohibit companies and their intermediaries from providing money or anything of value to officials of foreign governments, foreign political parties, or international organizations with the intent to obtain or retain business or seek a business advantage.

Recently, there has been a substantial increase in anti-bribery law enforcement activity by U.S. regulators, with more frequent and aggressive investigations and enforcement proceedings by both the Department of Justice and the SEC. A determination that our operations or activities are not, or were not, in compliance with United States or foreign laws or regulations could result in the imposition of substantial fines, interruptions of business, loss of supplier, vendor or other third-party relationships, termination of necessary licenses and permits, and other legal or equitable sanctions. Other internal or government investigations or legal or regulatory proceedings, including lawsuits brought by private litigants, may also follow as a consequence.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws involve substantial costs. It is possible that governmental authorities will conclude that our or our partners' business practices may not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws. If our operations are found to be in violation of any of these or any other healthcare regulatory laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, increased losses and diminished profits, additional oversight and reporting obligations if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations any of which could adversely affect our ability to operate our business and our financial results. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses or divert our management's attention from the operation of our business.

Significant disruptions of our information technology systems or data security incidents could result in significant financial, legal, regulatory, business and reputational harm to us.

We are increasingly dependent on information technology systems and infrastructure, including mobile technologies, to operate our business. In the ordinary course of our business, we collect, store, process and transmit large amounts of sensitive information, including intellectual property, proprietary business information, personal information and other confidential information. It is critical that we do so in a secure manner to maintain the confidentiality, integrity and availability of such sensitive information. We have also outsourced elements of our operations (including elements of our information technology infrastructure) to third parties, and as a result, we manage a number of third-party vendors who may or could have access to our computer networks or our confidential information. In addition, many of those third parties in turn subcontract or outsource some of their responsibilities to third parties. While all information technology operations are inherently vulnerable to inadvertent or intentional security breaches, incidents, attacks and exposures, the accessibility and distributed nature of our information technology systems, and the sensitive information stored on those systems, make such systems potentially vulnerable to unintentional or malicious internal and external attacks on our technology environment. Potential vulnerabilities can be exploited from inadvertent or intentional actions of our employees, third-party vendors, business partners, or by malicious third parties. Attacks of this nature are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives (including, but not limited to, industrial espionage) and expertise, including organized criminal groups, "hacktivists," nation states and others. In addition to the extraction of sensitive information, such attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. In addition, the prevalent use of mobile devices increases the risk of data security incidents.

Significant disruptions of our third-party vendors' and/or business partners' information technology systems or other similar data security incidents could adversely affect our business operations and result in the loss, misappropriation, and/or unauthorized access, use or disclosure of, or the prevention of access to, sensitive information, which could result in financial, legal, regulatory, business and reputational harm to us. In addition, information technology system disruptions, whether from attacks on our technology environment or from computer viruses, natural disasters, terrorism, war and telecommunication and electrical failures, could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

There is no way of knowing with certainty whether we have experienced any data security incidents that have not been discovered. While we have no reason to believe this to be the case, attackers have become very sophisticated in the way they conceal access to systems, and many companies that have been attacked are not aware that they have been attacked. Any event that leads to unauthorized access, use or disclosure of personal information, including but not limited to personal information regarding our patients or employees, could disrupt our business, harm our reputation, compel us to comply with applicable federal and state breach notification laws and foreign law equivalents, subject us to time consuming, distracting and expensive litigation, regulatory investigation and oversight, mandatory corrective action, require us to verify the correctness of database contents, or otherwise subject us to liability under laws, regulations and contractual obligations, including those that protect the privacy and security of personal information. This could result in increased costs to us, and result in significant legal and financial exposure and/or reputational harm. In addition, any failure or perceived failure by us or our vendors or business partners to comply with our privacy, confidentiality or data security-related legal or other obligations to third parties, or any further security incidents or other inappropriate access events that result in the unauthorized access, release or transfer of sensitive information, which could include personally identifiable information, may result in governmental investigations, enforcement actions, regulatory fines, litigation, or public statements against us by advocacy groups or others, and could cause third parties, including clinical sites, regulators or current and potential partners, to lose trust in us or we could be subject to claims by third parties that we have breached our privacy- or confidentiality-related obligations, which could materially and adversely affect our business and prospects. Moreover, data security incidents and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. While we have implemented security measures intended to protect our information technology systems and infrastructure, there can be no assurance that such measures will successfully prevent service interruptions or security incidents.

Business interruptions could delay our operations and sales efforts.

Our headquarters is located in the San Francisco Bay Area, near known earthquake fault zones and is vulnerable to significant damage from earthquakes. Our contract manufacturers, suppliers, clinical trial sites and local and national transportation vendors are all subject to business interruptions due to weather, outbreaks of pandemic diseases, natural disasters, or man-made incidents. We are also vulnerable to other types of natural disasters and other events that could disrupt our operations. If any of these events occurred and prevented us or third parties on which we rely from using all or a significant portion of our or their facilities, it may be difficult or, in certain cases, impossible for us to continue our business and operations for a substantial period of time.

We do not carry insurance for earthquakes or other natural disasters, and we may not carry sufficient business interruption insurance to compensate us for losses that may occur. Any losses or damages we incur could have a material adverse effect on our business operations.

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on principal members of our executive team, the loss of whose services may adversely impact the achievement of our objectives. While we have entered into offer letters with each of our executive officers, any of them could leave our employment at any time, as all of our employees are “at will” employees. Recruiting and retaining qualified scientific, manufacturing, and commercial personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. There is currently a shortage of skilled executives in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. In addition, failure to succeed in clinical trials, or delays in the regulatory approval process, may make it more challenging to recruit and retain qualified personnel. The inability to recruit or loss of the services of any executive or key employee might impede the progress of our research, development and commercialization objectives.

We may acquire companies, product candidates or products or engage in strategic transactions, which could divert our management’s attention and cause us to incur various costs and expenses.

We may acquire or invest in companies, product candidates or products that we believe could complement or expand our business or otherwise offer growth opportunities. The pursuit of potential acquisitions or investments may divert the attention of management and has caused, and in the future may cause, us to incur various costs and expenses in identifying, investigating, and pursuing them, whether or not they are consummated. We may not be able to identify desirable acquisitions or investments or be successful in completing or realizing anticipated benefits from such transactions. In addition, the acquisition of product candidates and products is a highly competitive area, and many other companies are pursuing the same or similar product candidates to those that we may consider attractive. Larger companies with more well-established and diverse revenue streams may have a competitive advantage over us due to their size, financial resources and more extensive clinical development and commercialization capabilities.

In addition, we receive inquiries relating to potential strategic transactions, including collaborations, licenses, and acquisitions. Such potential transactions may divert the attention of management and may cause us to incur various costs and expenses in investigating and evaluating such transactions, whether or not they are consummated.

We face potential product liability claims, and, if such claims are successful, we may incur substantial liability.

Our sales of DSUVIA/DZUVEO expose us to the risk of product liability claims. Product liability claims might be brought against us by patients, health care providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation;
- costs due to related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- the inability to commercialize our products; and
- decreased demand for our products.

Our current product liability insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. In addition, our current product liability insurance contains an exclusion related to any claims related to our products from a governmental body, or payer, or those claims arising from a multi-plaintiff action for bodily injury or property damage. Multi-plaintiff claims caused by product defects are covered. This exclusion does not apply to any bodily injury claim related to our products made by an individual. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated adverse effects. A successful product liability claim, or series of claims, brought against us could cause our stock price to decline and, if judgments are excluded from our insurance coverage or exceed our insurance coverage, could adversely affect our results of operations and business. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. There can be no assurance that such coverage will be adequate to protect us against any future losses due to liability.

Our employees, independent contractors, principal investigators, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk that our employees, independent contractors, investigators, consultants, commercial partners and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct that violates (1) regulations implemented by the FDA and similar foreign regulatory bodies; (2) laws requiring the reporting of true, complete and accurate information to such regulatory bodies; (3) healthcare fraud and abuse laws of the United States and similar foreign fraudulent misconduct laws; and (4) laws requiring the reporting of financial information or data accurately. The promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry are subject to extensive laws designed to prevent misconduct, including fraud, kickbacks, self-dealing and other abusive practices. These laws may restrict or prohibit a wide range of pricing, discounting, marketing, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials. It is not always possible to identify and deter employee and other third-party misconduct. The precautions we take to detect and prevent inappropriate conduct 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. If any such actions are instituted against us, and we are not successful in defending ourselves, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, imprisonment, additional oversight and reporting obligations if we become subject to a corporate integrity agreement or similar agreements to resolve allegations of non-compliance with these laws, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Risks Related to Our Intellectual Property

If we cannot defend our issued patents from third party claims or if our pending patent applications fail to issue, our business could be adversely affected.

To protect our proprietary technology, we rely on patents as well as other intellectual property protections including trade secrets, nondisclosure agreements, and confidentiality provisions. As of December 31, 2022, we are the owner of record of 94 issued patents worldwide drawn to AcelRx's sufentanil sublingual tablets and related medication delivery devices. These issued patents include 18 patents that we have listed in the FDA's Orange Book for DSUVIA, some of which have expiration dates that extend into 2031. These issued patents also include a European patent drawn to the DZUVEO device that has an expiration date that extends into 2036.

Because sufentanil is not a new chemical entity, potential regulatory (data) exclusivity periods for new formulation, dosage form and/or dosage strength sufentanil products in the United States is limited to three years under the Hatch-Waxman Act. While the FDA was not able to approve a 505(b)(2) NDA or an abbreviated new drug application, or ANDA, using DSUVIA as its reference listed drug prior to November 2, 2021, we may now be subject to a third party's Paragraph IV or other patent certification based on the patents we have listed in the FDA's Orange Book for DSUVIA and engage in litigation against such a 505(b)(2) or ANDA applicant at any time.

In addition, we are pursuing a number of U.S. patent applications and foreign national applications directed to DSUVIA, Niyad, and LTX-608. The patent applications that we have filed and have not yet been granted may fail to result in issued patents in the United States or in foreign countries. Even if the patents do successfully issue, third parties may challenge the patents. We have entered into the DSUVIA Agreement with Alora pursuant to which Alora, upon closing, will acquire all patents and trademarks related to DSUVIA and DZUVEO. At or prior to the closing of the DSUVIA Agreement, we and Alora will enter into an intellectual property agreement pursuant to which Alora will grant fully-paid, royalty-free and perpetual licenses to us under certain specified intellectual property rights acquired by Alora under the DSUVIA Agreement for, among other things, the development, manufacture, commercialization and exploitation of certain products, including Zalviso.

As we continue to develop our product candidates Fedsyra, phenylephrine, Niyad and LTX-608, we generally expect to pursue 505(b)(2) NDA application pathways with the exception of the first LTX-608 application which we expect to be treated as a new chemical entity. As a result of these filing avenues, we will need to include patent certifications regarding the reference listed drugs that our 505(b)(2) applications are based upon. These patent certifications could trigger patent litigation by the patent holders that we have certified against.

Our commercial success will depend in part on successfully defending our current patents against third party challenges and expanding our existing patent portfolio to provide additional layers of patent protection, as well as extending patent protection. There can be no assurance that we will be successful in defending our existing and future patents against third party challenges, or that our pending patent applications will result in additional issued patents.

The patent positions of pharmaceutical companies, including ours, can be highly uncertain and involve complex and evolving legal and factual questions. No consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the United States. Legal developments may preclude or limit the scope of available patent protection.

There is also no assurance that any patents issued to us will not become the subject of adversarial or post-issuance proceedings such as opposition, *inter partes* review, post-grant review, *ex parte* re-examination or other post-issuance proceedings. In addition, there is no assurance that the relevant patent office court or agency in such adversarial proceedings would not make unfavorable decisions, such as reducing the scope of a patent of ours, invalidating issued claims or determining that a patent of ours is invalid or unenforceable. There is also no assurance that any patents issued to us will provide us with competitive advantages, will not be challenged by any third parties, or that the patents of others will not prevent the commercialization of products incorporating our technology. Furthermore, there can be no guarantee that others will not independently develop similar products, duplicate any of our products, or design around our patents.

Litigation involving patents, patent applications and other proprietary rights is expensive and time consuming. If we are involved in such litigation, it could cause delays in bringing our products to market and interfere with our business.

Our commercial success depends in part on our not infringing patents or misappropriating trademarks or other third-party intellectual property rights. Although we are not currently aware of litigation or other proceedings or third-party claims of intellectual property infringement or misappropriation related to DSUVIA or our product candidates, the pharmaceutical industry is especially prone to extensive litigation proceedings between competitors regarding their patents and other intellectual property rights.

As we enter our target markets, it is possible that competitors or other third parties will claim that our products and/or processes infringe or misappropriate their intellectual property rights. These third parties may have obtained and may in the future obtain patents covering products or processes that are similar to our products, or may include composition or method claims that encompass our technology, allowing them to assert that our continued use of our own technologies infringes such newly emerging patent rights.

In the event that a patent infringement claim is asserted against us, we may counter, as an affirmative defense, that we do not infringe the relevant patent claims, that the patent is invalid or otherwise unenforceable or any combination thereof. The strength of our defenses will depend on the patents asserted, the interpretation of those patents, and our ability to establish the invalidity of the asserted patents. However, we could be unsuccessful in advancing non-infringement, invalidity or unenforceability arguments in our defense. In the United States, issued patents enjoy a presumption of validity, and the party challenging the validity of a patent claim must present clear and convincing evidence of invalidity, which is a high burden of proof. Conversely, the patent owner need only prove infringement by a preponderance of the evidence, which is a lower burden of proof.

If a court in a final and non-appealable decision were to hold that we have infringed someone else's valid patent claim, we could be prevented from using that third-party patented technology and may also be required to pay the owner of the patent for damages for past sales and need to seek license access to the patented technology for future sales. If we decide to pursue such a license to one or more of these patents, we may not be able to obtain a license on commercially reasonable terms, if at all, or the license we obtain may require us to pay substantial royalties or grant cross licenses to our patent rights. For example, if the relevant patent is owned by a competitor, that competitor may choose not to license patent rights to us. If we decide to develop alternative technology to avoid the third-party patent claims, we may not be able to do so in a timely or cost-effective manner, if at all.

In addition, because patent applications remain unpublished for 18 months from their initial filing date and some applications may be afforded confidentiality during prosecution that can take years to issue, there may currently be pending applications that are unknown to us and that may later result in issued patents that could cover one or more of our products.

It is possible that we may in the future receive communications from competitors and other companies alleging that we may be infringing their patents, misappropriating their trade secrets or otherwise violating their intellectual property rights, where they may offer license access to such intellectual property or threaten litigation. In addition to patent infringement claims, third parties may assert copyright, trademark or other intellectual property rights against us. We may need to expend considerable resources to counter such claims and may not be successful in our defense. Our business may suffer if a finding of infringement or misappropriation is established.

It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection.

The patent positions of pharmaceutical companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the United States. The pharmaceutical patent situation outside the United States is just as uncertain. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property estate.

We cannot predict the breadth of claims that may be allowed or enforced in the patents that may issue from the applications that we currently have pending, or may in the future file ourselves or acquire or license from third parties. Claims could be brought regarding the validity of our patents by third parties. Further, if any patent right that we obtain is deemed invalid and/or unenforceable, it could impact our ability to commercialize or partner our technology.

Competitors or third parties may infringe our patents. We may decide it is necessary to assert patent infringement claims against such entities, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours is not valid or is unenforceable, or that the third party's technology does not in fact infringe upon our patents. An adverse determination of any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our related pending patent applications at risk of not issuing. Litigation may fail and, even if successful, may result in substantial costs and be a distraction to our management. We may not be able to prevent misappropriation of our intellectual property rights, particularly in countries outside the United States where national laws and court systems are less robust, making patent rights more difficult to enforce, and very expensive to pursue. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential or sensitive information could be compromised by disclosure in the event of litigation. In addition, during the course of litigation there could 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 substantial adverse effect on the price of our common stock.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- we were the first to make the inventions covered by each of our pending patent applications or issued patents;
- our patent applications were filed before the inventions covered by each patent or patent application was published by a third-party;
- we were the first to file patent applications for these inventions;
- others will not independently develop similar or alternative technologies or duplicate any of our technologies;
- any patents issued to us or our collaborators will provide a basis for commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties; or
- the patents of others will not have an adverse effect on our business.

If we do not adequately protect our intellectual property rights, competitors may be able to use our technologies and erode or negate any competitive advantage we may have, which could materially harm our business, negatively affect our position in the marketplace, limit our or our current or potential partners' ability to commercialize DSUVIA/DZUVEO or any of our Fedsyra, phenylephrine, Niyad or LTX-608 product opportunities, if approved, and delay or render impossible our achievement of profitability.

We may be unable to adequately prevent disclosure of trade secrets and other proprietary information.

We rely on trade secrets to protect our proprietary know-how and technological advances, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our business partners, employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to protect our trade secrets and other proprietary information. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information without misappropriating our rights. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights. Failure to obtain or maintain trade secret protection could enable competitors to use our proprietary information to develop products that compete with our products or cause additional, material adverse effects upon our competitive business position.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and applications will be due to be paid to the United States Patent and Trademark Office and various foreign governmental patent agencies in several stages over the lifetime of the patents and/or applications.

We have systems in place, including use of third-party vendors, to manage payment of periodic maintenance fees, renewal fees, annuity fees and various other patent and application fees. The United States Patent and Trademark Office, or the USPTO, and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. There are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If this occurs, our competitors might be able to enter the market, which would have a material adverse effect on our business.

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

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to life sciences. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit.

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. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate. Additionally, claims may be brought regarding the validity of our patents by third parties in the United States and foreign countries. In addition, changes in the law and legal decisions by courts in the United States and foreign countries may affect our ability to obtain adequate protection for our technology and the enforcement of our intellectual property rights.

We have not yet registered our trademarks in all our potential markets, and failure to secure those registrations could adversely affect our business.

We have registered our ACELRX mark in the United States, Canada, the EU and India, and have registered our DSUVIA and DZUVIO marks in the United States and in Europe, respectively. Although we are not currently aware of any oppositions to or cancellations of our registered trademarks or pending applications, it is possible that one or more of the applications could be subject to opposition or cancellation after the marks are registered. The registrations will be subject to use and maintenance requirements. It is also possible that we have not yet registered all of our trademarks in all of our potential markets, such as securing the registration of DSUVIA in Canada, and that there are names or symbols other than "ACELRX" that may be protectable marks for which we have not sought registration, and failure to secure those registrations could adversely affect our business. Opposition or cancellation proceedings may be filed against our trademarks and our trademarks may not survive such proceedings. We have entered into the DSUVIA Agreement with Alora pursuant to which Alora, upon closing, will acquire all patents and trademarks related to DSUVIA and DZUVEO.

Risks Related to Ownership of Our Common Stock

The market price of our common stock has historically been and may continue to be highly volatile.

The trading price of our common stock has experienced significant volatility and is likely to be volatile in the future. For example, the closing price of our common stock ranged between $1.78 and $12.10 during the year ended December 31, 2022, and between $9.81 and $55.40 during the year ended December 31, 2021. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- failure to receive payments for the sale by Alora of DSUVIA in the United States, upon closing of the DSUVIA Agreement, or to successfully develop and commercialize our product candidates in the United States;
- inability to obtain additional funding needed to conduct our planned business operations;
- the integration and performance of any assets or businesses we acquire;
- our inability to develop and commercialize products and product candidates that we in-license;
- uncertainties regarding the magnitude and duration of impacts we are experiencing due to COVID-19;
- the perception of limited market sizes or pricing for our products;
- safety issues;
- adverse results or delays in future clinical trials;
- changes in laws or regulations applicable to our products;
- inability to obtain adequate product supply for our products, or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- changes in the structure of the healthcare payment systems;
- inability to maintain regulatory approval for DSUVIA in the U.S. and/or DZUVEO in the European Union, prior to closing of the DSUVIA Agreement;
- introduction of new products, services or technologies by our competitors;
- failure to meet or exceed financial projections we provide to the public;
- failure to meet or exceed the estimates and projections of the investment community;
- decisions by our collaboration partners regarding market access, pricing, and commercialization efforts in countries where they have the right to commercialize our products;
- failure to maintain our existing collaborations or enter into new collaborations;
- the perception of the pharmaceutical industry generally, and of opioid manufacturers more specifically, by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures, or other significant transactions, including disposition transactions, or capital commitments by us or our competitors;
- disputes or other developments relating to employment matters, business development efforts, proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;

- additions or departures of key management or scientific personnel;
- costs associated with potential governmental investigations, inquiries, regulatory actions or lawsuits that may be brought against us as a result of us being an opioid manufacturer;
- other types of significant lawsuits, including patent, stockholder, securities class action and derivative litigation;
- changes in the market valuations of similar companies;
- sales of our common stock by us or our stockholders in the future;
- our ability to maintain compliance with Nasdaq listing requirements;
- liquidity of our common stock; and
- trading volume of our common stock.

In addition, the stock market in general, and The Nasdaq Global Market, or Nasdaq, in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

Sales of a substantial number of shares of our common stock in the public market by us or our stockholders could cause our stock price to fall.

Because we will continue to need additional capital in the future to continue to expand our business and our research and development activities, among other things, we may conduct additional equity offerings. For example, under the universal shelf registration statement filed by us in June 2020 and declared effective by the SEC in July 2020, we may offer and sell any combination of common stock, preferred stock, debt securities and warrants in one or more offerings, up to a cumulative value of $150 million. To date, we have approximately $33.0 million remaining under such universal shelf registration statement. Sales of a substantial number of shares of our common stock in the public market 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. Our management is authorized to grant stock options and other equity-based awards to our employees, directors and consultants under our equity incentive plans. Grants under our equity incentive plans may also cause our stockholders to experience additional dilution, which could cause our stock price to fall. In May 2022 we filed a resale registration statement to permit the former stockholders of Lowell to sell the shares of common stock we issued such stockholders in exchange for their shares of Lowell capital stock. In addition, in November 2022 we filed a resale registration statement to permit Lincoln Park Capital Fund, LLC to sell the shares of common stock that are issuable upon conversion of the Series A Redeemable Convertible Preferred Stock and that are issuable upon exercise of the warrant, which were issued in a private placement transaction in August 2022. We may in the future issue additional shares of our common stock as consideration in mergers, acquisitions and other business development transactions. We are unable to predict the effect that sales may have on the prevailing market price of our common stock. All of our shares of common stock outstanding are eligible for sale in the public market, subject in some cases to the volume limitations and manner of sale requirements of Rule 144 under the Securities Act. Sales of stock by our stockholders could have a material adverse effect on the trading price of our common stock.

Our reverse stock split may not be successful.

At our Special Meeting of stockholders held on September 23, 2022, our stockholders approved a 1-for-20 reverse stock split of our common stock which was effective as of October 25, 2022 at 5:01 p.m. Eastern Time. There are risks associated with the reverse stock split and there is no assurance that:

- The market price per share of the common stock after the reverse stock split will rise in proportion to the reduction in the number of shares of the common stock outstanding before the reverse stock split or if it does rise that it will sustain the increase in the share price;
- the reverse stock split will result in a per share price that will attract brokers and investors who do not trade in lower priced stocks;
- the reverse stock split will result in a per share price that will increase our ability to attract and retain employees and other service providers; and
- the liquidity of the common stock will increase.

In order to maintain our listing on Nasdaq, we are required to comply with the Nasdaq requirements. Although we have completed our reverse stock split, there can be no assurance that we will continue to meet these listing requirements.

We have identified a material weakness in our internal control over financial reporting. This material weakness could continue to adversely affect our results of operations and financial condition. In the future, we may identify additional material weaknesses or otherwise fail to maintain an effective system of internal control over financial reporting or adequate disclosure controls and procedures, which may result in material errors in our financial statements or cause us to fail to meet our period reporting obligations.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, evaluating the effectiveness of our internal controls and disclosing any changes or material weaknesses identified through such evaluation. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis.

During the preparation of our consolidated financial statements for the year ended December 31, 2022, we identified an error within our earnings per share calculation for the three and six months ended June 30, 2022, and the nine months ended September 30, 2022, whereby we did not properly apply the two-class method of calculating earnings per share with respect to the warrants issued in November 2021. Our management subsequently concluded that a material weakness existed and our internal control over financial reporting was not effective as of June 30, 2022.

As a result, we determined that there were material errors in the financial statements that required a restatement of the unaudited condensed consolidated financial statements included in our Forms 10-Q for the quarterly periods ended June 30, 2022 and September 30, 2022. This was due to the inadequate design and implementation of controls related to the technical accounting review and analysis over earnings per share calculations which were insufficient to prevent or detect errors in the calculation. Specifically, the error was due to management's failure to identify warrants issued in November 2021 as participating securities and consequently attribute earnings to these securities as part of a two-class EPS calculation.

Management has implemented enhanced internal controls to remediate the material weakness. Specifically, we enhanced our processes to identify and appropriately apply applicable accounting requirements related to the earnings per share calculation to better evaluate and understand the nuances of the complex accounting standards that apply to our financial statements. We plan to continue to provide access to accounting literature, research materials and documents, enhance the review and analysis process around the earnings per share calculation and increase communications among our personnel and third-party professionals with whom we consult regarding complex accounting applications. The elements of our remediation plan can only be accomplished over time, and we can offer no assurance that these initiatives will ultimately have the intended effects.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. 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. If we are not able to comply with the requirements of the Sarbanes-Oxley Act or if we are unable to maintain effective internal control over financial reporting, we may not be able to produce timely and accurate financial statements or guarantee that information required to be disclosed by us in the reports that we file with the SEC, is recorded, processed, summarized, and reported within the time periods specified in SEC rules and forms. Any failure of our internal control over financial reporting or disclosure controls and procedures could cause our investors to lose confidence in our publicly reported information, cause the market price of our stock to decline, expose us to sanctions or investigations by the SEC or other regulatory authorities, or impact our results of operations.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We have never declared or paid any cash dividends on our capital stock, and we are prohibited from doing so under the terms of the Loan Agreement. Regardless of the restrictions in the Loan Agreement or the terms of any potential future indebtedness, we anticipate that we will retain all available funds and any future earnings to support our operations and finance the growth and development of our business and, therefore, we do not expect to pay cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our Board of Directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our Board of Directors may deem relevant.

Provisions in our amended and restated certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders or remove our current management.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders and may prevent attempts by our stockholders to replace or remove our current management. These provisions include:

- authorizing the issuance of "blank check" preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- limiting the removal of directors by the stockholders;
- a staggered Board of Directors;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders; and
- establishing advance notice requirements for nominations for election to our Board of Directors or for proposing matters that can be acted upon at stockholder meetings.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our Board of Directors, which is responsible for appointing the members of our management. In addition, we are subject to Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with an interested stockholder for a period of three years following the date on which the stockholder became an interested stockholder, unless such transactions are approved by our Board of Directors. This provision could have the effect of delaying or preventing a change of control, whether or not it is desired by or beneficial to our stockholders. Further, other provisions of Delaware law may also discourage, delay or prevent someone from acquiring us or merging with us.

Risks of a General Nature

Litigation may substantially increase our costs and harm our business.

We have been, are, and may in the future become, party to lawsuits including, without limitation, actions and proceedings in the ordinary course of business relating to our directors, officers, stockholders, intellectual property rights, employment matters and the safety or efficacy of our products, which will cause us to incur legal fees and other costs related thereto, including potential expenses for the reimbursement of legal fees of officers and directors under indemnification obligations. The expense of defending against such litigation may be significant and there can be no assurance that we will be successful in any defense. Further, the amount of time that may be required to resolve such lawsuits is unpredictable, and these actions may divert management's attention from the day-to-day operations of our business, which could adversely affect our business, results of operations, and cash flows. Our insurance carriers may deny coverage, may be inadequately capitalized to pay on valid claims, or our policy limits may be inadequate to fully satisfy any damage awards or settlements. If this were to happen, the payment of any such awards could have a material adverse effect on our consolidated operations, cash flows and financial position. Additionally, any such claims, whether or not successful, could damage our reputation and business. Litigation is subject to inherent uncertainties, and an adverse result in such matters that may arise from time to time could have a material adverse effect on our business, results of operations, and financial condition. Please see Note 13 to the consolidated financial statements in this Annual Report on Form 10-K for additional information about pending legal proceedings.

Our involvement in securities-related class action litigation could divert our resources and management's attention and harm our business.

The stock markets have from time-to-time experienced significant price and volume fluctuations that have affected the market prices for the common stock of pharmaceutical companies. These broad market fluctuations may cause the market price of our common stock to decline. In addition, the market price of our common stock may vary significantly based on AcelRx-specific events, such as receipt of Complete Response Letters, Warnings Letters, such as the Warning Letter we received from the FDA on February 11, 2021, negative clinical results, a negative vote or decision by an FDA advisory committee, or other negative feedback from the FDA, EMA, or other regulatory agencies. In the past, securities-related class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and biopharmaceutical companies often experience significant stock price volatility in connection with their investigational drug candidate development programs and the FDA's review of their NDAs. Following receipt of the FDA's Warning Letter, a securities class action complaint was filed against us and two of our officers on June 8, 2021 in the United States District Court for the Northern District of California. The amended securities class action complaint, which was filed on March 7, 2022, named a third officer as a defendant. On September 28, 2022, the Court issued a formal written opinion, or the Opinion, dismissing all of the plaintiff's claims against the Company and the named defendants. On November 28, 2022 the plaintiffs filed their second amended complaint, and on January 30, 2023 the Company filed its new motion to dismiss the complaint. Plaintiffs must file their opposition to our new motion to dismiss by or on March 16, 2023. On July 6, 2021, September 30, 2021, October 26, 2021 and November 17, 2021, four purported shareholder derivative complaints were filed in the United States District Court for the Northern District of California asserting state and federal claims based on the same alleged misstatements as the securities class action complaint. On December 6, 2021, the Court entered an order consolidating all four actions and staying the consolidated action pending the outcome of any motion to dismiss the securities class action. Please refer to Note 13 to the consolidated financial statements in this Annual Report on Form 10-K for additional information about these pending legal proceedings. Securities-related class action litigation often is expensive and diverts management's attention and our financial resources, which could harm our business. Additional lawsuits related to the pending litigation may follow. Moreover, if AcelRx experiences a decline in its stock price, we could face additional securities class action lawsuits.

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

As of December 31, 2022, we had federal net operating loss carryforwards of $346.4 million, of which $114.9 million federal net operating losses generated before January 1, 2018 will begin to expire in 2029. $231.5 million of such federal net operating losses were generated after December 31, 2017. As of December 31, 2022, we had state net operating loss carryforwards of $167.9 million, which begin to expire in 2028. Under current law, federal net operating losses generated in tax years beginning prior to January 1, 2018 generally will expire 20 years after they were generated if not used prior thereto; federal net operating losses generated in tax years beginning after December 31, 2017 will carryforward indefinitely, but the deductibility of such federal net operating losses generally is limited to 80% of current year taxable income. Many states have similar laws. Our ability to use our federal and state net operating losses to offset potential future taxable income and related income taxes that would otherwise be due is dependent upon our generation of future taxable income before the expiration dates of the net operating losses, and we cannot predict with certainty when, or whether, we will generate sufficient taxable income to use all of our net operating losses. Accordingly, our federal and state net operating losses could expire unused and be unavailable to offset future income tax liabilities. In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. The completion of the July 2013 public equity offering, together with our public equity offering in December 2012, our initial public offering, private placements and other transactions that have occurred, have triggered such an ownership change. We may experience additional ownership changes as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. Furthermore, our ability to utilize net operating losses of companies that we have acquired or may acquire in the future may be subject to limitations. In the future, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards or other tax attributes to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us and could adversely affect our business, results of operations, and cash flows.

Our effective tax rate may fluctuate, we may be adversely affected by changes in tax laws and regulations, and we may incur obligations in tax jurisdictions in excess of accrued amounts.

We are subject to taxation in numerous U.S. federal, state, and local jurisdictions. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various jurisdictions that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each jurisdiction. Nevertheless, our effective tax rate may be different than experienced in the past due to numerous factors, including changes in the mix of our profitability among the jurisdiction in which we operate, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and enactment of new tax laws. or changes in the interpretation and application of existing tax laws. New income, sales, use or other tax laws, rules, regulations, or ordinances could be enacted at any time. For example, recent legislation commonly referred to as the Inflation Reduction Act imposes a one percent excise tax on share buybacks imposed on the corporation repurchasing such stock, effective for tax years beginning after December 31, 2022. Also, effective for tax years beginning after December 31, 2021, the Tax Act eliminated the option to currently deduct research and development expenditures in the year incurred, and instead requires taxpayers to capitalize and amortize U.S.-based and non-U.S.-based research and development expenditures over five and fifteen years, respectively. Although there has been proposed legislation that would defer the capitalization requirement to later years, we have no assurance that the provision will be repealed, deferred, or otherwise modified. Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations and may result in tax obligations in excess of amounts accrued in our financial statements.

Macroeconomic uncertainties, including inflationary pressures, supply chain disruptions, labor shortages, significant volatility in global markets, recession risks, and the COVID-19 pandemic have in the past and may continue to adversely affect our business, future results of operations, and financial condition, the effects of which remain uncertain.

Global economic and business activities continue to face widespread macroeconomic uncertainties, including inflation, supply chain disruptions, labor shortages, as well as recession risks, which may continue for an extended period. In addition, the mitigation measures we have taken in responses to the COVID-19 pandemic have represented a significant disruption in how we operate our business, including a loss of productivity. The operations of our partners, suppliers, and other third parties with whom we have a business relationship have likewise been disrupted. While our offices are now reopened, many of our employees who were hired remotely during the pandemic continue to work remotely and others are working on a hybrid basis. We do not currently have visibility on whether we may return to normal operations of having everyone work in office on a full-time basis. Our efforts to keep our offices open safely may not be successful and could expose our employees to health risks. If there are further waves or variants of the virus, we may need to further modify our business practices in a manner that may impact our business. If our employees are not able to perform their job duties due to illness or are unable to perform them as efficiently at home for an extended period of time, we may not be able to deliver on our business priorities, and we may experience an overall lower productivity of our workforce.

The COVID-19 pandemic has already had an adverse effect on the global economy and our business. Actual and potential impacts include:

- the ability of our employees to travel has been limited and we have altered, postponed, or canceled planned industry events or shifted them to a virtual only format, and we may continue to do so;
- overall lower productivity of our workforce;
- extreme volatility in financial and other capital markets as a result of concerns over the economic impact of the COVID-19 pandemic, which have in the past and may in the future adversely affect our stock price and our ability to access capital markets.

We continue to monitor the impact of the COVID-19 pandemic and there may be additional costs or impacts to our business and operations, including in connection with returning to our offices, if we return to normal operations of having everyone work in office on a full-time basis. In addition, there is no guarantee that a future outbreak of this or any other widespread epidemics will not occur, or that the global economy will recover, either of which could seriously harm our business. The potential long-term impact of the COVID-19 pandemic or a similar health epidemic on our business, operations, or the global economy as a whole remains uncertain. Accordingly, it remains difficult for us to predict the duration and extent to which this will affect our business, future results of operations, and financial condition at this time.

To the extent that macroeconomic uncertainties and the COVID-19 pandemic continue to harm our business, many of the other risks described in these risk factors may be exacerbated.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We lease approximately 13,322 square feet of office space in Hayward, California under a sublease agreement that expires on January 30, 2023. We believe that our facilities are adequate to meet our current needs.

Item 3. Legal Proceedings

From time to time we may be involved in legal proceedings relating to intellectual property, commercial, employment and other matters arising in the ordinary course of business. Such matters are subject to uncertainty and there can be no assurance that such legal proceedings will not have a material adverse effect on our business, results of operations, financial position or cash flows. Please see the matters under the caption "Part II.—Item 8. Financial Statements and Supplementary Data—Note 13, Commitments and Contingencies—Litigation."

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 has been traded on The Nasdaq Global Market since February 11, 2011 under the symbol "ACRX". As of March 20, 2023, there were 31 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.

Reverse Stock Split

Effective as of 5:01 p.m. Eastern Time on October 25, 2022 (the "Effective Time"), we amended our charter to effect a reverse stock split at a ratio of 1-for-20. No fractional shares were issued in connection with the reverse stock split. Stockholders of record otherwise entitled to receive fractional shares of common stock received cash (without interest or deduction) in lieu of such fractional share interests.

The reverse stock split reduced the total number of shares of our common stock outstanding as of the Effective Time from approximately 148.1 million shares to approximately 7.4 million shares. The par value per share and other terms of our common stock were not affected by the reverse stock split, and the number of authorized shares of the Company's common stock remains at 200,000,000.

The reverse stock split was accounted for retroactively and is reflected in our common stock, stock option, restricted stock unit and warrant activity as of and during the years ended December 31, 2022 and 2021. Unless stated otherwise, all share data in this Annual Report on Form 10-K have been adjusted, as appropriate, to reflect the reverse stock split.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock, and we are prohibited from doing so under the terms of our Loan Agreement. Regardless of the restrictions in our Loan Agreement or the terms of any potential future indebtedness, we anticipate that we will retain all available funds and any future earnings to support our operations and finance the growth and development of our business and, therefore, we do not expect to pay cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our Board of Directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our Board of Directors may deem relevant.

Recent Sales of Unregistered Securities

None.

Item 6. Reserved

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

The following discussion and analysis should be read in conjunction with our audited financial statements and the related notes that appear elsewhere in this Annual Report on Form 10-K.

This discussion and analysis generally covers our financial condition and results of operations for the year ended December 31, 2022, including year-over-year comparisons versus the year ended December 31, 2021. Our Annual Report on Form 10-K for the year ended December 31, 2021 includes a discussion and analysis of our financial condition and results of operations for the year ended December 31, 2020 in Item 7 of Part II, "Management's Discussion and Analysis of Financial Condition and Results of Operations." This discussion and other parts of this Annual Report on Form 10-K contain forward-looking statements that involve risks and uncertainties, such as statements regarding our plans, objectives, expectations, intentions, and projections. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in "Part I, Item 1A – Risk Factors" of this Annual Report on Form 10-K.

Overview

We are a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for use in medically supervised settings. Our portfolio consists of nafamostat product candidates and pre-filled syringe product candidates, as further described in "Item 1. Business." We have signed an agreement with Alora to divest our sufentanil sublingual products (DSUVIA and DZUVEO) with the right to receive sales-based milestone and other payments, which we expect to close in April 2023. We do not have plans to further develop any sufentanil sublingual product candidates.

On January 7, 2022, we acquired Lowell Therapeutics, Inc., or Lowell, a privately held company, pursuant to the Agreement and Plan of Merger, dated as of November 14, 2021, or the Merger Agreement, in a transaction for consideration of approximately $32.5 million plus net cash acquired and certain other adjustments, and which includes up to approximately $26.0 million of contingent consideration payable in cash or stock at AcelRx's option, upon the achievement of regulatory and sales-based milestones, or the Merger Agreement. In connection with the Merger Agreement we acquired Niyad and LTX-608 (lyophilized vials of nafamostat for injection into the extracorporeal circuit or direct IV infusion to the patient, respectively), an in-process research and development, or IPR&D, asset. For additional information regarding the Merger Agreement, see Note 4, "Asset Acquisition" to the consolidated financial statements in this Annual Report on Form 10-K for additional information.

On July 14, 2021, we entered into a License and Commercialization Agreement, or the PFS Agreement, with Laboratoire Aguettant, or Aguettant, pursuant to which we obtained the exclusive right to develop and, subject to FDA approval, commercialize in the United States (i) an ephedrine pre-filled syringe containing 10 ml of a solution of 3 mg/ml ephedrine hydrochloride for injection and (ii) a phenylephrine pre-filled syringe containing 10 ml of a solution of 50 mcg/ml phenylephrine hydrochloride for injection. Aguettant will supply us with the products for use in commercialization and, if they are approved in the U.S., Aguettant is entitled to receive up to $24 million in sales-based milestone payments. In connection with our and Aguettant's agreement to enter into the Amended DZUVEO Agreement (as defined below) and the Amended and Restated Supply Agreement (as defined below), we will enter into an amendment to the PFS Agreement with Aguettant pursuant to which, effective on the later of the closing of the transaction contemplated under the DSUVIA Agreement (as defined below) and April 1, 2023, (a) Aguettant will pay us a complementary payment in the amount of €1.5 million, and (b) the maximum amount in sales-based milestone payments that Aguettant is entitled to receive will reduce to $21 million.

On July 14, 2021, we also entered into a License and Commercialization Agreement, or the DZUVEO Agreement, with Aguettant pursuant to which Aguettant obtained the exclusive right to develop and commercialize DZUVEO in the European Union, Norway, Iceland, Liechtenstein, Andorra, Vatican City, Monaco, Switzerland and the United Kingdom, or the DZUVEO Territory, for the management of acute moderate to severe pain in adults in medically monitored settings. We supply Aguettant with primary packaged product and Aguettant then completes secondary packaging of the finished product. Pursuant to the DSUVIA Agreement (as defined below), as a condition of the transaction contemplated thereunder, we and Aguettant will enter into an amendment to the DZUVEO Agreement, or the Amended DZUVEO Agreement, and an amendment and restatement to the supply agreement with respect to the manufacture and supply of DZUVEO, or the Amended and Restated Supply Agreement, in each case, in a form reasonably acceptable to Alora. The rights and obligations under the Amended DZUVEO Agreement and the Amended and Restated Supply Agreement will be assumed by Alora, as part of the DSUVIA asset divestment agreement. We received €2.5 million, or approximately $2.9 million, in 2021 under the DZUVEO Agreement. Refer to Note 6, "In-License Agreement", Note 7, "Out-License Agreements—DZUVEO" and Note 20, "Subsequent Events" to the consolidated financial statements in this Annual Report on Form 10-K for additional information.

On March 12, 2023, we entered into an asset purchase agreement, or the DSUVIA Agreement, with Alora pursuant to which Alora will acquire certain assets and assume certain liabilities relating to DSUVIA or DZUVEO, or any other single-dose pharmaceutical product for use in medically supervised settings containing a sublingual tablet that includes sufentanil as the sole active ingredient, as a 30 mcg tablet or other dosage form or strength as reasonably necessary for lifecycle management, or the Product. The Product expressly excludes Zalviso, any other multi-dose administration system containing sufentanil sublingual tablets (whether as the sole active ingredient or in combination with other active ingredients), and any single-dose formulation of sufentanil for use outside of a medically supervised setting. Subject to closing of the transaction contemplated under the DSUVIA Agreement, we will be entitled to receive quarterly payments in an amount equal to 15% of net Product sales to all customers excluding net sales to the Department of Defense and sales by or on behalf of Aguettant, and quarterly payments in an amount equal to 75% of net Product sales to the Department of Defense. Subject to closing of the transaction contemplated under the DSUVIA Agreement, we will also be entitled to receive sales milestones up to $116.5 million based on the achievement of Alora attaining certain levels of annual sales and 20% of any consideration, other than royalty payments, received by Alora and its affiliates in connection with a grant to any third party of a license related to any Product, or by Alora and its affiliates and equityholders in connection with a sale or transfer to any third party of an ownership interest in any assets acquired by Alora under the DSUVIA Agreement. We expect the transaction to close in April 2023 and we expect to support the transition to Alora under a Transition Services Agreement signed at or prior to the closing of the transaction contemplated under the DSUVIA Agreement. In addition, at or prior to the closing, we and Alora will enter into an intellectual property agreement pursuant to which Alora will grant fully-paid, royalty-free and perpetual licenses to us under certain specified intellectual property rights acquired by Alora under the DSUVIA Agreement for, among other things, the development, manufacture, commercialization and exploitation of certain products, including Zalviso. Refer to Note 20, "Subsequent Events" in the accompanying notes to the consolidated financial statements for additional information.

Our strategy is focused on developing, obtaining approval, and commercializing our product candidates, Niyad and the pre-filled syringes. Accordingly, we plan to divest DSUVIA to Alora in April 2023, who will continue to commercialize the product and pay us sales-based milestone and other payments. We believe this will maximize the value of DSUVIA as Alora has more available resources to invest on DSUVIA commercialization and as a result can execute a more robust commercial plan to support DSUVIA sales expansion, while we further reduce our operating costs. We have no plans on further developing or commercializing any of our other sufentanil sublingual products that were previously our product candidates. We are focused on achieving an Emergency Use Authorization, or EUA, for Niyad in 2023, and if successful, we expect to begin commercialization, while also initiating the clinical study for full regulatory approval.

On October 25, 2022, we filed a certificate of amendment to our amended and restated certificate of incorporation to effect a 1-for-20 reverse stock split of our outstanding common stock, effective as of 5:01 p.m. Eastern Time on October 25, 2022, or the Reverse Stock Split. Unless expressly stated herein, all share amounts of our common stock presented in this Annual Report have been adjusted to reflect the Reverse Stock Split. See Note 1 to the consolidated financial statements in this Annual Report on Form 10-K for additional information.

Product Development Programs

Our product development portfolio features Niyad (a regional anticoagulant for the dialysis circuit), two innovative therapies for the treatment of acute pain, two ready-to-use pre-filled syringe product candidates (Fedsyra and phenylephrine), and LTX-608 (a proprietary nafamostat formulation for direct IV infusion for disseminated intravascular coagulation, or DIC, for acute respiratory distress syndrome, or ARDS, as an anti-viral treatment for COVID-19, and for acute pancreatitis). Please refer to “Part I. Item 1. Business—Our Portfolio” for a detailed discussion of our approved products and product candidates.

General Trends and Outlook

COVID-19-related

Government-mandated orders and related safety policies on account of the COVID-19 pandemic have prevented us from operating our business in the normal course. We continue to adhere to the various and diverse orders issued by government officials in the jurisdictions in which we operate. In addition, some hospitals, ambulatory surgery centers and other healthcare facilities have barred visitors that are not caregivers or mission-critical and otherwise restricted access to such facilities. As a result, the educational and promotional efforts of our commercial and medical affairs personnel have been substantially reduced, and in some cases, stopped. Cancellation or delays of formulary committee meetings and delays of elective surgeries have also affected the pace of formulary approvals and, consequently, the rate of adoption and use of DSUVIA.

As a result of COVID-19 and related international travel restrictions, in addition to the testing requirements of our vendor, the timing for testing and acceptance of the installed DSUVIA automated packaging line, and subsequent FDA approval, was delayed. Refer to Note 20, “Subsequent Events” to the consolidated financial statements in this Annual Report on Form 10-K for additional information.

We will continue to engage with various elements of our supply chain and distribution channel, including our customers, contract manufacturers, and logistics and transportation providers, to meet demand for products and to remain informed of any challenges within our supply chain. We continue to monitor demand and intend to adapt our plans as needed to continue to drive our business and meet our obligations during the evolving COVID-19 pandemic. However, if the COVID-19 pandemic continues and persists for an extended period of time, we may face disruptions to our supply chain and operations, and associated delays in the manufacturing and supply of our products. Such supply disruptions may adversely impact our ability to generate sales of and revenues from our products and our business, financial condition, results of operations and growth prospects could be adversely affected.

As the global pandemic of COVID-19 continues to rapidly evolve, it could result in a significant long-term disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. The extent to which the COVID-19 pandemic continues to impact our business, our ability to generate sales of and revenues from our approved products, and our future clinical development and regulatory efforts will depend on future developments that are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the outbreak, travel restrictions, quarantines and social distancing requirements in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the virus.

Inflation

We do not believe that inflation has had a material impact on our business or operating results during the periods presented. However, inflation, led by supply chain constraints, federal stimulus funding, increases to household savings, and the sudden macroeconomic shift in activity levels arising from the loosening or removal of many government restrictions and the broader availability of COVID-19 vaccines, has had, and may continue to have, an impact on overhead costs and transportation costs and may in the future adversely affect our operating results. In addition, increased inflation has had, and may continue to have, an effect on interest rates. Increased interest rates may adversely affect our borrowing rate and our ability to obtain, or the terms under which we can obtain, any potential additional funding.

Department of Defense

In April 2020, DSUVIA achieved Milestone C approval by the Department of Defense, or DoD, a decision that clears the path for the DoD to begin placing orders for DSUVIA for inclusion in all Army Sets, Kits, and Outfits, or SKOs, for deployed/deploying troops. This SKO fulfillment is dependent on the Army's completion of their product information package including instructions on fulfillment and training which remains in process. In September 2020, we announced that DSUVIA was added to the DoD Joint Deployment Formulary, a core list of pharmaceutical products that are designated for deploying military units across all service branches. Also in September 2020, the U.S. Army awarded AcelRx with an initial contract of up to $3.6 million over four years for the purchase of DSUVIA to support a DoD-sponsored study, which is currently underway, to aid the development of clinical practice guidelines. Since the fourth quarter of 2020, DSUVIA orders are being fulfilled for the Army Prepositioned Stock Program, or APS. The aforementioned clinical and APS orders are separate from the planned SKO fulfillment. Upon closing of the transaction contemplated under the DSUVIA Agreement, Alora will be responsible for commercializing DSUVIA except that we will retain the responsibility for driving the demand within the Department of Defense, and we will receive quarterly payments in an amount equal to 75% of net Product sales to the Department of Defense. Refer to Note 20, "Subsequent Events" to the consolidated financial statements in this Annual Report on Form 10-K for additional information.

Financial Overview

Although the termination of the Royalty Monetization resulted in net income for the year ended December 31, 2022, we have incurred net losses and generated negative cash flows from operations since inception and expect to incur losses in the future as we continue commercialization activities to support the U.S. launch of DSUVIA, support European sales of DZUVEO by Aguettant, and fund any future research and development activities needed to support the FDA regulatory review of our product candidates.

Our net income was $47.8 million for the year ended December 31, 2022, and our net loss was $35.1 million for the year ended December 31, 2021. As of December 31, 2022, we had an accumulated deficit of $425.8 million. As of December 31, 2022, we had cash, cash equivalents, short-term investments and restricted cash totaling $20.8 million compared to $51.6 million as of December 31, 2021.

Critical Accounting Estimates

The accompanying discussion and analysis of our financial condition and results of operations are based upon our consolidated financial statements and the related disclosures, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates, assumptions and judgments that affect the reported amounts in our financial statements and accompanying notes. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. To the extent that there are material differences between these estimates and actual results, our future financial statement presentation, financial condition, results of operations and cash flows will be affected. Note 1, "Organization and Summary of Significant Accounting Policies" to the consolidated financial statements in this Annual Report on Form 10-K describes the significant accounting policies used in the preparation of the financial statements. Certain of these significant accounting policies are considered to be critical accounting policies, as defined below.

A critical accounting policy is defined as one that is both material to the presentation of our financial statements and requires management to make difficult, subjective or complex judgments that could have a material effect on our financial condition and results of operations. Specifically, critical accounting estimates have the following attributes: (i) we are required to make assumptions about matters that are highly uncertain at the time of the estimate; and (ii) different estimates we could reasonably have used, or changes in the estimate that are reasonably likely to occur, would have a material effect on our financial condition or results of operations.

We believe the following policies to be the most critical to an understanding of our financial condition and results of operations because they require us to make estimates, assumptions and judgments about matters that are inherently uncertain. Management has discussed the development, selection and disclosure of the following estimates with the Audit Committee.

Revenue from Contracts with Customers

We follow the provisions of Accounting Standards Codification, or ASC, Topic 606, *Revenue from Contracts with Customers*. The guidance provides a unified model to determine how revenue is recognized. We recognize revenue upon transfer of control of promised products or services to customers in an amount that reflects the consideration we expect to receive in exchange for those products or services. We sell our products primarily through wholesale and specialty distributors.

In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under our agreements, we perform the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations, including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) we satisfy each performance obligation.

Product sales revenue

We sell our product primarily through distributors. Revenues from product sales are recognized when distributors obtain control of our product, which occurs at a point in time, upon delivery to such distributors. These distributors subsequently resell the product to certified medically supervised healthcare settings. In addition to distribution agreements with these customers, we enter into arrangements with group purchasing organizations, or GPOs, and other certified medically supervised healthcare settings that provide for privately negotiated discounts with respect to the purchase of our products. For revenue recognition under bill-and-hold arrangements, wherein the customer agrees to buy product from us but requests delivery at a later date, we deem that control passes to the customer when the product is ready for delivery. We recognize revenue under these types of arrangements when a signed agreement is in place, the transaction is billable, the customer has significant risk and rewards for the product and the ability to direct the asset, the product has been set aside specifically for the customer, and the product cannot be redirected to another customer. Revenue from product sales is recorded at the transaction price, net of estimates for variable consideration consisting of chargebacks, government rebates, returns, distribution fees and GPO fees. Variable consideration is recorded at the time product sales are recognized resulting in a reduction in product revenue. The amount of variable consideration that is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Variable consideration is estimated using the most-likely amount method, which is the single-most likely outcome under a contract and is typically at the stated contractual rate. Where appropriate, these estimates take into consideration a range of possible outcomes that are probability-weighted in accordance with the expected value method under ASC Topic 606 for relevant factors. These factors include current contractual and statutory requirements, specific known market events and trends, industry data, and/or forecasted customer buying and payment patterns. Actual amounts of consideration ultimately received may differ from our estimates. If actual results vary materially from our estimates, we will adjust these estimates, which will affect revenue from product sales and earnings in the period such estimates are adjusted. These estimates include:

Chargebacks – Our customers subsequently resell our product to qualified healthcare providers. In addition to distribution agreements with customers, we enter into arrangements with qualified healthcare providers that provide discounts with respect to the purchase of our product. Chargebacks represent the estimated obligations resulting from contractual commitments to sell product to qualified healthcare providers at prices lower than the list prices charged to customers who directly purchase the product from us. Customers charge us for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue-related accrued liabilities on the consolidated balance sheets. Chargeback amounts are determined at the time of resale to the qualified healthcare providers by customers, and we issue credits for such amounts generally within a few weeks of the customer's notification to us of the resale. Reserves for chargebacks consists of credits that we expect to issue for units that remain in the distribution channel inventories at each reporting period end that we expect will be sold to the qualified healthcare providers, and chargebacks for units that our customers have sold to the qualified healthcare providers, but for which credits have not been issued.

Government Rebates – We are subject to discount obligations under state Medicaid programs. We estimate our Medicaid rebates and record them in the same period the related product revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability that is included in accrued liabilities on the consolidated balance sheets.

Returns – We allow our distributors to return product for credit 6 months prior to, and up to 12 months after, the product expiration date. As such, there may be a significant period of time between the time the product is shipped and the time the credit is issued on returned product.

Distribution Fees – Distribution fees include fees paid to certain customers for sales order management, data and distribution services. Distribution fees are recorded as a reduction of revenue in the period the related product revenue is recognized.

GPO Fees – We pay administrative fees to GPOs for services and access to data. These fees are based on contracted terms and are paid after the quarter in which the product was purchased by the GPOs' members.

Trade Discounts and Allowances – We provide our customers with discounts which include early payment incentives that are explicitly stated in our contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized.

We believe our estimated allowances for chargebacks, government rebates and product returns require a high degree of judgment and are subject to change based on our limited experience and certain quantitative and qualitative factors. We believe our estimated allowances for distribution fees, GPO fees and trade discounts and allowances do not require a high degree of judgment because the amounts are settled within a relatively short period of time. We will continue to assess our estimates of variable consideration as we accumulate additional historical data and will adjust these estimates accordingly. Changes in product revenue allowance estimates could materially affect our results of operations and financial position.

Contract and other collaboration revenue

We generate revenue from collaboration agreements. These agreements typically include payments for upfront signing or license fees, cost reimbursements for development and manufacturing services, milestone payments, product sales, and royalties on licensee's future product sales. Product sales related revenue under these collaboration agreements is classified as product sales revenue, while other revenue generated from collaboration agreements is classified as contract and other collaboration revenue.

Performance Obligations

A performance obligation is a promise in a contract to transfer a distinct good or service to the customer and is the unit of account in ASC Topic 606. Our performance obligations include delivering product to our distributors, commercialization license rights, development services, services associated with the regulatory approval process, joint steering committee services, demonstration devices, manufacturing services, material rights for discounts on manufacturing services, and product supply.

We have optional additional items in contracts, which are considered marketing offers and are accounted for as separate contracts when the customer elects such options. Arrangements that include a promise for future commercial product supply and optional research and development services at the customer's or our discretion are generally considered as options. We assess if these options provide a material right to the licensee and if so, such material rights are accounted for as separate performance obligations. If we are entitled to additional payments when the customer exercises these options, any additional payments are recorded in revenue when the customer obtains control of the goods or services.

Transaction Price

We have both fixed and variable consideration. Non-refundable upfront fees and product supply selling prices are considered fixed, while milestone payments are identified as variable consideration when determining the transaction price. Funding of research and development activities is considered variable until such costs are reimbursed at which point, they are considered fixed. We allocate the total transaction price to each performance obligation based on the relative estimated standalone selling prices of the promised goods or services for each performance obligation.

At the inception of each arrangement that includes milestone payments, we evaluate whether the milestones are considered probable of being achieved and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the value of the associated milestone (such as a regulatory submission by us) is included in the transaction price. Milestone payments that are not within our control, such as approvals from regulators, are not considered probable of being achieved until those approvals are received.

For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (a) when the related sales occur, or (b) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

Allocation of Consideration

As part of the accounting for these arrangements, we must develop assumptions that require judgment to determine the stand-alone selling price of each performance obligation identified in the contract. Estimated selling prices for license rights and material rights for discounts on manufacturing services are calculated using an income approach model and can include the following key assumptions: the development timeline, sales forecasts, costs of product sales, commercialization expenses, discount rate, the time which the manufacturing services are expected to be performed, and probabilities of technical and regulatory success. For all other performance obligations, we use a cost-plus margin approach.

Timing of Recognition

Significant management judgment is required to determine the level of effort required under an arrangement and the period over which we expect to complete our performance obligations under the arrangement. We estimate the performance period or measure of progress at the inception of the arrangement and re-evaluate it each reporting period. This re-evaluation may shorten or lengthen the period over which revenue is recognized. Changes to these estimates are recorded on a cumulative catch-up basis. If we cannot reasonably estimate when our performance obligations either are completed or become inconsequential, then revenue recognition is deferred until we can reasonably make such estimates. Revenue is then recognized over the remaining estimated period of performance using the cumulative catch-up method. Revenue is recognized for products at a point in time when control of the product is transferred to the customer in an amount that reflects the consideration we expect to be entitled to in exchange for those product sales, which is typically once the product physically arrives at the customer, and for licenses of functional intellectual property at the point in time the customer can use and benefit from the license. For performance obligations that are services, revenue is recognized over time proportionate to the costs that we have incurred to perform the services using the cost-to-cost input method.

Inventories

Inventories are valued at the lower of cost or net realizable value. Cost is determined using the first-in, first-out method for all inventories. Inventory includes the cost of the active pharmaceutical ingredients, or API, raw materials and third-party contract manufacturing and packaging services. Indirect overhead costs associated with production and distribution are allocated to the appropriate cost pool and then absorbed into inventory based on the units produced or distributed, assuming normal capacity, in the applicable period. Indirect overhead costs in excess of normal capacity are recorded as period costs in the period incurred. Prior to FDA approval, all manufacturing costs for our product candidates are expensed to research and development. Upon FDA approval, manufacturing costs for our approved products manufactured for commercial sale are capitalized.

Our policy is to write down inventory that has become obsolete, inventory that has a cost basis in excess of its expected net realizable value and inventory in excess of expected requirements. We periodically evaluate the carrying value of inventory on hand for potential excess amount over demand using the same lower of cost or net realizable value approach as that used to value the inventory. Because the predetermined, contractual transfer prices we received from Grünenthal GmbH, or Grünenthal, were less than the direct costs of manufacturing, all Zalviso inventories were carried at net realizable value.

Non-Cash Interest Expense on Liability Related to Sale of Future Royalties

In September 2015, we sold certain royalty and milestone payment rights from the sales of Zalviso in the European Union by our former commercial partner, Grünenthal pursuant to the Collaboration and License Agreement, dated as of December 16, 2013, as amended, to PDL BioPharma, Inc., or PDL, for an upfront cash purchase price of $65.0 million. Under the relevant accounting guidance, because of our significant continuing involvement, the Royalty Monetization was accounted for as a liability that was amortized using the effective interest method over the life of the arrangement. In order to determine the amortization of the liability, we were required to estimate the total amount of future royalty and milestone payments to be received by ARPI LLC and paid to PDL, up to a capped amount of $195.0 million, over the life of the arrangement. The aggregate future estimated royalty and milestone payments (subject to the capped amount), less the $61.2 million of net proceeds we received, were to be recorded as interest expense over the life of the liability. Consequently, we imputed interest on the unamortized portion of the liability and recorded interest expense related to the Royalty Monetization accordingly.

During the three months ended June 30, 2020, Grünenthal notified us that it was terminating the Amended License Agreement, effective November 13, 2020. The terms of the Grünenthal Agreements were extended to May 2021 to enable Grünenthal to sell down its Zalviso inventory, a right it had under the Grünenthal Agreements. The rights to market and sell Zalviso in the Territory reverted back to us in May 2021.

There was a continuing obligation on our part, through the term of the Royalty Monetization, to use commercially reasonable efforts to negotiate a replacement license agreement, or New Arrangement. However, without a New Arrangement to commercialize Zalviso in Europe, we were unable to reliably estimate the future payments to SWK Funding LLC, or SWK, (assignee of PDL) over the remaining life of the Royalty Monetization. Due to the significant judgments and factors related to the estimates of future payments under the Royalty Monetization, there were significant uncertainties surrounding the amount and timing of future payments and the probability of realization of any estimated contingent gain. While the expected payments under the Royalty Monetization were lower than the gross proceeds of $65.0 million received, we deferred recognition of any probable contingent gain until the Royalty Monetization liability expired.

On May 31, 2022, we entered into a Termination Agreement with SWK to fully terminate the Royalty Monetization for which we paid cash consideration of $0.1 million, and neither PDL nor SWK retains any further interest in the Royalty Monetization. Accordingly, effective May 31, 2022, the Royalty Monetization is no longer reflected on our financial statements or other records as a sale of assets to PDL or SWK and all security interests and other liens of every type held by the parties to the Royalty Monetization have been terminated and automatically released without further action by any party. The $84.1 million gain on extinguishment of the liability related to the sale of future royalties is recognized in the consolidated statements of operations as other income.

We recorded non-cash royalty revenues and non-cash interest (income) expense within our consolidated statements of operations over the term of the Royalty Monetization.

Acquisitions

We evaluate acquisitions of assets and other similar transactions to assess whether or not the transaction should be accounted for as a business combination or asset acquisition by first applying a screen test to determine whether substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset or group of similar identifiable assets. If so, the transaction is accounted for as an asset acquisition. If not, further determination is required as to whether or not we have acquired inputs and processes that have the ability to create outputs, which would meet the definition of a business. Significant judgment is required in the application of the screen test to determine whether an acquisition is a business combination or an acquisition of assets.

Acquisitions meeting the definition of business combinations are accounted for using the acquisition method of accounting, which requires that the purchase price be allocated to the net assets acquired at their respective fair values. In a business combination, any excess of the purchase price over the estimated fair values of the net assets acquired is recorded as goodwill.

For asset acquisitions, a cost accumulation model is used to determine the cost of an asset acquisition. Direct transaction costs are recognized as part of the cost of an asset acquisition. We also evaluate which elements of a transaction should be accounted for as a part of an asset acquisition and which should be accounted for separately. The cost of an asset acquisition, including transaction costs, is allocated to identifiable assets acquired and liabilities assumed based on a relative fair value basis. Goodwill is not recognized in an asset acquisition. Any difference between the cost of an asset acquisition and the fair value of the net assets acquired is allocated to the non-monetary identifiable assets based on their relative fair values. When a transaction accounted for as an asset acquisition includes an in-process research and development, or IPR&D, asset, the IPR&D asset is only capitalized if it has an alternative future use other than in a particular research and development project. For an IPR&D asset to have an alternative future use: (a) we must reasonably expect that we will use the asset acquired in the alternative manner and anticipate economic benefit from that alternative use, and (b) our use of the asset acquired must not be contingent on further development of the asset subsequent to the acquisition date (that is, the asset can be used in the alternative manner in the condition in which it existed at the acquisition date). Otherwise, amounts allocated to IPR&D that have no alternative use are expensed. Our asset acquisitions typically include contingent consideration arrangements that encompass obligations to make future payments to sellers contingent upon the achievement of future financial targets. Contingent consideration is not recognized until all contingencies are resolved and the consideration is paid or probable of payment, at which point the consideration is allocated to the assets acquired on a relative fair value basis.

Warrants Issued in Connection with Financings

We account for issued warrants as either liability or equity in accordance with ASC 480-10, *Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity*, or ASC 815-40, *Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock*. Under ASC 480-10, warrants are considered liability if they are mandatorily redeemable and they require settlement in cash or other assets, or a variable number of shares. If warrants do not meet liability classification under ASC 480-10, we consider the requirements of ASC 815-40 to determine whether the warrants should be classified as liability or equity. Under ASC 815-40, contracts that may require settlement for cash are liabilities, regardless of the probability of the occurrence of the triggering event. Liability-classified warrants are measured at fair value on the issuance date and at the end of each reporting period. Any change in the fair value of the warrants after the issuance date is recorded in the consolidated statements of operations. If warrants do not require liability classification under ASC 815-40, in order to conclude warrants should be classified as equity, we assess whether the warrants are indexed to our common stock and whether the warrants are classified as equity under ASC 815-40 or other applicable GAAP. Equity-classified warrants are accounted for at fair value on the issuance date with no changes in fair value recognized after the issuance date.

Net Income (Loss) per Share of Common Stock

Basic and diluted net income (loss) per common share, or EPS, are calculated in accordance with the provisions of FASB ASC Topic *260, Earnings per Share*.

We apply the two-class method to compute both basic and diluted net income or loss per share. The two-class method is an earnings allocation formula that treats participating securities as having rights to earnings that would otherwise have been available to common stockholders (including pre-funded warrants). Shares of common stock into which the pre-funded warrants may be exercised are considered outstanding for the purposes of computing net loss per share because the shares may be issued for little or no consideration and are exercisable after the original issuance date. In addition, we are required to calculate diluted net income or loss per share under the two-class method if the effect is more dilutive than the application of another dilutive method of calculating diluted EPS (i.e., the treasury stock, if-converted, or contingently issuable share method). In periods where there is a net loss, no allocation of undistributed net loss to the participating securities is performed if the holders of these securities are not contractually obligated to participate in our losses. Our participating securities include the November 2021 Financing Warrants and 2022 Warrants and the Series A Redeemable Convertible Preferred Stock.

For additional information regarding the net income (loss) per share, see Note 16, "Net Income (Loss) per Share of Common Stock" to the consolidated financial statements in this Annual Report on Form 10-K.

Results of Operations

We have realigned our cost structure from a focus on commercialization to a focus on advancing our recently acquired late-stage development pipeline. In 2022, we reduced our headcount-related expenses, primarily within the commercial organization. In the beginning of 2022, we employed 43 full-time employees. As of December 31, 2022, we employed 19 full-time employees. These reductions have resulted in, and will continue to result in, decreased operating expenses in 2022 and beyond. Our results of operations have fluctuated from period to period and may continue to fluctuate in the future, based upon our research and development efforts, variations in the level of expenditures related to development efforts and debt service obligations during any given period, and the uncertainty as to the extent and magnitude of the impact from the COVID-19 pandemic. Results of operations for any period may be unrelated to results of operations for any other period. In addition, historical results should not be viewed as indicative of future operating results.

Years Ended December 31, 2022 and 2021

Revenue

Product Sales Revenue

Product sales revenue consists of sales of DSUVIA in the U.S. and, prior to May 13, 2021, Zalviso in Europe.

Product sales revenue by product for the years ended December 31, 2022 and 2021, was as follows (in thousands, except percentages):

	Years Ended December 31,		$ Change	% Change
	2022	2021	2022 vs. 2021	2022 vs. 2021
DSUVIA	$ 1,771	$ 735	$ 1,036	141%
Zalviso	—	270	(270)	(100)%
Total product sales revenue	$ 1,771	$ 1,005	$ 766	76%

The increase in DSUVIA product sales revenue for the year ended December 31, 2022, as compared to the year ended December 31, 2021, was primarily the result of increased sales volume and prices for DSUVIA and DZUVEO, partially due to purchases from our distributors in advance of our October 1, 2022 price increase. We expect inventory levels to decrease at these distributors over the next quarter or two and do not expect any returned product as a result of these sales. For the year ended December 31, 2021, there was an approximate $0.3 million reduction in revenue related to product returns and $0.3 million in product sales revenue of Zalviso by Grünenthal. In May 2020, Grünenthal terminated the Collaboration and License Agreement and the Manufacture and Supply Agreement, or together, the Grünenthal Agreements, accordingly the rights to market and sell Zalviso in Europe reverted back to us on May 12, 2021. In July 2022, the European Marketing Authorization for Zalviso was withdrawn.

Contract and Other Collaboration Revenue

Contract and other collaboration revenue included revenue under the Grünenthal Agreements, related to research and development services, non-cash royalty revenue related to the sale of the majority of our royalty rights and certain commercial sales milestones to SWK under the Royalty Monetization, and royalty revenue for sales of Zalviso in Europe.

On July 14, 2021, we granted Aguettant the license rights to DZUVEO in the European Union. Accordingly, for the year ended December 31, 2021, we recognized $1.7 million of the $2.9 million upfront fee as license revenue under the DZUVEO Agreement. Total contract and other collaboration revenue for the year ended December 31, 2021 was $1.8 million. For the year ended December 31, 2022, we did not record any contract and other collaboration revenue. As of December 31, 2022, we had deferred revenue of $1.2 million, $0.1 million of which represented the current portion, for the portion of the upfront fee received under the DZUVEO Agreement allocated to the material right for discounted price on future optional product supply which has not yet been satisfied. Refer to Note 20, “Subsequent Events” to the consolidated financial statements in this Annual Report on Form 10-K for additional information.

Cost of goods sold

Total costs of goods sold for the years ended December 31, 2022 and 2021, were as follows (in thousands, except percentages):

	Years Ended December 31,		$ Change	% Change
	2022	2021	2022 vs. 2021	2022 vs. 2021
Direct costs	$ 615	$ 1,204	$ (589)	(49)%
Indirect costs	1,976	2,549	(573)	(22)%
Total costs of goods sold	$ 2,591	$ 3,753	$ (1,162)	(31)%

Direct costs from contract manufacturers for DSUVIA totaled $0.6 million in the year ended December 31, 2022, while direct costs from contract manufacturers for DSUVIA and Zalviso totaled $1.2 million in the year ended December 31, 2021. Direct cost of goods sold for DSUVIA and Zalviso includes the inventory costs of the active pharmaceutical ingredient, or API, third-party contract manufacturing costs, estimated warranty costs, packaging and distribution costs, shipping, handling and storage costs.

We periodically evaluate the carrying value of inventory on hand for potential excess amounts over demand using the same lower of cost or net realizable value approach as that used to value the inventory. During the year ended December 31, 2021, we recorded inventory impairment charges of $0.8 million, primarily as a result of DSUVIA inventory that may expire before being sold. There was no such inventory impairment for the year ended December 31, 2022.

The indirect costs to manufacture DSUVIA totaled $2.0 million in the year ended December 31, 2022, while the indirect costs to manufacture DSUVIA and Zalviso totaled $2.5 million in the year ended December 31, 2021. Indirect costs include internal personnel and related costs for purchasing, supply chain, quality assurance, depreciation and related expenses. Indirect costs declined primarily due to the reduction in personnel expenses attributed to DSUVIA and Zalviso production.

Research and Development Expenses

The majority of our operating expenses to date have been for research and development activities related to Zalviso and DSUVIA. Research and development expenses included the following:

- expenses incurred under agreements with contract research organizations and clinical trial sites;
- employee-related expenses, which include salaries, benefits and stock-based compensation;
- payments to third party pharmaceutical and engineering development contractors;
- payments to third party manufacturers;
- depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities and equipment, and equipment and laboratory and other supply costs; and
- costs for equipment and laboratory and other supplies.

We expect to incur future research and development expenditures to support the FDA regulatory review of our product candidates and anticipated activities required for the development of our nafamostat product candidates, and the preparation and submission of the NDAs for our two in-licensed pre-filled syringe, or PFS, product candidates from Aguettant.

We track external development expenses on a program-by-program basis. Our development resources are shared among all our programs. Compensation and benefits, facilities, depreciation, stock-based compensation, and development support services are not allocated specifically to projects and are considered research and development overhead.

Below is a summary of our research and development expenses for the years ended December 31, 2022 and 2021 (in thousands, except percentages):

	Years Ended December 31,		$ Change	% Change
	2022	2021	2022 vs. 2021	2022 vs. 2021
DSUVIA	$ 1,507	$ 1,401	$ 106	8%
PFS	313	50	263	526%
Niyad	405	—	405	100%
Other product candidates	58	49	9	18%
Overhead	2,910	2,595	315	12%
Total research and development expenses	$ 5,193	$ 4,095	$ 1,098	27%

Research and development expenses during the year ended December 31, 2022, as compared to the year ended December 31, 2021, increased by $1.1 million primarily due to PFS and Niyad development activities, increased DSUVIA manufacturing-related development costs, depreciation expense and compensation costs.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consisted primarily of salaries, benefits and stock-based compensation for personnel engaged in commercialization, administration, finance and business development activities. Other significant expenses included allocated facility costs and professional fees for general legal, audit and consulting services.

Total selling, general and administrative expenses for the years ended December 31, 2022 and 2021, were as follows (in thousands, except percentages):

	Years Ended December 31,		$ Change	% Change
	2022	2021	2022 vs. 2021	2022 vs. 2021
Selling, general and administrative expenses	$ 25,672	$ 30,935	$ (5,263)	(17)%

Selling, general and administrative expenses decreased by $5.3 million during the year ended December 31, 2022, as compared to the year ended December 31, 2021. The decrease is primarily due to a decline of $3.2 million in personnel-related expenses (primarily commercial personnel), $2.3 million in DSUVIA-related selling expenses, and $1.4 million in non-cash stock-based compensation expense. This was partially offset by $1.6 million in financing transaction related costs, $0.8 million of which were cash transaction costs, with the remaining $0.8 million attributed to the accounting for the warrant issued in the December 2022 financing.

Impairment of Property and Equipment

We have decided to not focus any development resources on Zalviso in the United States and do not expect to resubmit the Zalviso NDA in the foreseeable future. In addition, we do not expect any revenues from Zalviso in Europe in the foreseeable future. Accordingly, we determined that it is no longer probable that we will realize the future economic benefit associated with the costs of the Zalviso-related purchased equipment and manufacturing-related facility improvements we have made at our contract manufacturer and, therefore, recorded a non-cash impairment charge of $4.9 million to the Zalviso-related assets for the year ended December 31, 2022.

Other Income

Total other income for the years ended December 31, 2022 and 2021, was as follows (in thousands, except percentages):

	Years Ended December 31,		$ Change	% Change
	2022	2021	2022 vs. 2021	2022 vs. 2021
Interest expense	$ (1,153)	$ (2,291)	$ 1,138	(50)%
Interest income and other income, net	366	124	242	195%
Non-cash interest income on liability related to sale of future royalties	1,136	3,038	(1,902)	(63)%
Gain on extinguishment of liability related to sale of future royalties	84,052	—	(84,052)	(100)%
Total other income	$ 84,401	$ 871	$ 83,530	9,590%

Interest expense consisted primarily of interest accrued or paid on our debt obligation agreements and amortization of debt discounts. Interest expense decreased for the year ended December 31, 2022, as compared to the year ended December 31, 2021, primarily as a result of a lower average outstanding loan balance. As of December 31, 2022, the outstanding balance due under the Loan Agreement with Oxford was $5.4 million. Refer to Note 9, "Long-Term Debt" to the consolidated financial statements in this Annual Report on Form 10-K for additional information.

Interest income and other income for the years ended December 31, 2022 and 2021 primarily consisted of interest earned on our investments and the change in the fair value of our contingent put option. The increase in interest income and other income in the year ended December 31, 2022, compared to the year ended December 31, 2021, was primarily due to higher yields on our investments and the change in the fair value of our contingent put option.

The non-cash interest income on the liability related to the sale of future royalties is attributable to the Royalty Monetization that we completed in September 2015. As described in Note 11, "Liability Related to Sale of Future Royalties" to the consolidated financial statements in this Annual Report on Form 10-K, the Royalty Monetization has been recorded as debt under the applicable accounting guidance. The effective interest income rate for the years ended December 31, 2022 and 2021, was approximately 3.2% and 3.5%, respectively.

On May 31, 2022, we entered into a Termination Agreement with SWK to fully terminate the Royalty Monetization and we recognized an $84.1 million gain on extinguishment of the liability related to the sale of future royalties.

Liquidity and Capital Resources

Liquidity and Going Concern

The termination of the Royalty Monetization resulted in net income for the year ended December 31, 2022; however, before this, we had incurred losses and generated negative cash flows from operations since inception and we expect to continue to incur operating losses and negative cash flows in the future. These conditions raise substantial doubt about our ability to continue as a going concern. Considering our current cash resources and current and expected levels of operating expenses for the next twelve months, we expect to need additional capital to fund our planned operations prior to the twelve-month anniversary of the filing date of this Annual Report on Form 10-K. We may seek to raise such additional capital through public or private equity offerings, including under the Controlled Equity Offering℠ Sales Agreement, or the ATM Agreement, with Cantor Fitzgerald & Co., or Cantor, debt securities, monetize or securitize certain assets, refinance our loan agreement, enter into product development, license or distribution agreements with third parties, or divest any of our product candidates. While we believe our plans to raise additional funds will alleviate the conditions that raise substantial doubt about our ability to continue as a going concern, these plans are not entirely within our control and cannot be assessed as being probable of occurring. Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available, we may be required to further reduce our workforce, reduce the scope of, or cease, the development of our product candidates in advance of the date on which our cash resources are exhausted to ensure that we have sufficient capital to meet its obligations and continue on a path designed to preserve stockholder value. In addition, if we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish rights to our technologies, future revenue streams or product candidates, or to grant licenses on terms that may not be favorable to us.

We have funded our operations primarily through issuance of equity securities, borrowings, payments from Grünenthal, monetization of certain future royalties and commercial sales milestones from the European sales of Zalviso by Grünenthal, funding of approximately $22.6 million from the DoD, and more recently with revenues from sales of DSUVIA since the commercial launch in the first quarter of 2019 and the upfront payment under the DZUVEO Agreement with Aguettant.

As of December 31, 2022, we had cash, cash equivalents and investments totaling $20.8 million, compared to $51.6 million as of December 31, 2021. The decrease was primarily due to cash required to fund our continuing operations, including debt service, development activities for our newly acquired late-stage pipeline product candidates, commercialization activities for DSUVIA, including installation of the automated packaging line for DSUVIA, and business development activities. Our existing capital resources will not be sufficient to fund our operations until such time as we may be able to generate sufficient revenues to sustain our operations.

On December 29, 2022, we completed a registered direct offering with an institutional investor, or the Purchaser, in which we issued and sold 748,744 shares of our common stock, pre-funded warrants exercisable for an aggregate of 2,632,898 shares of common stock, and common warrants exercisable for an aggregate of 4,227,052 shares of common stock. The shares of common stock and accompanying common warrants were sold at a combined offering price of $2.22625 per share and accompanying common warrant, and the pre-funded warrants and accompanying common warrants were sold at a combined offering price of $2.22615 per pre-funded warrant and accompanying common warrant. The pre-funded warrants were immediately exercisable following closing of the offering, have an unlimited term, and have an exercise price of $0.0001 per share. The common warrants will not be exercisable until after the six-month anniversary of the closing of the offering, will have an exercise price of $2.07 per share and will expire on December 29, 2028. Total net proceeds from the offering were approximately $6.6 million, after deducting fees payable to the placement agent and other estimated offering expenses payable by us, excluding the proceeds, if any, from the exercise of the pre-funded warrants and the common warrants. As of December 31, 2022, the 2,632,898 pre-funded warrants and the 4,227,052 common warrants remain outstanding.

On August 3, 2022, we entered into a securities purchase agreement with Lincoln Park Capital Fund, LLC, or LPC, pursuant to which we issued, in a private placement transaction, 3,000 shares of Series A Redeemable Convertible Preferred Stock, par value $0.001 per share, with $100 per share stated value, together with a warrant to purchase up to an aggregate of 81,150 shares of common stock at an exercise price of $4.07 per share (subject to adjustment for stock splits, reverse stock splits and similar recapitalization events), for $0.3 million, and became immediately exercisable and has a term ending on February 3, 2028. Upon the closing of the December 29, 2022 registered direct offering, we modified the previously issued warrant to LPC to reduce the exercise price to $2.07 per share in accordance with the warrant's down round feature. As of December 31, 2022, this warrant had not been exercised and was still outstanding.

On November 17, 2021, we completed a registered direct offering in which we issued and sold 875,000 shares of our common stock at a price of $16.00 per share and warrants exercisable for an aggregate of 875,000 shares of our common stock at a price of $20.00 per share. The total net proceeds from this offering were approximately $13.9 million. Upon the closing of the December 29, 2022 registered direct offering, we agreed to amend a previously issued warrant held by the Purchaser to purchase up to 750,000 shares of common stock in this November 17, 2021 registered direct offering to reduce the exercise price to $2.07 per share and to extend the expiration date to December 29, 2028. The remaining warrants issued in the November 17, 2021 registered direct offering for 125,000 shares of our common stock are currently exercisable at a price of $20.00 per share and expire on November 15, 2026. All of the warrants exercisable for a total of 875,000 shares of our common stock issued in connection with this registered direct offering remain outstanding at December 31, 2022.

On January 22, 2021, we completed an underwritten public offering in which we issued and sold 725,000 shares of our common stock to the underwriter at a price of $35.25 per share. On January 27, 2021, the underwriters exercised their option in full and purchased an additional 108,750 shares at a price of $35.25 per share. The total net proceeds from this offering of an aggregate 833,750 shares were approximately $28.9 million.

We entered into a Controlled Equity Offering℠ Sales Agreement, or, as amended, the ATM Agreement, with Cantor Fitzgerald & Co., or Cantor, as agent, pursuant to which we may offer and sell, from time to time through Cantor, shares of our common stock. During the year ended December 31, 2022, we issued and sold approximately 0.1 million shares of common stock pursuant to the ATM Agreement and received net proceeds of $0.5 million, after deducting fees and expenses. During the year ended December 31, 2021, we had issued and sold an aggregate of approximately 0.2 million shares of common stock pursuant to the ATM Agreement, for which we had received net proceeds of approximately $7.5 million, after deducting fees and expenses. As of December 31, 2022, we had the ability to sell approximately $35.6 million of our common stock under the ATM Agreement.

On May 30, 2019, we entered into the Loan Agreement with Oxford. Under the Loan Agreement, we borrowed an aggregate principal amount of $25.0 million under a term loan. After deducting all loan initiation costs and outstanding interest on the prior loan agreement with Hercules, we received $15.9 million in net proceeds. As of December 31, 2022, the outstanding balance under the Loan Agreement was $5.4 million. For more information, see Note 9, "Long-Term Debt" to the consolidated financial statements in this Annual Report on Form 10-K for additional information.

Our cash and investment balances are held in a variety of interest-bearing instruments, including obligations of commercial paper, corporate debt securities, U.S. government sponsored enterprise debt securities and money market funds. Cash in excess of immediate requirements is invested with a view toward capital preservation and liquidity. We do not expect COVID-19 to have a material impact on our high quality, short-dated investments.

Cash Flows

	Years Ended December 31,	
	2022	**2021**
Net cash used in operating activities	$ (28,331)	$ (30,002)
Net cash provided by/(used in) investing activities	36,450	(26,123)
Net cash (used in)/provided by financing activities	(507)	41,514

Cash Flows from Operating Activities

The primary use of cash for our operating activities during these periods was to fund commercial activities for DSUVIA. Our cash used in operating activities also reflected changes in our working capital, net of adjustments for non-cash charges, such as depreciation and amortization of our fixed assets, stock-based compensation, non-cash interest income (expense) related to the sale of future royalties and interest expense related to our debt financings.

Cash used in operating activities of $28.3 million during the year ended December 31, 2022, reflected net income of $47.8 million, offset by aggregate non-cash items of $74.7 million and an approximate $1.4 million net change in our operating assets and liabilities. Non-cash inflows included an $84.2 million gain on the termination of the Royalty Monetization, partially offset by a $4.9 million charge for the impairment of Zalviso-related property and equipment, $2.9 million in stock-based compensation expense and $1.7 million in depreciation and amortization expense. The net change in our operating assets and liabilities included a $1.6 million decrease in accrued liabilities.

Cash used in operating activities of $30.0 million during the year ended December 31, 2021, reflected a net loss of $35.1 million, partially offset by aggregate non-cash charges of $4.9 million and included an approximate $0.2 million net change in our operating assets and liabilities. Non-cash charges included $4.6 million for stock-based compensation expense, $3.0 million in non-cash interest income on the liability related to the Royalty Monetization, and $2.0 million in depreciation and amortization expense. The net change in our operating assets and liabilities included a $1.2 million increase in deferred revenue and a $0.9 million increase in prepaid expenses and other assets.

Cash Flows from Investing Activities

Our investing activities have consisted primarily of our capital expenditures and purchases and sales and maturities of our available-for-sale investments.

During the year ended December 31, 2022, cash provided by investing activities of $36.5 million was primarily the net result $46.4 million in proceeds from maturity of investments partially offset by $7.9 million for purchases of investments and $1.7 million in cash paid for the Lowell asset acquisition, net of cash acquired.

During the year ended December 31, 2021, cash used in investing activities of $26.1 million was primarily the net result of $70.5 million for purchases of investments, $1.8 million for purchases of property and equipment, and $0.8 million in asset acquisition costs related to our acquisition of Lowell, partially offset by $47.0 million in proceeds from the sale and maturity of investments.

Cash Flows from Financing Activities

Cash flows from financing activities primarily reflect proceeds from the sale of our securities and payments made on debt financings.

During the year ended December 31, 2022, cash used in financing activities of $0.5 million was primarily due to $8.4 million in long-term debt payments, including $8.3 million under the Loan Agreement with Oxford, partially offset by $7.9 million in net proceeds received in connection with equity financings.

During the year ended December 31, 2021, cash provided by financing activities of $41.5 million was primarily due to $50.3 million in net proceeds received in connection with equity financings, including the issuance of warrants and shares sold under our ATM Agreement, partially offset by $8.8 million used for payment of long-term debt.

Capital Commitments and Capital Resources

Our current operating plan includes expenditures related to the development of our product candidates. In addition, on January 7, 2022, we acquired Lowell in a transaction for consideration of approximately $32.5 million plus net cash acquired and certain other adjustments, inclusive of approximately $26.0 million of contingent consideration payable in cash or stock at AcelRx's option, upon the achievement of regulatory and sales-based milestones. For additional information regarding the acquisition of Lowell, see Note 4, "Asset Acquisition" to the consolidated financial statements in this Annual Report on Form 10-K for additional information. Our operating plan includes anticipated activities required for the development and supply of our nafamostat product candidates, and the preparation and submission of the NDAs for our two in-licensed PFS product candidates from Aguettant. These assumptions may change as a result of many factors. We will continue to evaluate the work necessary to gain approval of our product candidates in the United States and intend to update our cash forecasts accordingly. Considering our current cash resources and current and expected levels of operating expenses for the next twelve months, we expect to need additional capital to fund our planned operations for at least the next twelve months.

Our future capital requirements may vary materially from our expectations based on numerous factors, including, but not limited to, the following:

- the ability to retain the listing of our common stock on the Nasdaq exchange;
- expenditures related to the potential commercialization of our product candidates, if approved;
- expenditures related to drafting and submission of new drug or device regulatory applications with the U.S. Food and Drug Administration, or the FDA, for our developmental product candidates and payment of statutory filing fees and related application prosecution costs arising from such submissions;
- costs associated with business development activities and licensing transactions;
- the outcome and timing of the regulatory submissions for our product candidates, including our two in-licensed product candidates from Aguettant, and any approvals for our product candidates;
- the outcome, timing and cost of the development of our nafamostat product candidates;
- the initiation, progress, timing and completion of any post-approval clinical trials for our product candidates, if approved;
- changes in the focus and direction of our business strategy and/or research and development programs;
- milestone and royalty revenue we receive under our collaborative development and commercialization arrangements;
- delays that may be caused by changing regulatory requirements;
- the costs involved in filing and prosecuting patent applications and enforcing and defending patent claims;
- the timing and terms of future in-licensing and out-licensing transactions;
- the cost and timing of establishing sales, marketing, manufacturing and distribution capabilities;
- the cost of procuring clinical supplies of our product candidates, and commercial supplies, if approved;
- the cost of establishing new supply chains and related third party logistics to support our developmental product candidates;
- the extent to which we acquire or invest in businesses, products and product candidates or technologies; and
- the expenses associated with litigation.

In the long-term, our existing capital resources will not be sufficient to fund our operations until such time as we may be able to generate sufficient revenues to sustain our operations. We will have to raise additional funds through the sale of our equity securities, monetization of current and future assets, issuance of debt or debt-like securities or from development and licensing arrangements to sustain our operations and continue our development programs.

Please see "Part II., Item 1A. Risk Factors—Risks Related to Our Financial Condition and Need for Additional Capital."

We have material cash requirements and other contractual obligations related to our Loan Agreement with Oxford (as described in Note 9, "Long-Term Debt"), contract manufacturing services and office rent (as described in Note 10, "Leases" to the consolidated financial statements in this Annual Report on Form 10-K).

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

We are a smaller reporting company as defined by Rule 12b-2 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and are not required to provide the information specified under this item.

Item 8. Financial Statements and Supplementary Data

The financial statements required by this item are attached to this Form 10-K beginning with page F-1.

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

None.

Item 9A. Controls and Procedures

We maintain disclosure controls and procedures (as defined in Exchange Act Rule 13a–15(e) and 15d-15(e)) that are designed to ensure that information required to be disclosed in our reports under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and the rules and regulations thereunder, 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, to allow for timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and management is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Evaluation of Disclosure Controls and Procedures

We have carried out an evaluation, under the supervision, and with the participation, of management including our principal executive officer and principal financial officer, of our disclosure controls and procedures (as defined in Rule 13a-15(e)) of the Securities Exchange Act of 1934, as amended, or the Exchange Act) as of the end of the period covered by this Annual Report on Form 10–K. Based on the evaluation of our disclosure controls and procedures as of December 31, 2022, our chief executive officer and principal financial officer have concluded that our disclosure controls and procedures were not effective to ensure that the information required to be disclosed by the Company in reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, due to the material weakness in our internal control over financial reporting described below.

Management's Annual Report on Internal Control over Financial Reporting

The following report is provided by management in respect of AcelRx Pharmaceuticals' internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act):

1. AcelRx Pharmaceuticals' management is responsible for establishing and maintaining adequate internal control over financial reporting.

2. AcelRx Pharmaceuticals' management has used the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, framework (2013 framework) to evaluate the effectiveness of internal control over financial reporting. Management believes that the COSO framework is a suitable framework for its evaluation of financial reporting because it is free from bias, permits reasonably consistent qualitative and quantitative measurements of AcelRx Pharmaceuticals' internal control over financial reporting, is sufficiently complete so that those relevant factors that would alter a conclusion about the effectiveness of AcelRx Pharmaceuticals' internal control over financial reporting are not omitted and is relevant to an evaluation of internal control over financial reporting.

3. Management has assessed the effectiveness of AcelRx Pharmaceuticals' internal control over financial reporting as of December 31, 2022 and has concluded that such internal control over financial reporting was not effective.

Management has concluded that there is a material weakness in the review procedures related to the technical accounting review and analysis over earnings per share calculations that were insufficient to prevent or detect errors in the calculation. Specifically, the error was due to management's failure to identify warrants issued in November 2021 as participating securities and consequently attribute earnings to these securities as part of a two-class EPS calculation. This material weakness resulted in the restatement of our unaudited condensed consolidated financial statements for the quarterly periods ended June 30, 2022 and September 30, 2022. Additionally, this material weakness could result in a misstatement of the calculation of earnings per share and related disclosures that would result in a material misstatement to the annual or interim consolidated financial statements that would not be prevented or detected. As a result, our previously issued unaudited condensed consolidated financial statements for the quarterly periods ended June 30, 2022 and September 30, 2022 have been restated. Based on this assessment, management believes that our internal control over financial reporting was not effective as of December 31, 2022.

This Annual Report does not include an attestation report of our registered public accounting firm regarding internal control over financial reporting. Management's report was not subject to attestation by our registered public accounting firm pursuant to the rules of the Securities and Exchange Commission applicable to smaller reporting companies that permit us to provide only management's report in this Annual Report.

Changes in Internal Control over Financial Reporting

Except for the material weakness noted above, there has been no change in the Company's internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) that occurred during the quarter ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Remediation Plan for Material Weakness

Management has actively initiated remediation efforts to address the material weakness. Specifically, we have enhanced our processes to identify and appropriately apply applicable accounting requirements related to the earnings per share calculation to better evaluate and understand the nuances of the complex accounting standards that apply to our financial statements. Our plans at this time include to continue to provide access to accounting literature, research materials and documents, enhance the review and analysis process around the earnings per share calculation and increase communications among our personnel and third-party professionals with whom we consult regarding complex accounting applications. The elements of our remediation plan can only be accomplished over time, and we can offer no assurance that these initiatives will ultimately have the intended effects.

Limitations on the Effectiveness of Controls.

A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Because of inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues, if any, within an organization have been detected. Accordingly, our disclosure controls and procedures and our internal control over financial reporting are designed to provide reasonable, not absolute, assurance that the objectives of the control system are met. We continue to implement, improve and refine our disclosure controls and procedures and our internal control over financial reporting.

Item 9B. Other Information

In connection with the Company's year-end financial statement close and preparation of its Annual Report on Form 10-K for the year ended December 31, 2022, an error in the earnings per share calculations was identified in the interim financial statements (the "Prior Period Financial Statements") for the three and six months ended June 30, 2022 and nine months ended September 30, 2022 (the "Interim Periods"). The error in the earnings per share calculation was due to the Company not properly applying the two-class method of calculating earnings per share with respect to, or disclose that, the warrants issued in November 2021 are participating securities. The financial statements for the year ended December 31, 2021 and the three months ended March 31, 2022, did not require the application of the two-class method of calculating earnings per share, and therefore were not impacted by the issuance of the warrants in November 2021.

The error has no impact on the Company's cash balance, liquidity, revenues, operating expenses, or total net income. Further, there is no impact to the Company's balance sheet accounts or cash flows.

On March 30, 2023, the Company's management and the Audit Committee of the Company, in discussion with the Company's independent registered accounting firm, WithumSmith+Brown PC, determined that the Company's Prior Period Financial Statements for the Interim Periods, should no longer be relied upon because of the error in the earnings per share calculations. The Company's management and the Audit Committee concluded that it is appropriate to restate the Prior Period Financial Statements for the Interim Periods noted above.

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

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Information regarding our directors and executive officers set forth under the headings "Proposal No.1—Election of Directors," "Information Regarding the Board of Directors and Corporate Governance," and "Executive Officers of the Registrant" of the 2023 Proxy Statement is incorporated herein by reference.

Information regarding our Audit Committee, including the members of our Audit Committee, set forth under the heading "Information Regarding the Board of Directors and Corporate Governance—Audit Committee" of the 2023 Proxy Statement is incorporated herein by reference.

Information regarding the procedures by which our shareholders may recommend nominees to our Board of Directors set forth under the heading "Information Regarding the Board of Directors and Corporate Governance—Nominating and Corporate Governance Committee" of the 2023 Proxy

Statement is incorporated herein by reference.

Information regarding our Code of Business Conduct and Ethics set forth under the heading “Information Regarding the Board of Directors and Corporate Governance—Code of Business Conduct and Ethics” of the 2023 Proxy Statement is incorporated herein by reference.

Item 11. Executive Compensation

Information regarding executive compensation and director compensation set forth under the headings “Executive Compensation” and “Director Compensation,” respectively, of the 2023 Proxy Statement is incorporated herein by reference.

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

Information contained in the sections captioned “Security Ownership of Certain Beneficial Owners and Management” and “Equity Compensation Plan Information” of the 2023 Proxy Statement is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions and Director Independence

Information contained in the section captioned “Related Person Transactions and Indemnification” of the 2023 Proxy Statement is incorporated herein by reference.

Information regarding director independence set forth under the heading "Information Regarding the Board of Directors and Corporate Governance" of the 2023 Proxy Statement is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services

Information regarding our independent auditor fees and services in the section captioned "Proposal No. 2—Ratification of Selection of Independent Registered Public Accounting Firm" of the 2023 Proxy Statement is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) The following documents are filed as part of this Form 10-K:

1. Financial Statements:

See Index to Financial Statements in Item 8 of this Form 10-K.

2. Financial Statement Schedules:

Reference is made to the financial statement schedules included under Item 8 of Part II hereof. All other schedules are omitted because they are not applicable, not required or the information is shown in the financial statements or the notes thereto.

(b) Exhibits

Exhibit Number	Exhibit Description	Incorporation By Reference			
		Form	SEC File No.	Exhibit	Filing Date
2.1§	Agreement and Plan of Merger, dated as of November 14, 2021, by and among the Registrant, Lowell, Merger Sub 1, Merger Sub 2 and the Stockholder Representative.	10-Q	001-35068	2.1	11/15/2021
3.1	Amended and Restated Certificate of Incorporation of the Registrant.	8-K	001-35068	3.1	2/18/2011
3.2	Certificate of Amendment of Amended and Restated Certificate of Incorporation of the Registrant.	8-K	001-35068	3.1	6/25/2019
3.3	Certificate of Amendment of Amended and Restated Certificate of Incorporation of the Registrant.	8-K	001-35068	3.1	10/25/2022
3.4	Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock of the Registrant.	8-K	001-35068	3.1	08/04/2022
3.5	Certificate of Elimination of Series A Convertible Preferred Stock of the Registrant.	8-K	001-35068	3.2	10/25/2022
3.6	Amended and Restated Bylaws of the Registrant.	8-K	001-35068	3.1	08/12/2022
4.1	Description of Capital Stock.	10-K	001-35068	4.1	3/15/2021
4.2	Reference is made to Exhibits 3.1 through 3.3.				
4.3	Specimen Common Stock Certificate of the Registrant.	S-1	333-170594	4.2	1/31/2011
4.4	Form of Warrant to Purchase Common Stock of the Registrant, dated as of May 30, 2019.	8-K	001-35068	4.1	6/3/2019

Exhibit Number	Exhibit Description	Incorporation By Reference			
		Form	SEC File No.	Exhibit	Filing Date
4.5	Form of Warrant to Purchase Common Stock of the Registrant, dated as of November 15, 2021.	8-K	001-35068	4.1	11/15/2021
4.6	Warrant to Purchase Common Stock of the Registrant, dated as of August 3, 2022.	8-K	001-35068	4.1	08/04/2022
4.7	Form of Common Warrant (December 2022).	8-K	001-35068	4.1	12/28/2022
4.8	Form of Pre-Funded Warrant (December 2022).	8-K	001-35068	4.2	12/28/2022
4.9	Form of Common Warrant, as amended (November 2022).	8-K	001-35068	4.3	12/28/2022
10.1+	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers.	S-1	333-170594	10.1	1/7/2011
10.2+	2011 Equity Incentive Plan.	S-8	333-172409	99.3	2/24/2011
10.3+	Forms of Stock Option Grant Notice, Notice of Exercise and Option Agreement under 2011 Equity Incentive Plan.	10-K	001-35068	10.5	3/30/2011
10.4+	Forms of Restricted Stock Unit Grant Notice and Restricted Stock Unit Agreement under 2011 Equity Incentive Plan.	10-K	001-35068	10.6	3/30/2011
10.5+	Amended and Restated 2020 Equity Incentive Plan.	8-K	001-350683	10.1	6/17/2021
10.6+	Forms of Stock Option Grant Notice, Stock Option Agreement and Notice of Exercise under the Amended and Restated 2020 Equity Incentive Plan.	S-8	333-239213	99.2	6/16/2020
10.7+	Forms of RSU Award Grant Notice and Award Agreement (RSU Award) under the Amended and Restated 2020 Equity Incentive Plan.	S-8	333-239213	99.3	6/16/2020
10.8+	Amended and Restated 2011 Employee Stock Purchase Plan.	S-8	333-239213	99.4	6/16/2020
10.9+	Amended and Restated Offer Letter between the Registrant and Badri (Anil) Dasu, dated December 30, 2010.	S-1	333-170594	10.15	1/7/2011
10.10+	Amended and Restated Offer Letter between the Registrant and Pamela Palmer, dated December 29, 2010.	S-1	333-170594	10.16	1/7/2011
10.11+	Offer Letter between the Registrant and Vincent J. Angotti, effective as of March 6, 2017.	10-Q	001-35068	10.4	5/8/2017
10.12+	Offer Letter between the Registrant and Raffi Asadorian, dated July 18, 2017.	8-K	001-35068	10.1	7/19/2017
10.13+	Non-Employee Director Compensation Policy.	10-K	001-35068	10.13	3/10/2022
10.14+	Amended and Restated Severance Benefit Plan effective as of February 7, 2017.	8-K	001-35068	10.2	2/9/2017
10.15§	Sublease for a Single Sublessee, dated March 26, 2021, by and between the Registrant and Weichert Workforce Mobility Inc., as successor in interest to The MI Group, Inc.	10-Q	001-35068	10.3	5/17/2021
10.16§#	License and Commercialization Agreement (DZUVEO), dated July 14, 2021, between the Registrant and Laboratoire Aguettant.	10-Q	001-35068	10.1	11/15/2021
10.17§#	License and Commercialization Agreement (PFS), dated July 14, 2021, between the Registrant and Laboratoire Aguettant.	10-Q	001-35068	10.2	11/15/2021

Exhibit Number	Exhibit Description	Incorporation By Reference			
		Form	SEC File No.	Exhibit	Filing Date
10.18	Contingent Value Rights Agreement, dated as of January 7, 2022, by and among AcelRx Pharmaceuticals, Inc., James Wilkie, solely in his capacity as the representative of the Lowell stockholders and option holders, and Computershare Inc., and its wholly-owned subsidiary, Computershare Trust Company, N.A., a federally chartered trust company, collectively as Rights Agent	8-K	001-35068	10.1	1/12/2022
10.19§#	Commercial Supply Agreement, effective March 31, 2021 by and between the Registrant and Catalent Pharma Solutions, LLC.	10-Q	001-35068	10.1	8/16/2021
10.20#	Manufacturing Services Agreement between Registrant and Patheon Pharmaceuticals, Inc., dated as of January 18, 2013.	10-Q	001-35068	10.1	5/8/2013
10.21#	Amended and Restated Capital Expenditure Agreement between Registrant and Patheon Pharmaceuticals, Inc., effective as of December 12, 2012.	10-Q	001-35068	10.2	5/8/2013
10.22	Second Amendment to Amended and Restated Capital Expenditure and Equipment Agreement, between the Registrant and Patheon Pharmaceuticals, Inc. effective as of January 30, 2014.	10-Q	001-35068	10.4	5/8/2014
10.23#	Amendment #1 to Manufacturing Services Agreement between the Registrant and Patheon Pharmaceuticals, Inc., effective as of December 12, 2012.	10-Q	001-35068	10.6	5/2/2016
10.24#	Amendment #2 to Manufacturing Services Agreement between the Registrant and Patheon Pharmaceuticals, Inc., effective as of August 4, 2017.	10-Q	001-35068	10.1	11/9/2017
10.25#	Purchase and Sale Agreement between Registrant and ARPI LLC, dated as of September 18, 2015.	10-Q	001-35068	10.6	11/3/2015
10.26#	Subsequent Purchase and Sale Agreement between ARPI LLC (a wholly owned subsidiary of the Registrant) and SWK Funding, LLC (assigned of PDL BioPharma, Inc.), dated as of September 18, 2015.	10-Q	001-35068	10.7	11/3/2015
10.27	Controlled Equity Offering℠ Sales Agreement between the Registrant and Cantor Fitzgerald & Co., dated as of June 21, 2016.	8-K	001-35068	10.1	6/21/2016
10.28	Amendment No. 1 to the Controlled Equity Offering℠ Sales Agreement between the Registrant and Cantor Fitzgerald & Co., dated as of August 29, 2020.	S-3	333-239156	1.3	6/12/2020
10.29	Loan and Security Agreement between the Registrant and Oxford Finance, LLC, dated as of May 30, 2019.	8-K	001-35068	10.1	6/3/2019
10.30	First Amendment to Loan and Security Agreement between the Registrant and Oxford Finance, LLC, dated as of May 5, 2021.	10-Q	001-35068	10.4	11/15/2021
10.31	Second Amendment to Loan and Security Agreement between the Registrant and Oxford Finance, LLC, dated as of November 14, 2021.	10-K	001-35068	10.31	3/10/2022
10.32#	Agreement between the Registrant and SpecGX, LLC, dated June 16, 2017.	10-Q	001-35068	10.1	11/7/2019

Exhibit Number	Exhibit Description	Incorporation By Reference			
		Form	SEC File No.	Exhibit	Filing Date
10.33	Amendment to Agreement between the Registrant and SpecGX, LLC, dated September 23, 2019.	10-Q	001-35068	10.2	11/7/2019
10.34	Securities Purchase Agreement, between the Registrant and Lincoln Park Capital Fund, LLC, dated as of August 3, 2022.	8-K	001-35068	10.1	08/04/2022
10.35	Registration Rights Agreement, between the Registrant and Lincoln Park Capital Fund, LLC, dated as of August 3, 2022.	8-K	001-35068	10.2	08/04/2022
23.1	Consent of Withum Smith & Brown, LLP, Independent Registered Public Accounting Firm.				
24.1	Power of Attorney (included in signature page).				
31.1	Certification of Principal Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.				
31.2	Certification of Principal Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.				
32.1	Certifications of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				
101.INS	XBRL Instance Document- the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.				
101.SCH	Inline XBRL Taxonomy Schema Document				
101.CAL	Inline XBRL Taxonomy Calculation Linkbase Document				
101.DEF	Inline XBRL Taxonomy Definition Linkbase Document				
101.LAB	Inline XBRL Taxonomy Label Linkbase Document				
101.PRE	Inline XBRL Taxonomy Presentation Linkbase Document				
104	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101.INS, 101.SCH, 101.CAL, 101.DEF, 101.LAB, and 101.PRE).				

§ Schedules omitted pursuant to Item 601(a)(5) of Regulation S-K. The Registrant agrees to furnish supplementally a copy of any omitted schedule upon request by the SEC.

+ Indicates management contract or compensatory plan.

Material in the exhibit marked with am "[*]" has been omitted because it is confidential, not material, and would be competitively harmful if publicly disclosed.

The certifications attached as Exhibit 32.1 accompany this Annual Report on Form 10-K pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, and shall not be deemed "filed" by the Registrant for purposes of Section 18 of the Securities Exchange Act of 1934, as amended.

Item 16. Form 10-K Summary

None.

SIGNATURES

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

Date: March 31, 2023

AcelRx Pharmaceuticals, Inc.
(Registrant)

/s/ Vincent J. Angotti

Vincent J. Angotti
Chief Executive Officer and Director
(Principal Executive Officer)

/s/ Raffi Asadorian

Raffi Asadorian
Chief Financial Officer
(Principal Financial and Accounting Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Vincent J. Angotti and Raffi Asadorian, and each of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution for him or her, and in his or her name in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, and any of them, his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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

Signature	Title	Date
/s/ Vincent J. Angotti **Vincent J. Angotti**	Chief Executive Officer and Director *(Principal Executive Officer)*	March 31, 2023
/s/ Raffi Asadorian **Raffi Asadorian**	Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 31, 2023
/s/ Adrian Adams **Adrian Adams**	Chairman	March 31, 2023
/s/ Richard Afable, M.D. **Richard Afable, M.D.**	Director	March 31, 2023
/s/ Marina Bozilenko **Marina Bozilenko**	Director	March 31, 2023
/s/ Jill Broadfoot **Jill Broadfoot**	Director	March 31, 2023
/s/ Stephen J. Hoffman, Ph.D., M.D. **Stephen J. Hoffman, Ph.D., M.D.**	Director	March 31, 2023
/s/ Pamela P. Palmer, M.D., Ph.D. **Pamela P. Palmer, M.D., Ph.D.**	Director	March 31, 2023
/s/ Howard B. Rosen **Howard B. Rosen**	Director	March 31, 2023
/s/ Mark Wan **Mark Wan**	Director	March 31, 2023

ACELRX PHARMACEUTICALS, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of
AcelRx Pharmaceuticals, Inc.
Hayward, California

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of AcelRx Pharmaceuticals, Inc. (the "Company") as of December 31, 2022 and 2021, the related consolidated statements of operations, changes in redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the two years in the period ended December 31, 2022, and the related notes and schedule II (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2022, in conformity with accounting principles generally accepted in the United States of America.

Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has suffered recurring operating losses and negative cash flows from operating activities since inception, and expects to continue incurring operating losses and negative cash flows in the future. These matters raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We are a public accounting firm registered with the 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 audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

Emphasis of the Matter – Restatement of Unaudited Interim Financial Statements

As disclosed in Note 21 of the consolidated financial statements, the unaudited interim financial statements as of and for the periods ended June 30, 2022 and September 30, 2022 have been restated to correct an error within the earnings per share calculation.

Critical Audit Matters

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

Product Revenue Allowances for Chargebacks, Government Rebates and Product Returns

Description of the Matter
As described in Note 1 to the consolidated financial statements, revenue from product sales is recognized net of estimates for variable consideration consisting of chargebacks, government rebates, returns, distribution fees, GPO fees and product returns. This variable consideration is recorded in the same period that the related revenue is recognized and creates variability for the consideration that the Company expects to receive. Liabilities related to government rebates and rebate programs of managed healthcare organizations involve the use of significant assumptions and judgments that include consideration of legal interpretations of applicable laws and regulations, historical claims experience, the payer channel mix, current contract prices, unbilled claims, claims submission time lags, and inventory levels in the distribution channel. Estimates for product returns consider existing return policies with customers, historical sales and return rates, inventory levels in the distribution channel, and product shelf lives.

Management's estimated allowance for chargebacks, government rebates, and product returns requires a high degree of judgment and is subject to change based on various quantitative and qualitative factors. Accordingly, extensive audit effort and a high degree of auditor judgment were needed to evaluate management's estimates and assumptions used in the determination of chargebacks, government rebates, and product returns.

How We Addressed the Matter in Our Audit
We obtained an understanding of and evaluated the design of controls relating to the Company's processes for estimating chargebacks, government rebates, and product returns.

We evaluated the significant accounting policies relating to chargebacks, government rebates, and product returns, as well as management's application of the policies, for appropriateness and reasonableness.

To test management's estimates of chargebacks, rebates and returns, we obtained management's calculations for the respective estimates and performed one or more of the following procedures: clerically tested the calculation, agreed relevant inputs to the terms of relevant contracts, performed retrospective reviews, performed a sensitivity analysis on the inputs and assumptions used in the estimates and assessed subsequent events, evaluated the methodologies and assumptions used and the underlying data used by the Company, evaluated the assumptions used by management against historical trends, evaluated the change in estimated accruals from the prior periods, and assessed the historical accuracy of the Company's estimates against actual results.

/s/ WithumSmith+Brown, PC

We have served as the Company's auditor since 2015.

San Francisco, California
March 31, 2023

PCAOB ID Number 100

AcelRx Pharmaceuticals, Inc.

Consolidated Balance Sheets
(in thousands, except share data)

	December 31, 2022	December 31, 2021
Assets		
Current Assets:		
Cash and cash equivalents	$ 15,275	$ 7,663
Restricted cash	5,000	—
Short-term investments	495	38,967
Accounts receivable, net	309	160
Inventories, net	1,178	1,111
Prepaid expenses and other current assets	2,309	2,588
Total current assets	24,566	50,489
Operating lease right-of-use assets	3,595	4,302
Property and equipment, net	10,261	15,928
In-process research and development asset	8,819	—
Other assets	246	2,174
Restricted cash, net of current portion	—	5,000
Total assets	$ 47,487	$ 77,893
Liabilities and Stockholders' Equity (Deficit)		
Current Liabilities:		
Accounts payable	$ 2,040	$ 2,121
Accrued and other liabilities	4,266	6,524
Long-term debt, current portion	5,763	8,796
Operating lease liabilities, current portion	1,701	1,068
Total current liabilities	13,770	18,509
Long-term debt, net of current portion	—	5,007
Deferred revenue, net of current portion	1,036	1,151
Operating lease liabilities, net of current portion	2,959	3,750
Warrant liability	7,098	—
Liability related to the sale of future royalties	—	85,288
Other long-term liabilities	810	81
Total liabilities	25,673	113,786
Commitments and Contingencies		
Stockholders' Equity (Deficit)*:		
Common stock, $0.001 par value—200,000,000 shares authorized as of December 31, 2022 and 2021; 8,243,680 and 6,840,967 shares issued and outstanding as of December 31, 2022 and 2021, respectively	8	7
Additional paid-in capital	447,635	437,684
Accumulated deficit	(425,829)	(473,584)
Total stockholders' equity (deficit)	21,814	(35,893)
Total Liabilities and Stockholders' Equity (Deficit)	$ 47,487	$ 77,893

* Adjusted to give retroactive effect to a 1-for-20 reverse stock split effective as of 5:01 p.m. Eastern Time on October 25, 2022.

See notes to consolidated financial statements.

AcelRx Pharmaceuticals, Inc.

Consolidated Statements of Operations
(in thousands, except share and per share data)

	Year Ended December 31,	
	2022	**2021**
Revenue:		
Product sales	$ 1,771	$ 1,005
Contract and other collaboration	—	1,813
Total revenue	1,771	2,818
Operating costs and expenses:		
Cost of goods sold	2,591	3,753
Research and development	5,193	4,095
Selling, general and administrative	25,672	30,935
Impairment of property and equipment	4,948	—
Total operating costs and expenses	38,404	38,783
Loss from operations	(36,633)	(35,965)
Other income:		
Interest expense	(1,153)	(2,291)
Interest income and other income, net	366	124
Non-cash interest income on liability related to sale of future royalties	1,136	3,038
Gain on extinguishment of liability related to the sale of future royalties	84,052	—
Total other income	84,401	871
Net income (loss) before provision for income taxes	47,768	(35,094)
Provision for income taxes	13	5
Net income (loss)	$ 47,755	$ (35,099)
Deemed dividend related to Series A Redeemable Convertible Preferred Stock	(186)	—
Income allocated to participating securities	(5,240)	—
Net income (loss) attributable to Common Shareholders, basic	$ 42,329	$ (35,099)
Net income (loss) per share of common stock, basic	$ 5.73	$ (5.86)
Shares used in computing net income (loss) per share of common stock, basic–(Note 16)	7,385,348	5,993,013
Net income (loss) attributable to Common Shareholders, diluted	$ 42,342	$ (35,099)
Net income (loss) per share of common stock, diluted	$ 5.72	$ (5.86)
Shares used in computing net income (loss) per share of common stock, diluted –(Note 16)	7,406,986	5,993,013

See notes to consolidated financial statements.

AcelRx Pharmaceuticals, Inc.

Consolidated Statements of Changes in Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands, except share data)
1-for-20 reverse stock split reflected for all years presented

	Series A Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount			
Balance as of December 31, 2020	—	$ —	4,940,590	$ 5	$ 382,730	$ (438,485)	$ (55,750)
Stock-based compensation	—	—	—	—	4,609	—	4,609
Issuance of common stock upon vesting of restricted stock units, net of shares withheld for employee taxes	—	—	24,433	—	(249)	—	(249)
Net proceeds from issuance of common stock in connection with equity financings	—	—	1,860,078	2	44,714	—	44,716
Net proceeds from issuance of warrants in connection with equity financings	—	—	—	—	5,562	—	5,562
Issuance of common stock upon exercise of stock options	—	—	969	—	17	—	17
Issuance of common stock upon ESPP purchase	—	—	14,897	—	301	—	301
Net loss	—	—	—	—	—	(35,099)	(35,099)
Balance as of December 31, 2021	—	—	6,840,967	7	437,684	(473,584)	(35,893)
Issuance of Series A Redeemable Convertible Preferred Stock and Warrants	3,000	129	—	—	110	—	110
Deemed dividends related to Series A Redeemable Convertible Preferred Stock		186			(186)		(186)
Redemption of Series A Redeemable Convertible Preferred Stock and Warrants	(3,000)	(315)	—	—	—	—	—
Stock-based compensation	—	—	—	—	2,889	—	2,889
Issuance of common stock in connection with asset purchase	—	—	481,026	—	5,511	—	5,511
Net proceeds from issuance of common stock and pre-funded warrants in connection with equity financings	—	—	873,074	1	789	—	790
Modification of equity-classified warrants	—	—	—	—	822	—	822
Issuance of common stock upon vesting of restricted stock units, net of shares withheld for employee taxes	—	—	37,672	—	(58)	—	(58)
Issuance of common stock upon ESPP purchase	—	—	10,941	—	74	—	74
Net income	—	—	—	—	—	47,755	47,755
Balance as of December 31, 2022	—	$ —	8,243,680	$ 8	$ 447,635	$ (425,829)	$ 21,814

See notes to consolidated financial statements.

AcelRx Pharmaceuticals, Inc.

Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,	
	2022	**2021**
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net income (loss)	$ 47,755	$ (35,099)
Adjustments to reconcile net income (loss) to net cash used in operating activities:		
Non-cash royalty revenue related to royalty monetization	—	(83)
Non-cash interest income on liability related to royalty monetization	(1,136)	(3,038)
Depreciation and amortization	1,647	1,973
Non-cash interest expense related to debt financing	393	761
Non-cash issuance costs for warrant liability	775	—
Stock-based compensation	2,889	4,609
Non-cash gain on termination of liability related to royalty monetization	(84,152)	—
Impairment of property and equipment	4,948	—
Inventory impairment charge	—	810
Other	(60)	(138)
Changes in operating assets and liabilities:		
Accounts receivable	(149)	475
Inventories	(107)	(295)
Prepaid expenses and other assets	299	(908)
Accounts payable	551	111
Accrued liabilities	(1,613)	79
Operating lease liabilities	(285)	(447)
Deferred revenue	(86)	1,188
Net cash used in operating activities	(28,331)	(30,002)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchase of property and equipment	(364)	(1,827)
Purchase of investments	(7,861)	(70,459)
Cash paid for asset acquisition, net of cash acquired	(1,687)	(821)
Proceeds from sale of investments	—	2,996
Proceeds from maturities of investments	46,362	43,988
Net cash provided by (used in) investing activities	36,450	(26,123)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Payment of long-term debt	(8,433)	(8,833)
Net proceeds from issuance of Series A Redeemable Convertible Preferred Stock and Warrants	239	—
Redemption of Series A Redeemable Convertible Preferred Stock	(315)	—
Proceeds from issuance of common stock, accompanying warrants and pre-funded warrants in December 2022 registered direct offering	7,528	—
Net proceeds from issuance of common stock and warrants in connection with November 2021 registered direct offering	—	13,918
Net proceeds from issuance of common stock and warrants in connection with 2021 underwritten public offering	—	28,886
Net proceeds from issuance of common stock in connection with at-the-market sales agreement.	458	7,474
Net proceeds from issuance of common stock through equity plans	74	318
Tax payments related to shares withheld for restricted stock units vested	(58)	(249)
Net cash (used in) provided by financing activities	(507)	41,514
NET INCREASE (DECREASE) IN CASH, CASH EQUIVALENTS AND RESTRICTED CASH	7,612	(14,611)
CASH, CASH EQUIVALENTS AND RESTRICTED CASH —Beginning of year	12,663	27,274
CASH, CASH EQUIVALENTS AND RESTRICTED CASH —End of year	$ 20,275	$ 12,663
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:		
Cash paid for interest	$ 824	$ 1,595
Income taxes paid	$ 13	$ 5
NONCASH INVESTING AND FINANCING ACTIVITIES:		
Purchases of property and equipment in accounts payable and accrued expenses	$ 825	$ 1,095
Equity issuance costs from modification of November 2021 Financing Warrants	$ 47	$ —
Equity issuance costs in accounts payable and accrued expenses	$ 51	$ —
Liability for held back shares in connection with asset acquisition in other long-term liabilities	$ 800	$ —
Issuance of common stock in connection with asset acquisition	$ 5,511	$ —
Asset acquisition costs in accounts payable and accrued expenses	$ —	$ 1,087
Establishment of right-of-use asset and lease liability	$ 127	$ 4,669
Write-off of right-of-use asset and lease liability	$ —	$ (3,128)
Gain on termination of sublease	$ —	$ 522

See notes to consolidated financial statements.

1. Organization and Summary of Significant Accounting Policies

The Company

AcelRx Pharmaceuticals, Inc., or the Company, or AcelRx, was incorporated in Delaware on July 13, 2005 as SuRx, Inc. The Company subsequently changed its name to AcelRx Pharmaceuticals, Inc. The Company's operations are based in Hayward, California.

AcelRx is a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for use in medically supervised settings. DSUVIA® (known as DZUVEO® in Europe) is focused on the treatment of acute pain, and utilizes sufentanil, delivered via a non-invasive route of sublingual administration, exclusively for use in medically supervised settings. On November 2, 2018, the U.S. Food and Drug Administration, or FDA, approved DSUVIA for use in adults in a certified medically supervised healthcare setting, such as hospitals, surgical centers, and emergency departments, for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. The commercial launch of DSUVIA in the United States occurred in the first quarter of 2019. In June 2018, the European Commission, or EC, granted marketing approval of DZUVEO for the management of acute moderate to severe pain in adults in medically monitored settings. Zalviso was approved in Europe and was commercialized by Grünenthal GmbH, or Grünenthal, through May 12, 2021 (see *Termination of Grünenthal Agreements* below). In July 2022, the European Marketing Authorization for Zalviso was withdrawn.

On March 12, 2023, the Company entered into an asset purchase agreement, or the DSUVIA Agreement, with Vertical Pharmaceuticals, LLC, a wholly owned subsidiary of Alora Pharmaceuticals, LLC, or together Alora, pursuant to which Alora will acquire certain assets and assume certain liabilities relating to DSUVIA or DZUVEO, or any other single-dose pharmaceutical product for use in medically supervised settings containing a sublingual tablet that includes sufentanil as the sole active ingredient, as a 30 mcg tablet or other dosage form or strength as reasonably necessary for lifecycle management, or the Product. See Note 20, "Subsequent Events" below.

In July 2021, the Company entered into a License and Commercialization Agreement with Laboratoire Aguettant, or Aguettant, for Aguettant to commercialize DZUVEO in the European Union, Norway, Iceland, Liechtenstein, Andorra, Vatican City, Monaco, Switzerland and the United Kingdom, or the DZUVEO Agreement. See Note 20, "Subsequent Events" below.

In July 2021, the Company also entered into a separate License and Commercialization Agreement with Aguettant, or the PFS Agreement, pursuant to which the Company obtained the exclusive right to develop and, subject to FDA approval, commercialize in the United States (i) an ephedrine pre-filled syringe containing 10 ml of a solution of 3 mg/ml ephedrine hydrochloride for injection, and (ii) a phenylephrine pre-filled syringe containing 10 ml of a solution of 50 mcg/ml phenylephrine hydrochloride for injection. Aguettant will supply the Company with the products for use in commercialization and, if they are approved in the U.S., Aguettant is entitled to receive up to $24 million in sales-based milestone payments. See Note 20, "Subsequent Events" below.

On January 7, 2022, the Company acquired Lowell Therapeutics, Inc., or Lowell, a privately held company (see Note 4, "Asset Acquisition" below), and, as a result acquired Niyad™, a regional anticoagulant for the dialysis circuit during continuous renal replacement therapy, or CRRT, for acute kidney injury, or AKI, patients in the hospital, and for chronic kidney disease patients undergoing intermittent hemodialysis, or IHD, in dialysis centers. The Company plans to study Niyad, which has received Breakthrough Device Designation status from the FDA and an ICD-10 procedural code from the U.S. Centers for Medicare & Medicaid Services, under an investigational device exemption. While not approved for commercial use in the United States, the active drug component of Niyad, nafamostat, has been approved in Japan and South Korea as a regional anticoagulant for the dialysis circuit, disseminated intravascular coagulation, and acute pancreatitis. Niyad is a lyophilized formulation of nafamostat, a broad-spectrum, synthetic serine protease inhibitor, which has a half-life of 8 minutes, with anticoagulant, anti-inflammatory and potential anti-viral activities. In addition, the Company acquired LTX-608, a proprietary nafamostat formulation for direct IV infusion that it intends to develop for the treatment of acute respiratory distress syndrome, or ARDS, and disseminated intravascular coagulation, or DIC.

Termination of Grünenthal Agreements

On December 16, 2013, AcelRx and Grünenthal entered into a Collaboration and License Agreement, or the License Agreement, which was amended effective July 17, 2015, and September 20, 2016, or the Amended License Agreement, which granted Grünenthal rights to commercialize Zalviso in Europe. In September 2015, the European Commission granted marketing approval for the marketing authorization application, or MAA, for Zalviso for the management of acute moderate-to-severe post-operative pain in adult patients. On December 16, 2013, AcelRx and Grünenthal entered into a Manufacture and Supply Agreement, or the MSA, which was amended effective July 15, 2015, or the Amended MSA, and together with the Amended License Agreement, the Grünenthal Agreements. Under the Amended MSA, the Company exclusively manufactured and supplied Zalviso for Grünenthal's European sales.

On May 18, 2020, the Company received a notice from Grünenthal that it had exercised its right to terminate the Grünenthal Agreements, effective November 13, 2020. The terms of the Grünenthal Agreements were extended to May 12, 2021 to enable Grünenthal to sell down its Zalviso inventory, a right it had under the Grünenthal Agreements. The rights to market and sell Zalviso in the Zalviso Territory reverted back to the Company on May 12, 2021. In July 2022, the European Marketing Authorization for Zalviso was withdrawn.

Termination of Royalty Monetization

On September 18, 2015, the Company sold the majority of the royalty rights and certain commercial sales milestones it was entitled to receive under the Amended License Agreement with Grünenthal to PDL BioPharma, Inc., or PDL, in a transaction referred to as the Royalty Monetization. On August 31, 2020, PDL announced it sold its royalty interest for Zalviso to SWK Funding, LLC, or SWK. On May 31, 2022, the Company entered into a Termination Agreement with SWK to fully terminate the Royalty Monetization for which the Company paid cash consideration of $0.1 million. Neither PDL nor SWK retains any further interest in the Royalty Monetization. Accordingly, effective May 31, 2022, the Royalty Monetization is no longer reflected on the Company's consolidated financial statements or other records as a sale of assets to PDL or SWK, and all security interests and other liens of every type held by the parties to the Royalty Monetization have been terminated and automatically released without further action by any party. The $84.1 million gain on extinguishment of the liability related to the sale of future royalties is recognized in the consolidated statements of operations as other income.

Liquidity and Going Concern

The consolidated financial statements for the year ended December 31, 2022 were prepared on the basis of a going concern, which contemplates that the Company will be able to realize assets and discharge liabilities in the normal course of business. The termination of the Royalty Monetization resulted in net income for the year ended December 31, 2022; however, before this, the Company had incurred recurring operating losses and negative cash flows from operating activities since inception and expects to continue to incur operating losses and negative cash flows in the future. These conditions raise substantial doubt about the Company's ability to continue as a going concern. Considering the Company's current cash resources and its current and expected levels of operating expenses for the next twelve months, management expects to need additional capital to fund its planned operations prior to the 12 month anniversary of the date this Annual Report on Form 10-K is filed with the United States Securities and Exchange Commission, or the SEC. Management may seek to raise such additional capital through public or private equity offerings, including under the Controlled Equity Offering℠ Sales Agreement, or the ATM Agreement, with Cantor Fitzgerald & Co., or Cantor, debt securities, monetize or securitize certain assets, refinance its loan agreement, enter into product development, license or distribution agreements with third parties, or divest DSUVIA in the United States, DZUVEO in Europe, or any of the Company's product candidates. While management believes its plans to raise additional funds will alleviate the conditions that raise substantial doubt about the Company's ability to continue as a going concern, these plans are not entirely within the Company's control and cannot be assessed as being probable of occurring. Additional funds may not be available when the Company needs them on terms that are acceptable to the Company, or at all. If adequate funds are not available, the Company may be required to further reduce its workforce, reduce the scope of, or cease, the commercial launch of DSUVIA, or delay the development of its regulatory filing plans for its product candidates in advance of the date on which the Company's cash resources are exhausted to ensure that the Company has sufficient capital to meet its obligations and continue on a path designed to preserve stockholder value. In addition, if additional funds are raised through collaborations, strategic alliances or licensing arrangements with third parties, the Company may have to relinquish rights to its technologies, future revenue streams or product candidates, or to grant licenses on terms that may not be favorable to the Company.

Reverse Stock Split

On September 23, 2022, at a special meeting of stockholders, the Company's stockholders authorized the Company's Board of Directors to effect a reverse stock split of all outstanding shares of common stock in a range of 1-for-10 to 1-for-30. The Board of Directors subsequently approved a reverse stock split with a ratio of 1-for-20, or the Reverse Stock Split. On October 25, 2022, following the filing of a certificate of amendment to the Company's amended and restated certificate of incorporation, every 20 shares of the Company's common stock that were issued and outstanding automatically converted into one outstanding share of common stock. The Reverse Stock Split affected all shares of common stock outstanding immediately prior to the effective time of the Reverse Stock Split, as well as the number of shares of common stock available for issuance under the Company's equity incentive and employee stock purchase plans. Outstanding stock options, restricted stock units and warrants were proportionately reduced and the respective exercise prices, if applicable, were proportionately increased. The Reverse Stock Split affected all holders of common stock uniformly and did not affect any stockholder's percentage of ownership interest. The par value of the Company's common stock remained unchanged at $0.001 per share and the number of authorized shares of common stock remained the same after the Reverse Stock Split.

As the par value per share of the Company's common stock remained unchanged at $0.001 per share, the change in the common stock recorded at par value has been reclassified to additional paid-in capital on a retroactive basis. All references to shares of common stock, stock options, restricted stock units and warrants and per share data for all periods presented in the accompanying consolidated financial statements and notes thereto have been adjusted to reflect the Reverse Stock Split on a retroactive basis.

Basis of Presentation

The preparation of financial statements in conformity with accounting principles generally accepted in the United States, or GAAP, requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and the accompanying notes. Actual results could differ from those estimates.

Reclassifications

Certain prior year amounts in the consolidated financial statements have been reclassified to conform to the current year's presentation. In particular, the restricted cash classified as "Cash and cash equivalents" has been reclassified to "Restricted cash, net of current portion" in the consolidated balance sheets as of December 31, 2021 and in the consolidated statement of cash flows as of December 31, 2022 and December 31, 2021. See "—Cash, Cash Equivalents and Restricted Cash" below.

Principles of Consolidation

The consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries. All intercompany accounts 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 the amounts reported in the consolidated financial statements and accompanying notes. Management believes its most significant accounting estimates relate to revenue recognition, inventory valuation and the liability related to the sale of future royalties. Management evaluates its estimates on an ongoing basis including critical accounting policies. Estimates are based on historical experience and on various other market-specific and other relevant assumptions that the Company believes to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results could differ from those estimates.

Cash, Cash Equivalents, Restricted Cash and Short-Term Investments

The Company considers all highly liquid investments with an original maturity (at date of purchase) of three months or less to be cash equivalents. Cash and cash equivalents consist of cash on deposit with banks.

On May 30, 2019, the Company entered into a Loan Agreement with Oxford Finance LLC, or Oxford, or the Lender. The Loan Agreement requires that the Company always maintain unrestricted cash of not less than $5.0 million in accounts subject to control agreements in favor of the Lender, tested monthly as of the last day of the month. The Company has classified these unrestricted funds as restricted cash on the consolidated balance sheets.

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported within the consolidated balance sheets that sum to the total of the same such amounts in the consolidated statements of cash flows:

	Balance as of	
	December 31, 2022	December 31, 2021
Cash and cash equivalents	$ 15,275	$ 7,663
Restricted cash	5,000	—
Restricted cash, net of current portion	—	5,000
Total cash, cash equivalents, and restricted cash	$ 20,275	$ 12,663

All marketable securities are classified as available for sale and consist of commercial paper, U.S. government sponsored enterprise debt securities and corporate debt securities. These securities are carried at estimated fair value, which is based on quoted market prices or observable market inputs of almost identical assets, with unrealized gains and losses included in accumulated other comprehensive income (loss). The amortized cost of securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion is included in interest income or expense. The cost of securities sold is based on specific identification. The Company's investments are subject to a periodic impairment review for other-than-temporary declines in fair value. The Company's review includes the consideration of the cause of the impairment including the creditworthiness of the security issuers, the number of securities in an unrealized loss position, the severity and duration of the unrealized losses and the Company's intent and ability to hold the investment for a period of time sufficient to allow for any anticipated recovery in the market value. When the Company determines that the decline in fair value of an investment is below its accounting basis and this decline is other than temporary, it reduces the carrying value of the security it holds and records a loss in the amount of such decline.

Fair Value of Financial Instruments

The Company measures and reports its cash equivalents, investments and financial liabilities at fair value. Fair value is defined as the exchange price that would be received for an asset or an exit price paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. The fair value hierarchy defines a three-level valuation hierarchy for disclosure of fair value measurements as follows:

Level I—Unadjusted quoted prices in active markets for identical assets or liabilities;

Level II—Inputs other than quoted prices included within Level I that are observable, unadjusted quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and

Level III—Unobservable inputs that are supported by little or no market activity for the related assets or liabilities.

The categorization of a financial instrument within the valuation hierarchy is based upon the lowest level of input that is significant to the fair value measurement.

Segment Information

The Company operates in a single segment, the development and commercialization of innovative therapies for use in medically supervised settings. The Company's product sales revenue consists of sales of DSUVIA in the United States, DZUVEO in Europe by Aguettant, and, through May 2021, sales of Zalviso in Europe by Grünenthal. The Company's contract and collaboration revenue consists of non-cash royalty revenue, royalty revenue, and other revenue under the Grünenthal Agreements and license revenue under the DZUVEO Agreement. See Note 8, "Revenue from Contracts with Customers" below.

Concentration of Risk

The Company invests cash that is currently not being used for operational purposes in accordance with its investment policy in debt securities of U.S. government sponsored agencies, commercial paper and overnight deposits. The Company is exposed to credit risk in the event of default by the institutions holding the cash equivalents and available-for-sale securities to the extent recorded on the consolidated balance sheets. The Company has significant cash balances at financial institutions which throughout the year regularly exceed the federally insured limit of $250,000. Any loss incurred or a lack of access to such funds could have a significant adverse impact on the Company's financial condition, results of operations, and cash flows.

The Company relies on a single third-party supplier for the supply of sufentanil, the active pharmaceutical ingredient in DSUVIA and various sole-source third-party contract manufacturer organizations to manufacture the DSUVIA single-dose applicator, or SDA.

DSUVIA sales are concentrated with the DoD and with a limited number of wholesalers in the United States. Zalviso was sold in Europe by Grünenthal through May 2021. In July 2021, Aguettant was granted an exclusive license to commercialize DZUVEO in Europe. DZUVEO sales in Europe by Aguettant have recently commenced.

Revenue and accounts receivable have been concentrated with these customers.

Revenues from customers that accounted for 10% or more of the Company's total revenues during the years ended December 31, 2022 and 2021 were as follows:

	Year Ended December 31,	
Percent of Total Revenue	**2022**	**2021**
Aguettant	10%	62%
Grünenthal	0%	12%
Wholesaler A	25%	16%
Wholesaler B	12%	8%
Distributor A	28%	5%
Distributor B	12%	2%

Accounts Receivable, Net

The need for a bad debt allowance is evaluated each reporting period based on the Company's assessment of the creditworthiness of its customers or any other potential circumstances that could result in bad debt.

The Company believes that the entire accounts receivable balance as of December 31, 2022 is collectible, and there was no bad debt allowance provided as of December 31, 2022 or 2021.

Accounts receivable, net from customers that accounted for 10% or more of the Company's total accounts receivable balance as of December 31, 2022 and 2021 were as follows:

	As of December 31,	
Percent of Accounts Receivable, Net	**2022**	**2021**
Customer A	58%	0%
Customer B	19%	73%
Customer C	15%	9%

Inventories, Net

Inventories are valued at the lower of cost or net realizable value. Cost is determined using the first-in, first-out method for all inventories. Inventory includes the cost of the active pharmaceutical ingredients, or API, raw materials and third-party contract manufacturing and packaging services. Indirect overhead costs associated with production and distribution are allocated to the appropriate cost pool and then absorbed into inventory based on the units produced or distributed, assuming normal capacity, in the applicable period. Indirect overhead costs in excess of normal capacity are recorded as period costs in the period incurred.

The Company's policy is to write down inventory that has become obsolete, inventory that has a cost basis in excess of its expected net realizable value and inventory in excess of expected requirements. The Company periodically evaluates the carrying value of inventory on hand for potential excess amount over demand using the same lower of cost or net realizable value approach as that used to value the inventory.

Property and Equipment, Net

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets, generally three to five years. Leasehold improvements are amortized over the shorter of the estimated useful life of the improvements or the remaining lease term. Expenditures for repairs and maintenance, which do not extend the useful life of the property and equipment, are expensed as incurred. Upon retirement, the asset cost and related accumulated depreciation are relieved from the accompanying consolidated balance sheets. Gains and losses associated with dispositions are reflected as a component of interest income and other income, net in the accompanying consolidated statements of operations.

Impairment of Long-Lived Assets

The Company periodically assesses the impairment of long-lived assets and, if indicators of asset impairment exist, the Company assesses the recoverability of the affected long-lived assets by determining whether the carrying value of such assets can be recovered through an analysis of the undiscounted future expected operating cash flows. If impairment is indicated, the Company records the amount of such impairment for the excess of the carrying value of the asset over its estimated fair value. See Note 5, "Property and Equipment, Net" below.

Acquisitions

The Company evaluates acquisitions of assets and other similar transactions to assess whether or not the transaction should be accounted for as a business combination or asset acquisition by first applying a screen test to determine whether substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset or group of similar identifiable assets. If so, the transaction is accounted for as an asset acquisition. If not, further determination is required as to whether or not the Company has acquired inputs and processes that have the ability to create outputs, which would meet the definition of a business. Significant judgment is required in the application of the screen test to determine whether an acquisition is a business combination or an acquisition of assets.

Acquisitions meeting the definition of business combinations are accounted for using the acquisition method of accounting, which requires that the purchase price be allocated to the net assets acquired at their respective fair values. In a business combination, any excess of the purchase price over the estimated fair values of the net assets acquired is recorded as goodwill.

For asset acquisitions, a cost accumulation model is used to determine the cost of an asset acquisition. Direct transaction costs are recognized as part of the cost of an asset acquisition. The Company also evaluates which elements of a transaction should be accounted for as a part of an asset acquisition and which should be accounted for separately. The cost of an asset acquisition, including transaction costs, is allocated to identifiable assets acquired and liabilities assumed based on a relative fair value basis. Goodwill is not recognized in an asset acquisition. Any difference between the cost of an asset acquisition and the fair value of the net assets acquired is allocated to the non-monetary identifiable assets based on their relative fair values. When a transaction accounted for as an asset acquisition includes an in-process research and development, or IPR&D, asset, the IPR&D asset is only capitalized if it has an alternative future use other than in a particular research and development project. For an IPR&D asset to have an alternative future use (a) the Company must reasonably expect that it will use the asset acquired in the alternative manner and anticipate economic benefit from that alternative use, and (b) the Company's use of the asset acquired is not contingent on further development of the asset subsequent to the acquisition date (that is, the asset can be used in the alternative manner in the condition in which it existed at the acquisition date). Otherwise, amounts allocated to IPR&D that have no alternative use are expensed. Asset acquisitions may include contingent consideration arrangements that encompass obligations to make future payments to sellers contingent upon the achievement of future financial targets. Contingent consideration is not recognized until all contingencies are resolved and the consideration is paid or probable of payment, at which point the consideration is allocated to the assets acquired on a relative fair value basis.

Leases

The Company follows the provisions of Accounting Standards Update, or ASU, 2016-02, *Leases (Topic 842)*. At the inception of an arrangement, the Company determines whether the arrangement is, or contains, a lease based on the unique facts and circumstances present. Operating lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the expected lease term. The interest rate implicit in lease contracts is typically not readily determinable. As such, the Company utilizes its incremental borrowing rate, which is the rate incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment. Certain adjustments to the right-of-use asset may be required for items such as initial direct costs paid or incentives received.

Lease expense is recognized over the expected term on a straight-line basis. Operating leases are recognized on the consolidated balance sheets as operating lease right-of-use assets, operating lease liabilities current and operating lease liabilities non-current.

Revenue from Contracts with Customers

The Company follows the provisions of Accounting Standards Codification, or ASC, Topic 606, *Revenue from Contracts with Customers*. This guidance provides a unified model to determine how revenue is recognized. The Company recognizes revenue upon transfer of control of promised products or services to customers in an amount that reflects the consideration the Company expects to receive in exchange for those products or services. The Company sells its products primarily through wholesale and specialty distributors.

In determining the appropriate amount of revenue to be recognized as it fulfills its obligations under its agreements, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations, including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation.

Product Sales Revenue

The Company sells its product primarily through distributors. Revenues from product sales are recognized when distributors obtain control of the Company's product, which occurs at a point in time, upon delivery to such distributors. These distributors subsequently resell the product to certified medically supervised healthcare settings. In addition to distribution agreements with these customers, the Company enters into arrangements with group purchasing organizations, or GPOs, and other certified medically supervised healthcare settings that provide for privately negotiated discounts with respect to the purchase of its products. For revenue recognition under bill-and-hold arrangements, wherein the customer agrees to buy product from the Company but requests delivery at a later date, the Company deems that control passes to the customer when the product is ready for delivery. The Company recognizes revenue under these types of arrangements when a signed agreement is in place, the transaction is billable, the customer has significant risk and rewards for the product and the ability to direct the asset, the product has been set aside specifically for the customer, and the product cannot be redirected to another customer. Revenue from product sales is recorded at the transaction price, net of estimates for variable consideration consisting of chargebacks, government rebates, returns, distribution fees, GPO fees and product returns. Variable consideration is recorded at the time product sales are recognized resulting in a reduction in product revenue. The amount of variable consideration that is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Variable consideration is estimated using the most-likely amount method, which is the single-most likely outcome under a contract and is typically at the stated contractual rate. Where appropriate, these estimates take into consideration a range of possible outcomes that are probability-weighted in accordance with the expected value method under ASC Topic 606 for relevant factors. These factors include current contractual and statutory requirements, specific known market events and trends, industry data, and/or forecasted customer buying and payment patterns. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results vary materially from the Company's estimates, the Company will adjust these estimates, which will affect revenue from product sales and earnings in the period such estimates are adjusted. These estimates include:

Chargebacks – The Company's customers subsequently resell its product to qualified healthcare providers. In addition to distribution agreements with customers, the Company enters into arrangements with qualified healthcare providers that provide discounts with respect to the purchase of its product. Chargebacks represent the estimated obligations resulting from contractual commitments to sell product to qualified healthcare providers at prices lower than the list prices charged to customers who directly purchase the product from the Company. Customers charge the Company for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue-related accrued liabilities on the consolidated balance sheets. Chargeback amounts are determined at the time of resale to the qualified healthcare providers by customers, and the Company issues credits for such amounts generally within a few weeks of the customer's notification to the Company of the resale. Reserves for chargebacks consists of credits that the Company expects to issue for units that remain in the distribution channel inventories at each reporting period end that the Company expects will be sold to the qualified healthcare providers, and chargebacks for units that the Company's customers have sold to the qualified healthcare providers, but for which credits have not been issued.

Government Rebates – The Company is subject to discount obligations under state Medicaid programs. The Company estimates its Medicaid rebates, and reserves are recorded in the same period the related product revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability that is included in accrued liabilities on the consolidated balance sheets.

Returns – The Company allows its distributors to return product for credit 6 months prior to, and up to 12 months after, the product expiration date. As such, there may be a significant period of time between the time the product is shipped and the time the credit is issued on returned product.

Distribution Fees – Distribution fees include fees paid to certain customers for sales order management, data and distribution services. Distribution fees are recorded as a reduction of revenue in the period the related product revenue is recognized.

GPO Fees – The Company pays administrative fees to GPOs for services and access to data. These fees are based on contracted terms and are paid after the quarter in which the product was purchased by the GPOs' members.

Trade Discounts and Allowances - The Company provides its customers with discounts which include early payment incentives that are explicitly stated in its contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized.

The Company believes its estimated allowances for chargebacks, government rebates and product returns require a high degree of judgment and are subject to change based on its limited experience and certain quantitative and qualitative factors. The Company believes its estimated allowances for distribution fees, GPO fees and trade discounts and allowances do not require a high degree of judgment because the amounts are settled within a relatively short period of time. The Company will continue to assess its estimates of variable consideration as it accumulates additional historical data and will adjust these estimates accordingly. Changes in product revenue allowance estimates could materially affect the Company's results of operations and financial position.

Contract and Other Collaboration Revenue

The Company generates revenue from collaboration agreements. These agreements typically include payments for upfront signing or license fees, cost reimbursements for development and manufacturing services, milestone payments, product sales, and royalties on licensee's future product sales. Product sales related revenue under these collaboration agreements is classified as product sales revenue, while other revenue generated from collaboration agreements is classified as contract and other collaboration revenue.

Performance Obligations

A performance obligation is a promise in a contract to transfer a distinct good or service to the customer and is the unit of account in ASC Topic 606. The Company's performance obligations include delivering products to its distributors, commercialization license rights, development services, services associated with the regulatory approval process, joint steering committee services, demonstration devices, manufacturing services, material rights for discounts on manufacturing services, and product supply.

The Company has optional additional items in contracts, which are considered marketing offers and are accounted for as separate contracts when the customer elects such options. Arrangements that include a promise for future commercial product supply and optional research and development services at the customer's or the Company's discretion are generally considered as options. The Company assesses if these options provide a material right to the licensee and if so, such material rights are accounted for as separate performance obligations. If the Company is entitled to additional payments when the customer exercises these options, any additional payments are recorded in revenue when the customer obtains control of the goods or services.

Transaction Price

The Company has both fixed and variable consideration. Variable consideration for product revenue is described as Net product sales in the consolidated statements of operations. For collaboration agreements, non-refundable upfront fees and product supply selling prices are considered fixed, while milestone payments are identified as variable consideration when determining the transaction price. Funding of research and development activities is considered variable until such costs are reimbursed at which point, they are considered fixed. The Company allocates the total transaction price to each performance obligation based on the relative estimated standalone selling prices of the promised goods or services for each performance obligation.

At the inception of each arrangement that includes milestone payments, the Company evaluates whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the value of the associated milestone (such as a regulatory submission by the Company) is included in the transaction price. Milestone payments that are not within the control of the Company, such as approvals from regulators, are not considered probable of being achieved until those approvals are received.

For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (a) when the related sales occur, or (b) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

Allocation of Consideration

As part of the accounting for collaboration arrangements, the Company must develop assumptions that require judgment to determine the stand-alone selling price of each performance obligation identified in the contract. Estimated selling prices for license rights and material rights for discounts on manufacturing services are calculated using an income approach model and can include the following key assumptions: the development timeline, sales forecasts, costs of product sales, commercialization expenses, discount rate, the time which the manufacturing services are expected to be performed, and probabilities of technical and regulatory success. For all other performance obligations, the Company uses a cost-plus margin approach.

Timing of Recognition

Significant management judgment is required to determine the level of effort required under collaboration arrangements and the period over which the Company expects to complete its performance obligations under the arrangement. The Company estimates the performance period or measure of progress at the inception of the arrangement and re-evaluates it each reporting period. This re-evaluation may shorten or lengthen the period over which revenue is recognized. Changes to these estimates are recorded on a cumulative catch-up basis. If the Company cannot reasonably estimate when its performance obligations either are completed or become inconsequential, then revenue recognition is deferred until the Company can reasonably make such estimates. Revenue is then recognized over the remaining estimated period of performance using the cumulative catch-up method. Revenue is recognized for products at a point in time when control of the product is transferred to the customer in an amount that reflects the consideration the Company expects to be entitled to in exchange for those product sales, which is typically once the product physically arrives at the customer, and for licenses of functional intellectual property at the point in time the customer can use and benefit from the license. For performance obligations that are services, revenue is recognized over time proportionate to the costs that the Company has incurred to perform the services using the cost-to-cost input method.

Cost of Goods Sold

Cost of goods sold for product revenue includes third-party manufacturing costs, shipping and handling costs, and indirect overhead costs associated with production and distribution which are allocated to the appropriate cost pool and recognized when revenue is recognized. Indirect overhead costs in excess of normal capacity are recorded as period costs in the period incurred.

Under the Grünenthal Agreements, the Company sold Zalviso to Grünenthal at predetermined, contractual transfer prices that were less than the direct costs of manufacturing and recognized indirect costs as period costs where they were in excess of normal capacity and not recoverable on a lower of cost or net realizable value basis. Cost of goods sold for Zalviso shipped to Grünenthal included the inventory costs of API, third-party contract manufacturing costs, packaging and distribution costs, shipping, handling and storage costs, depreciation and costs of the employees involved with production.

Research and Development Expenses

Research and development costs are charged to expense when incurred. Research and development expenses include salaries, employee benefits, including stock-based compensation, consultant fees, laboratory supplies, costs associated with clinical trials and manufacturing, including contract research organization fees, other professional services and allocations of corporate costs. The Company reviews and accrues clinical trial expenses based on work performed, which relies on estimates of total costs incurred based on patient enrollment, completion of patient studies and other events.

Stock-Based Compensation

Compensation expense for all stock-based payment awards made to employees and directors, including employee stock options and restricted stock units related to the 2020 Equity Incentive Plan, or 2020 EIP, the 2011 Equity Incentive Plan, or 2011 EIP, and employee share purchases related to the Amended and Restated 2011 Employee Stock Purchase Plan, or ESPP, is based on estimated fair values at grant date. The Company determines the grant date fair value of the awards using the Black-Scholes option-pricing model and generally recognizes the fair value as stock-based compensation expense on a straight-line basis over the vesting period of the respective awards. The Company applies the graded-vesting attribution method to awards with market conditions that include graded-vesting features. Additionally, the Company uses the Monte Carlo Simulation model to evaluate the derived service period and fair value of awards with market conditions, including assumptions of historical volatility and risk-free interest rate commensurate with the vesting term.

The Black-Scholes option pricing model requires inputs such as expected term, expected volatility and risk-free interest rate. These inputs are subjective and generally require significant analysis and judgment to develop. The expected term, which represents the period of time that options granted are expected to be outstanding, is derived by analyzing the historical experience of similar awards, giving consideration to the contractual terms of the stock-based awards, vesting schedules and expectations of future employee behavior. Expected volatilities are estimated using the historical stock price performance over the expected term of the option, which are adjusted as necessary for any other factors which may reasonably affect the volatility of AcelRx's stock in the future. The risk-free interest rate is based on the U.S. Treasury yield in effect at the time of the grant for the expected term of the award. The Company recognizes forfeitures when they occur and does not anticipate paying dividends in the near future.

Warrants Issued in Connection with Financings

The Company accounts for issued warrants as either liability or equity in accordance with ASC 480-10, *Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity*, or ASC 815-40, *Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock*. Under ASC 480-10, warrants are considered liability if they are mandatorily redeemable and they require settlement in cash or other assets, or a variable number of shares. If warrants do not meet liability classification under ASC 480-10, the Company considers the requirements of ASC 815-40 to determine whether the warrants should be classified as liability or equity. Under ASC 815-40, contracts that may require settlement for cash are liabilities, regardless of the probability of the occurrence of the triggering event. Liability classified warrants are measured at fair value on the issuance date and at the end of each reporting period. Any change in the fair value of the warrants after the issuance date is recorded in the consolidated statements of operations. If warrants do not require liability classification under ASC 815-40, in order to conclude warrants should be classified as equity, the Company assesses whether the warrants are indexed to its common stock and whether the warrants are classified as equity under ASC 815-40 or other applicable GAAP. Equity classified warrants are accounted for at fair value on the issuance date with no changes in fair value recognized after the issuance date.

Restructuring Costs

The Company's restructuring costs consist of employee termination benefit costs. Liabilities for costs associated with the cost reduction plan are recognized when the liability is incurred and are measured at fair value. One-time termination benefits are expensed at the date the Company notifies the employee, unless the employee must provide future service, in which case the benefits are expensed ratably over the future service period.

In May 2022, the Company initiated a reorganization that eliminated approximately 40% of its employees, primarily within the commercial organization. For the year ended December 31, 2022, the Company incurred approximately $0.5 million in employee termination benefits related to this restructuring, all of which has been paid. This headcount reduction was completed in the second quarter of 2022. No additional expenses are anticipated in connection with this cost reduction plan.

Non-Cash Interest Income (Expense) on Liability Related to Sale of Future Royalties

In September 2015, the Company sold certain royalty and milestone payment rights from the sales of Zalviso in the European Union by Grünenthal to PDL for gross proceeds of $65.0 million. Grünenthal terminated the Grünenthal Agreements effective November 13, 2020. The terms of the Grünenthal Agreements were extended to May 2021 to enable Grünenthal to sell down its Zalviso inventory. The rights to market and sell Zalviso in the Territory reverted back to the Company in May 2021.

Under the Royalty Monetization, the Company had a continuing obligation to use commercially reasonable efforts to negotiate a replacement license agreement, or New Arrangement. Under the relevant accounting guidance, because of the Company's significant continuing involvement, the Royalty Monetization was accounted for as a liability that is being amortized using the effective interest method over the life of the arrangement. In order to determine the amortization of the liability, the Company was required to estimate the total amount of future royalty and milestone payments to be received by ARPI LLC and payments made to PDL, up to a capped amount of $195.0 million, over the life of the arrangement. The aggregate future estimated royalty and milestone payments (subject to the capped amount), less the $61.2 million of net proceeds the Company received, was to be amortized as interest expense over the life of the liability. Consequently, the Company imputed interest on the unamortized portion of the liability and recorded interest expense, or interest income, as these estimates were updated and recorded non-cash royalty revenues and non-cash interest income (expense), net, within its consolidated statements of operations over the term of the Royalty Monetization.

When the expected payments under the Royalty Monetization were lower than the gross proceeds of $65.0 million received, the Company deferred recognition of any probable contingent gain until the Royalty Monetization liability expired. See Note 11, “Liability Related to Sale of Future Royalties”.

Comprehensive Loss

Comprehensive loss is comprised of net loss and other comprehensive income (loss) and is disclosed in the consolidated statements of operations. For the Company, other comprehensive income (loss) consists of changes in unrealized gains and losses on the Company’s investments.

Income Taxes

Deferred tax assets and liabilities are measured based on differences between the financial reporting and tax basis of assets and liabilities using enacted rates and laws that are expected to be in effect when the differences are expected to reverse. The Company records a valuation allowance for the full amount of deferred assets, which would otherwise be recorded for tax benefits relating to operating loss and tax credit carryforwards, as realization of such deferred tax assets cannot be determined to be more likely than not.

Net Income (Loss) per Share of Common Stock

Basic and diluted net income (loss) per common share, or EPS, are calculated in accordance with the provisions of Financial Accounting Standards Board, or FASB, ASC Topic *260, Earnings per Share*.

The Company applies the two-class method to compute basic and , if more dilutive than other methods, diluted net income or loss per share. The two-class method is an earnings allocation formula that treats participating securities as having rights to earnings that would otherwise have been available to common stockholders (including pre-funded warrants). Shares of common stock into which the pre-funded warrants may be exercised are considered outstanding for the purposes of computing net loss per share because the shares may be issued for little or no consideration and are exercisable after the original issuance date. In addition, the Company is required to calculate diluted net income or loss per share under the two-class method if the effect is more dilutive than the application of another dilutive method of calculating diluted EPS (i.e., the treasury stock, if-converted, or contingently issuable share method). In periods where there is a net loss, no allocation of undistributed net loss to participating securities is performed if the holders of these securities are not contractually obligated to participate in the Company’s losses. The Company’s participating securities include the November 2021 Financing Warrants, 2022 Warrants and the Series A Redeemable Convertible Preferred Stock (see Note 12, “Warrants” and Note 14, “Stockholder’s Equity (Deficit)” below).

For additional information regarding the net income (loss) per share, see Note 16, “Net Income (Loss) per Share of Common Stock”.

Recently Adopted Accounting Pronouncements

In May 2021, the FASB issued ASU 2021-04, *Earnings Per Share (Topic 260), Debt-Modifications and Extinguishments (Subtopic 470-50), Compensation-Stock Compensation (Topic 718), and Derivatives and Hedging-Contracts in Entity's Own Equity (Subtopic 815-40): Issuer's Accounting for Certain Modifications or Exchanges of Freestanding Equity-Classified Written Call Options (a consensus of the FASB Emerging Issues Task Force)*, or ASU-2021-14, which provides guidance on modifications or exchanges of a freestanding equity-classified written call option that is not within the scope of another topic. An entity should treat a modification of the terms or conditions or an exchange of a freestanding equity-classified written call option that remains equity classified after modification or exchange as an exchange of the original instrument for a new instrument, and provides further guidance on measuring the effect of a modification or an exchange of a freestanding equity-classified written call option that remains equity classified after modification or exchange. ASU 2021-04 also provides guidance on the recognition of the effect of a modification or an exchange of a freestanding equity-classified written call option that remains equity classified after modification or exchange on the basis of the substance of the transaction, in the same manner as if cash had been paid as consideration. ASU 2021-04 is effective for all entities for fiscal years beginning after December 15, 2021, including interim periods within those fiscal years. An entity should apply ASU 2021-04 prospectively to modifications or exchanges occurring on or after the effective date of ASU 2021-04.

The Company adopted ASU 2021-04 effective January 1, 2022, on a prospective basis. In conjunction with the warrant amendments discussed in Note 12, "Warrants", the Company recorded issuance costs of $0.7 million as an expense and $0.1 million as a reduction of proceeds in additional paid-in capital for the corresponding increase to the remeasured fair value of the equity-classified warrants as of the modification date.

Recently Issued Accounting Pronouncements

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments – Credit Losses: Measurement of Credit Losses on Financial Instruments,* or ASU 2016-13. ASU 2016-13 replaces the incurred loss impairment model in current GAAP with a model that reflects expected credit losses and requires consideration of a broader range of reasonable and supportable information to determine credit loss estimates. ASU 2016-13 is effective for the Company beginning January 1, 2023, with early adoption allowed beginning January 1, 2020. In May 2019, the FASB issued ASU 2019-05, *Financial Instruments – Credit Losses,* or ASU 2019-05, to allow entities to irrevocably elect the fair value option for certain financial assets previously measured at amortized cost upon adoption of the new credit losses standard. The new effective dates and transition align with those of ASU 2016-13. Management does not anticipate adoption of these new standards to have a material impact on the Company's financial position, results of operations or cash flows.

2. Investments and Fair Value Measurement

Investments

The Company classifies its marketable securities as available for sale and records its investments at fair value. Available-for-sale securities are carried at estimated fair value based on quoted market prices or observable market inputs of almost identical assets, with the unrealized holding gains and losses included in accumulated other comprehensive income (loss). Marketable securities which have maturities beyond one year as of the end of the reporting period are classified as non-current.

The tables below summarize the Company's cash, cash equivalents and investments (in thousands):

	As of December 31, 2022			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash, cash equivalents and restricted cash:				
Cash	$ 13,275	$ —	$ —	$ 13,275
Money market funds	321	—	—	321
U.S. government agency securities	2,444	—	—	2,444
Commercial paper	4,235	—	—	4,235
Total cash, cash equivalents and restricted cash	20,275	—	—	20,275
Short-term investments:				
Commercial paper	495	—	—	495
Total short-term investments	495	—	—	495
Total cash, cash equivalents, restricted cash and short-term investments	$ 20,770	$ —	$ —	$ 20,770

	As of December 31, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash, cash equivalents and restricted cash:				
Cash	$ 1,443	$ —	$ —	$ 1,443
Money market funds	2,822	—	—	2,822
Commercial paper	8,398	—	—	8,398
Total cash, cash equivalents and restricted cash	12,663	—	—	12,663
Short-term investments:				
Commercial paper	29,504	—	—	29,504
Corporate debt securities	9,463	—	—	9,463
Total short-term investments	38,967	—	—	38,967
Total cash, cash equivalents, restricted cash and short-term investments	$ 51,630	$ —	$ —	$ 51,630

None of the available-for-sale securities held by the Company had material unrealized losses and there were no realized losses for the years ended December 31, 2022 and 2021. There were no other-than-temporary impairments for these securities as of December 31, 2022 or 2021. No gross realized gains or losses were recognized on the available-for-sale securities and, accordingly, there were no amounts reclassified out of accumulated other comprehensive income (loss) to earnings during the years ended December 31, 2022 and 2021.

As of December 31, 2022 and 2021, the contractual maturity of all investments held was less than one year.

Fair Value Measurement

The Company's financial instruments consist of Level I and II assets. Money market funds are highly liquid investments and are actively traded. The pricing information on these investment instruments are readily available and can be independently validated as of the measurement date. This approach results in the classification of these securities as Level 1 of the fair value hierarchy. For Level II instruments, the Company estimates fair value by utilizing third-party pricing services in developing fair value measurements where fair value is based on valuation methodologies such as models using observable market inputs, including benchmark yields, reported trades, broker/dealer quotes, bids, offers and other reference data. Such Level II instruments typically include U.S. Treasury, U.S. government agency securities and commercial paper. As of December 31, 2022, the Company held, in addition to Level II assets, a warrant liability related to the 2022 Warrants (see Note 12, "Warrants" for further description). The fair value of the warrant liability was estimated using the Black Scholes Model which uses as inputs the following weighted average assumptions: dividend yield, expected term in years; equity volatility; and risk-free interest rate. The Company follows the guidance in ASC 820 for its financial assets and liabilities that are re-measured and reported at fair value at each reporting period. The estimated fair value of the warrant liability represents a Level III measurement. Changes to the estimated fair value of these liabilities are recorded in interest income and other income, net in the consolidated statements of operations.

The following tables set forth the fair value of the Company's financial assets by level within the fair value hierarchy (in thousands):

	As of December 31, 2022			
	Fair Value	Level I	Level II	Level III
Assets				
Money market funds	$ 321	$ 321	$ —	$ —
U.S. government agency securities	2,444	—	2,444	—
Commercial paper	4,730	—	4,730	—
Total assets measured at fair value	7,495	321	7,174	
Liabilities				
Warrant liability	7,098	—	—	7,098
Total liabilities measured at fair value	7,098	—	—	$ 7,098

	As of December 31, 2021			
	Fair Value	Level I	Level II	Level III
Assets				
Money market funds	$ 2,822	$ 2,822	$ —	$ —
Commercial paper	37,902	—	37,902	—
Corporate debt securities	9,463	—	9,463	—
Total assets measured at fair value	$ 50,187	$ 2,822	$ 47,365	$ —

3. Inventories, Net

Inventories consist of finished goods, raw materials and work in process and are stated at the lower of cost or net realizable value and consist of the following (in thousands):

	As of December 31,	
	2022	2021
Raw materials	$ 796	$ 722
Work in process	338	159
Finished goods	44	230
Inventories	$ 1,178	$ 1,111

The Company did not record any inventory impairment charges for the year ended December 31, 2022. During the year ended December 31, 2021, the Company recorded inventory impairment charges of approximately $0.8 million, primarily as a result of DSUVIA inventory that may expire before being sold.

4. Asset Acquisition

On January 7, 2022, the Company closed its acquisition of Lowell and acquired the product nafamostat, and the associated patents and historical know-how. The acquisition was valued at approximately $32.5 million plus cash acquired of $3.5 million and certain other adjustments. All options to purchase capital stock and all shares of Lowell capital stock issued and outstanding immediately before the effective time of the merger were cancelled in exchange for the right to receive (i) 450,477 shares of AcelRx common stock issued at a five day daily volume weighted average price of $11.46 per share as of January 7, 2022, or the Acquisition Date, valued at $5.2 million on closing, (ii) cash in the amount of $3.5 million, (iii) 69,808 shares of AcelRx common stock to be held back to satisfy any potential indemnification and other obligations of Lowell and its securityholders valued at $0.8 million, (iv) $0.5 million cash and stock paid for sellers' transaction costs and (v) up to $26.0 million of contingent consideration payable in cash or stock at AcelRx's option, upon the achievement of regulatory and sales-based milestones.

The shares issued in the merger were issued in a private placement pursuant to the exemption from registration under Section 4(a)(2) of the Securities Act of 1933, as amended, or the Securities Act, including Rule 506 of Regulation D promulgated under the Securities Act, or Regulation D, without general solicitation as a transaction not involving any public offering.

The merger has been accounted for as an asset acquisition of a single IPR&D asset that has an alternative future use. The initial measurement of the asset purchased of $8.8 million was based on the purchase cost of $12.4 million including (i) $6.0 million common stock fair value on the closing date (issued and held back on the acquisition date), (ii) $0.5 million seller's costs paid by the Company, (iii) $3.5 million cash and (iv) approximately $2.5 million of transaction costs less purchase price allocated to cash acquired of $3.5 million. Due to the nature of regulatory and sales-based milestones, the contingent consideration of up to $26.0 million was not included in the initial cost of the assets purchased as they are contingent upon events that are outside the Company's control, such as regulatory approvals and issuance of patents, and are not considered probable until notification is received. However, upon achievement or anticipated achievement of each milestone, the Company shall recognize the related, appropriate payment as an additional cost of the acquired IPR&D asset. As of December 31, 2022, none of the contingent events has occurred.

The following table summarizes the total consideration for the acquisition and the value of the IPR&D asset acquired (in thousands):

Consideration		
Cash	$	3,536
Issuance of common stock to Lowell security holders in connection with asset acquisition		5,161
Issuance of common stock to settle Lowell's transaction costs in connection with asset acquisition		350
Liability for issuance of 69,808 hold back shares to Lowell securityholders[(1)]		800
Transaction costs		2,521
Total consideration	$	12,368
IPR&D Asset Acquired		
Purchase price	$	12,368
Cash acquired		(3,549)
Total IPR&D asset acquired[(2)]	$	8,819

(1) Recorded as Other long-term liabilities in the consolidated balance sheets.

(2) Recorded as In-process research and development asset in the consolidated balance sheets.

The IPR&D asset will be initially accounted for as an indefinite-lived asset, and as a long-lived asset, it will be reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of the asset may not be recoverable. If the IPR&D asset achieves regulatory approval and the asset life is determined to be finite, the asset's useful life will be estimated, and the asset will be amortized over its remaining useful life. No impairment losses were recorded on the IPR&D asset during the year ended December 31, 2022.

5. Property and Equipment, Net

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

	Balance as of	
	December 31, 2022	December 31, 2021
Laboratory equipment	$ 4,396	$ 4,406
Leasehold improvements	5,838	5,838
Computer equipment and software	1,565	1,589
Construction in process	8,979	13,805
Tooling	826	826
Furniture and fixtures	250	250
	21,854	26,714
Less accumulated depreciation and amortization	(11,593)	(10,786)
Property and equipment, net	$ 10,261	$ 15,928

The Company decided to realign its cost structure from a focus on commercialization to a focus on advancing its recently acquired late-stage development pipeline, namely the pre-filled syringes and Niyad product candidates. As a result, the Company decided to not focus any development resources on Zalviso in the United States, and does not expect to resubmit the Zalviso NDA in the foreseeable future. In addition, due to the termination of the agreements with Grünenthal for Zalviso in Europe and the related withdrawal of the Marketing Authorization in Europe in July 2022, the Company does not expect any revenues from Zalviso in Europe in the foreseeable future. Accordingly, the Company determined that it is no longer probable that it will realize the future economic benefit associated with the costs of the Zalviso-related purchased equipment and manufacturing-related facility improvements the Company has made at its contract manufacturer and, therefore, recorded a non-cash impairment charge of $4.9 million to the Zalviso-related assets for the year ended December 31, 2022. The impairment charge was recorded as operating expense in the consolidated statement of operations. Depreciation and amortization expense was $0.8 million and $1.1 million for the years ended December 31, 2022 and 2021, respectively.

6. In-License Agreement

On July 14, 2021, the Company entered into a License and Commercialization Agreement, or the PFS Agreement, with Aguettant pursuant to which the Company obtained the exclusive right to develop and, subject to FDA approval, commercialize in the United States (i) an ephedrine pre-filled syringe containing 10 ml of a solution of 3 mg/ml ephedrine hydrochloride for injection, and (ii) a phenylephrine pre-filled syringe containing 10 ml of a solution of 50 mcg/ml phenylephrine hydrochloride for injection. Aguettant will supply the Company with the products for use in commercialization, if they are approved in the United States.

The PFS Agreement has an initial term of ten (10) marketing years, with the first marketing year ending on December 31 of the calendar year after the first launch of a product (or December 31 of the same calendar year if the first launch of a product occurs between January 1 and April 30 of a calendar year). The term will automatically renew for successive five marketing year periods unless a party notifies the other party of its intention not to renew at least six (6) months prior to the expiration of the then-current term.

Aguettant is entitled to receive up to $24.0 million in sales-based milestone payments. The Company will purchase each product from Aguettant at an agreed price, or the PFS Purchase Price, subject to adjustment. The Company will also make revenue share payments that, combined with the PFS Purchase Price, will range from 40% to 45% of net sales in the United States.

The Company and Aguettant will agree on minimum sales obligations twelve (12) months prior to the launch of each product.

The Company has the right to grant sublicenses to its affiliates or, with the prior approval of Aguettant, third parties, subject to certain limitations.

As of December 31, 2022, there have been no payments by the Company to Aguettant under the PFS Agreement.

See Note 20, “Subsequent Events” below.

7. Out-License Agreements

DZUVEO

On July 14, 2021, the Company entered into a License and Commercialization Agreement, or the DZUVEO Agreement, with Aguettant, pursuant to which Aguettant obtained the exclusive right to develop and commercialize DZUVEO in the European Union, Norway, Iceland, Liechtenstein, Andorra, Vatican City, Monaco, Switzerland and the United Kingdom, or the DZUVEO Territory, for the management of acute moderate to severe pain in adults in medically monitored settings. The Company will supply Aguettant with product.

The DZUVEO Agreement has an initial term of ten (10) marketing years, with the first marketing year ending on December 31 of the calendar year after the launch of DZUVEO (or December 31, 2022, if the launch occurs between January 1, 2022 and April 30, 2022). The term will automatically renew for successive five marketing year periods unless a party notifies the other party of its intention not to renew at least six (6) months prior to the expiration of the then-current term. The DZUVEO Agreement may be terminated for cause by either party based on uncured material breach by the other party, insolvency of the other party, or force majeure event. Upon early termination, all ongoing activities under the agreement and all rights and commercialization licenses and sublicenses with respect to DZUVEO will terminate. Additionally, if terminated early by either party, any accrued liability at the time of such termination will not be released.

The Company is entitled to receive up to €47.0 million in a combination of up-front and sales-based milestone payments, of which the Company received €2.5 million, or approximately $2.9 million, in the third quarter of 2021, for which it recognized revenue of $1.7 million in the third quarter of 2021. Aguettant will purchase product from the Company at an agreed price, or the DZUVEO Purchase Price, subject to adjustment. Aguettant will also make revenue share payments that, combined with the DZUVEO Purchase Price, range from 35% to 45% of net sales in the DZUVEO Territory.

Beginning in the third marketing year, the parties will establish binding annual minimums for purchase orders to be submitted by Aguettant. Aguettant has the right to grant sublicenses to its affiliates or, with the prior approval of the Company, third parties, subject to certain limitations.

The DZUVEO Agreement also provides Aguettant with a right of first negotiation for eighteen (18) months before the Company can enter into a collaboration regarding Zalviso in Europe.

See Note 20, “Subsequent Events” below.

Zalviso

On May 18, 2020, the Company received a notice from Grünenthal that it had exercised its right to terminate the Grünenthal Agreements, effective November 13, 2020. The terms of the Grünenthal Agreements were extended to May 12, 2021 to enable Grünenthal to sell down its Zalviso inventory, a right it had under the Grünenthal Agreements. The rights to market and sell Zalviso in the Zalviso Territory reverted back to the Company on May 12, 2021. In July 2022, the European Marketing Authorization for Zalviso was withdrawn.

8. Revenue from Contracts with Customers

The following table summarizes revenue from contracts with customers for the years ended December 31, 2022 and 2021 into categories that depict how the nature, amount, timing and uncertainty of revenue and cash flows are affected by economic factors (in thousands):

	December 31,	
	2022	2021
Product sales:		
DSUVIA	$ 1,588	$ 735
DZUVEO	183	—
Zalviso	—	270
Total product sales	1,771	1,005
Contract and collaboration revenue:		
License revenue	—	1,696
Non-cash royalty revenue related to Royalty Monetization (Note 11)	—	83
Royalty revenue	—	28
Other revenue	—	6
Total revenues from contract and other collaboration	—	1,813
Total revenue	$ 1,771	$ 2,818

For additional detail on the Company's accounting policy regarding revenue recognition, refer to Note 1, "Organization and Summary of Significant Accounting Policies - Revenue from Contracts with Customers."

Product Sales

The Company's commercial launch of DSUVIA in the United States occurred in the first quarter of 2019. See Note 20, "Subsequent Events" below.

Zalviso was sold in Europe by the Company's collaboration partner, Grünenthal, through May 12, 2021, at which time, due to the termination of the Grünenthal Agreements, the rights to market and sell Zalviso in Europe reverted back to the Company. In July 2022, the European Marketing Authorization for Zalviso was withdrawn. DZUVEO sales in Europe by the Company's collaboration partner, Aguettant, have recently commenced. See Note 20, "Subsequent Events" below.

Contract and Other Collaboration

Contract and other collaboration revenue includes revenue under the Grünenthal Agreements related to research and development services, non-cash royalty revenue related to the Royalty Monetization and royalty revenue for sales of Zalviso in Europe and license revenue recognized under the DZUVEO Agreement. For the year ended December 31, 2022, the Company did not record any contract and other collaboration revenue.

The Company concluded that Aguettant is a customer and therefore revenue recognition for the DZUVEO Agreement in Europe should be accounted for in accordance with ASC Topic 606, *Revenue from Contracts with Customers*, because the Company granted to Aguettant licenses and will provide the supply of product, as defined below, all of which are outputs of the Company's ongoing activities, in exchange for consideration.

The Company identified the following promises under the DZUVEO Agreement at inception, namely: (a) granting of the licenses, (b) manufacturing services inclusive of quality control testing and stability testing which are options in the initial arrangement, and (c) a material right associated with the discounted price for future optional orders of DZUVEO commercial product supply.

The licenses are considered to be functional intellectual property. The Company determined that the licenses are capable of being distinct because Aguettant can benefit from the license on its own by commercializing the underlying product using its own resources. The Company manufacturing services are not highly specialized in nature and can be performed by third-party contract manufacturing organizations. There are no binding commitments for manufacturing purchase orders at inception of the arrangement. Therefore, the manufacturing services are considered to be an option and not a performance obligation in the initial arrangement. However, the Company has determined that the discounted price per unit on future optional product orders constitutes a material right and is a performance obligation. The right to purchase at a discount is capable of being used by the customer on a standalone basis, because this relates to future product purchases and occur after the licenses' performance obligations are transferred.

The Company evaluated if there is an interdependence between the performance obligations and determined that the licenses are a combined solution and the predominant performance obligation. The material right is separately identifiable in the context of the contract and is not modified by, and does not modify, the license performance obligation and is not highly interdependent or interrelated with the material right performance obligations in the contract.

The transaction price at the inception of the DZUVEO Agreement consisted of the upfront fee of €2.5 million, or approximately $2.9 million. The variable consideration related to product supply and reimbursables has been constrained as of December 31, 2022 as there has been no forecast provided by Aguettant. The Company will re-evaluate the transaction price each reporting period and as uncertain events are resolved or other changes in circumstances occur.

The Company determined that the $52.2 million sales-based milestone payments and revenue share payments were probable of significant revenue reversal, as their achievement was highly dependent on factors outside the Company's control. As a result, these payments were fully constrained and were not included in the transaction price. Any variable consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur, as they were determined to relate predominantly to the licenses granted to Aguettant and the optional manufacturing services provided by the Company.

The transaction price is allocated to the performance obligations based on relative standalone selling price which were determined for the licenses using the adjusted market approach, and for the manufacturing services and the material right associated with discounted DZUVEO product supply using the cost-plus reasonable margin approach. Variable consideration is allocated to the specific performance obligations to which it relates.

For revenue recognition purposes, the Company determined that the duration of the contract began on the effective date in July 2021 and ends after an initial term of 10 marketing years, unless it automatically renews for a successive five marketing years. The Company also analyzed the impact if Aguettant terminated the agreement prior to the end of the term and determined, considering both quantitative and qualitative factors, that there were substantive non-monetary penalties to Aguettant for doing so.

Revenue for the granting of the licenses was recognized on the effective date of the DZUVEO Agreement at the point in time that the licenses are effective. The manufacturing services inclusive of quality control testing and stability testing will be recognized at a point in time when, or as, the Company transfers the associated promised goods and services to Aguettant. The material right for the discounted price per unit on future optional orders will be recognized over time with the measure of progress being straight-line over the period in which the Company stands ready to provide the discounted price per unit on the manufacturing services.

No contract and other collaboration revenue was recorded related to the DZUVEO Agreement for the year ended December 31, 2022. For the year ended December 31, 2021, the Company recorded $1.7 million in contract and other collaboration revenue as a result of satisfying its licenses performance obligation by transferring the license rights to Aguettant.

See Note 20, "Subsequent Events" below.

Contract Liabilities

A contract liability of $1.2 million was recorded on the consolidated balance sheets as deferred revenue as of December 31, 2022, $0.1 million of which represented the current portion, for the portion of the upfront fee received under the DZUVEO Agreement allocated to the material right for discounted price on future optional product supply which has not yet been satisfied. There was no contract asset as of December 31, 2022 associated with the DZUVEO Agreement.

As of December 31, 2022, deferred contract acquisition costs were negligible and deferred contract acquisition costs amortized during the years ended December 31, 2022 and 2021 were $0 and $0.3 million, respectively.

The following table presents changes in the Company's contract liability for the years ended December 31, 2022 and 2021 (in thousands):

Balance at January 1, 2021	$	49
Additions[1]		1,237
Deductions for performance obligations satisfied:		
In current period		(49)
Balance at December 31, 2021	$	1,237
Deductions for performance obligations satisfied:		
In current period		(86)
Balance at December 31, 2022	$	1,151

[1] Deferred revenue under the DZUVEO Agreement with Aguettant.

See Note 20, "Subsequent Events" below.

9. Long-Term Debt

Loan Agreement with Oxford

On May 30, 2019, the Company entered into the Loan Agreement with Oxford as the Lender. Under the Loan Agreement, the Lender made a term loan to the Company in an aggregate principal amount of $25.0 million, or the Loan, which was funded on May 30, 2019. The Company used approximately $8.9 million of the proceeds from the Loan to repay its outstanding obligations under its prior debt agreement. After deducting all loan initiation costs and outstanding interest on the prior debt agreement, the Company received $15.9 million in net proceeds.

The interest rate is calculated at a rate equal to the sum of (a) the greater of (i) the 30-day U.S. LIBOR rate reported in *The Wall Street Journal* on the last business day of the month that immediately precedes the month in which the interest will accrue and (ii) 2.50%, plus (b) 6.75%. Payments on the Loan were interest-only until July 1, 2020 followed by equal principal payments and monthly accrued interest payments through the scheduled maturity date of June 1, 2023. The Company's obligations under the Loan Agreement are secured by a security interest in all the assets of the Company, other than the Company's intellectual property which is subject to a negative pledge.

The Company may prepay the Loan at any time. If the Loan is paid prior to the maturity date, the Company will pay the Lender a prepayment charge, based on a percentage of the then outstanding principal balance, equal to 1%. Upon voluntary or mandatory prepayment, in addition to the prepayment charge, the Company is required to pay the EOT Fee, Lender's expenses and all outstanding principal and accrued interest through the prepayment date.

The Loan Agreement includes customary representations and covenants that, subject to exceptions, will restrict the Company's ability to do the following things: declare dividends or redeem or repurchase equity interests; incur additional liens; make loans and investments; incur additional indebtedness; engage in mergers, acquisitions, and asset sales; transact with affiliates; undergo a change in control; add or change business locations; and engage in businesses that are not related to its existing business. The Loan Agreement requires that the Company always maintain unrestricted cash of not less than $5.0 million in accounts subject to control agreements in favor of Lender, tested monthly as of the last day of the month.

The Loan Agreement also includes standard events of default, including payment defaults, breaches of covenants following any applicable cure period, a material impairment in the perfection or priority of the Lender's security interest or in the value of the collateral, a material adverse change in business, operations or the prospect of repayment, events relating to bankruptcy or insolvency. The Loan also contains a cross default provision, under which if a third party (under any agreement) has the right to accelerate indebtedness greater than $250,000, the Loan would also be considered in default. In addition, the Loan defines events which negatively impact government approvals, judgments in excess of $500,000 and the delisting of the Company's shares of common stock on the Nasdaq Global Market, or Nasdaq, as events of default. Upon the occurrence of an event of default, a default interest rate of an additional 5% may be applied to the outstanding loan balances, and the Lender may declare all outstanding obligations immediately due and payable and take such other actions as set forth in the Loan Agreement. Acceleration would result in the payment of any applicable prepayment charges and application of the default interest rate to the outstanding balance until payment is made in full. The Company bifurcated a compound derivative liability related to a contingent interest feature and acceleration upon default provision (contingent put option) provided to the Lender. The bifurcated embedded derivative must be valued and separately accounted for in the Company's consolidated financial statements. The contingent put option liability is classified as a component of other long-term liabilities. As of December 31, 2022, the estimated fair value of the contingent put option liability was $10,000 which was determined by using a risk-neutral valuation model, wherein the fair value of the underlying debt facility is estimated, both with and without the presence of the default provisions, holding all other assumptions constant.

In connection with the Loan Agreement, on May 30, 2019, the Company issued warrants to the Lender and its affiliates, which are exercisable for an aggregate of 8,833 shares of the Company's common stock with a per share exercise price of $56.60, or the Warrants. The Warrants have been classified within stockholders' equity (deficit) and accounted for as a discount to the loan by allocating the gross proceeds on a relative fair value basis. For further discussion, see Note 12, "Warrants".

The outstanding balance due under the Loan Agreement was $5.4 million and $13.3 million at December 31, 2022 and 2021, respectively. Interest expense related to the Loan Agreement was $1.1 million, of which $0.4 million represented amortization of the debt discount, and $2.2 million, $0.7 million of which represented amortization of the debt discount, for the years ended December 31, 2022 and 2021, respectively, and the effective interest rate was approximately 13.6% and 13.2% for the years ended December 31, 2022 and 2021, respectively.

Non-Interest Bearing Payments for the Construction of Leasehold Improvements

In August 2019, the Company entered into a Site Readiness Agreement, or SRA, with a potential Contract Manufacturing Organization, or CMO, in contemplation of entering into a commercial supply agreement for its product DSUVIA at a future date. Under the SRA, the Company is building out a suite within the CMO's production facility. If additional equipment and facility modifications are required to meet the Company's product needs, the Company may be required to contribute to the cost of such additional equipment and facility modifications. The Company has determined that it is the owner of the leasehold improvements related to the build-out which will be paid for in four annual installments of $0.5 million each. As of December 31, 2022 and 2021, the accrued balance under the SRA was $0.4 million and $1.7 million of these leasehold improvements had been capitalized. The effective interest rate related to the payments at December 31, 2022 and 2021 was approximately 14.4%. The leasehold improvements are recorded as property and equipment, net, in the consolidated balance sheets. See Note 20, "Subsequent Events" below.

Future Payments on Long-Term Debt

The following table summarizes the outstanding future payments associated with the Company's long-term debt as of December 31, 2022 (in thousands):

2023	$ 5,951
Total payments	5,951
Less amount representing interest	(134)
Notes payable, gross	5,817
Less: Unamortized portion of EOT Fee	(26)
Less: Unamortized discount on notes payable	(28)
Long-term debt	5,763
Less current portion	(5,763)
Long-term debt, net of current portion	$ —

10. Leases

Office Lease

The Company leased office and laboratory space for its former corporate headquarters, located at 301 – 351 Galveston Drive, Redwood City, California, and entered into an agreement to sublease approximately 12,106 square feet of this office and laboratory space.

On March 26, 2021, the Company entered into a Lease Termination Agreement with its landlord and a Sublease Termination Agreement with its sublessee, to terminate the lease and sublease agreements at its former corporate headquarters. The termination of both the lease and sublease was effective on April 30, 2021. As of the date of the Lease Termination Agreement, the Company remeasured its lease liability and recorded a gain of $0.5 million upon derecognition of the lease liability and right of use asset for the master lease, which was included in operating expenses for the year ended December 31, 2021. In connection with the Sublease Termination, the remaining deferred costs of $0.3 million were fully amortized through April 30, 2021, the effective date of the Sublease Termination, and included in operating expenses for the year ended December 31, 2021.

On March 26, 2021, the Company entered into a Sublease Agreement to sublet space for its new corporate headquarters, located at 25821 Industrial Boulevard, Hayward, California. The Sublease Agreement commencement date was April 1, 2021. The Sublease Agreement is for a period of two years and three months with monthly rental payments of $17,000, including one month of abated rent. On the lease commencement date, the Company recognized an operating lease right-of-use asset in the amount of $0.4 million.

Contract Manufacturing Leases

On December 12, 2012, the Company entered into an agreement for commercial supply manufacturing services related to the Company's Zalviso drug product with Patheon Pharmaceuticals Inc. ("Patheon"), a contract manufacturing organization. The initial term of the agreement was through December 31, 2017, which term automatically renews in two-year increments unless earlier terminated by either party by giving eighteen months' notice. Commencing in 2013, the Company is required to make overhead fee payments each year of $0.2 million, prorated based on aggregate revenues. The Company has determined that this fee is an in-substance fixed lease payment as it represents the minimum annual payment under the contract. The Company concluded that this agreement contains an embedded lease as the clean rooms have been built specifically for production of the Company's product and their use is effectively controlled by the Company as it has priority over the space during the term of the agreement.

On November 29, 2022, the Company received notice from Patheon that it intends to terminate the agreement for commercial supply manufacturing services related to the Company's Zalviso drug product. Based on Patheon's date of notice, the agreement will terminate on May 31, 2024. Patheon will continue to supply product under the agreement until the Termination Date.

On April 21, 2021, the Company entered into a Commercial Supply Agreement, or the CSA, with Catalent Pharma Solutions, LLC, or Catalent, effective March 31, 2021, under which Catalent provides certain services to the Company in connection with the processing and packaging of a packaged single dose applicator containing the sublingual tablet 30 mcg sufentanil dosage form contained in the pharmaceutical product, DSUVIA (sufentanil), intended for commercialization.

The term of the CSA is for a period of five years from the first date upon which the FDA approves Catalent as a manufacturer of DSUVIA in the United States, or the Commencement Date. The term shall automatically be extended for successive two-year periods, unless and until one party gives the other party at least 24 months' prior written notice of its desire to terminate as of the end of the then-current term.

The Company will pay Catalent an annual fee of $1.0 million beginning January 1, 2022. Pursuant to the CSA, the Company will purchase each 10-pack carton of DSUVIA from Catalent at an agreed price through December 31, 2022, and pay other fees set forth in the CSA. All pricing and fees, with the exception of raw materials, may be adjusted on an annual basis, effective on January 1 of each calendar year, beginning with January 1, 2023, subject to certain limitations. Price increases for raw materials will be passed through to the Company.

The Company has determined that the fixed fees in the CSA are in-substance lease payments. The Company concluded that this agreement contains an embedded lease as the clean rooms have been built specifically for production of the Company's product and their use is effectively controlled by the Company as it has sole use over the space during the term of the agreement. The Company accounts for the agreement as an operating lease and has evaluated the non-cancelable lease term to be through the binding commitment date of May 15, 2027. See Note 20, "Subsequent Events" below.

The components of lease expense are presented in the following table (in thousands):

	Year ended December 31, 2022	Year ended December 31, 2021
Operating lease costs	$ 1,373	$ 1,467
Gain on derecognition of operating lease	—	(522)
Sublease income	—	(199)
Loss on termination of sublease	—	331
Net lease costs	$ 1,373	$ 1,077

The weighted average remaining lease term and discount rate related to the operating leases are presented in the following table:

	December 31, 2022	December 31, 2021
Weighted-average remaining lease term – operating leases (in years)	4.1	5.0
Weighted-average remaining discount rate – operating leases	12.8%	12.8%

Maturities of lease liabilities as of December 31, 2022 are presented in the following table (in thousands):

Year:		
2023	$	2,127
2024		1,090
2025		1,040
2026		1,040
2027		415
Thereafter		—
Total future minimum lease payments		5,712
Less imputed interest		(1,052)
Total	$	4,660
Reported as:		
Operating lease liabilities	$	4,660
Operating lease liabilities, current portion		(1,701)
Operating lease liabilities, net of current portion	$	2,959

11. Liability Related to Sale of Future Royalties

On September 18, 2015, the Company entered into the Royalty Monetization with PDL for which it received gross proceeds of $65.0 million. Under the Royalty Monetization, PDL was to receive 75% of the European royalties under the Amended License Agreement with Grünenthal, as well as 80% of the first four commercial milestones worth $35.6 million (or 80% of $44.5 million), up to a capped amount of $195.0 million over the life of the arrangement.

The Company periodically assessed the expected royalty and milestone payments using a combination of historical results, internal projections and forecasts from external sources. To the extent such payments were greater or less than the Company's initial estimates or the timing of such payments is materially different than its original estimates, the Company prospectively adjusted the amortization of the liability and the effective interest rate. Grünenthal notified the Company that it was terminating the Amended License Agreement effective November 13, 2020. On August 31, 2020, PDL sold its royalty interest for Zalviso to SWK Funding, LLC, or SWK, under the Royalty Monetization. The terms of the Grünenthal Agreements were extended to May 12, 2021 to enable Grünenthal to sell down its Zalviso inventory. The rights to market and sell Zalviso in the Zalviso Territory reverted back to the Company on May 12, 2021.

On May 31, 2022, the Company entered into a Termination Agreement with SWK to fully terminate the Royalty Monetization for which the Company paid cash consideration of $0.1 million, and neither PDL nor SWK retains any further interest in the Royalty Monetization. Accordingly, effective May 31, 2022, the Royalty Monetization is no longer reflected on the Company's consolidated financial statements or other records as a sale of assets to PDL or SWK and all security interests and other liens of every type held by the parties to the Royalty Monetization have been terminated and automatically released without further action by any party. The $84.1 million gain on extinguishment of the liability related to the sale of future royalties is recognized in the consolidated statements of operations as other income.

The effective interest income rate for the years ended December 31, 2022 and 2021 was approximately 3.2% and 3.5%, respectively.

The following table shows the activity within the liability account during the year ended December 31, 2022 (in thousands):

	Year ended December 31, 2022	Period from inception to December 31, 2022
Liability related to sale of future royalties — beginning balance	$ 85,288	$ —
Proceeds from sale of future royalties	—	61,184
Non-cash royalty revenue	—	(1,083)
Non-cash interest (income) expense recognized	(1,136)	24,051
Consideration paid for termination of Royalty Monetization	(100)	(100)
Gain on termination of liability related to sale of future royalties	(84,052)	(84,052)
Liability related to sale of future royalties as of December 31, 2022	$ —	$ —

As mentioned above, the Royalty Monetization was terminated on May 31, 2022.

12. Warrants

December 2022 Financing Warrants

On December 27, 2022, the Company entered into a securities purchase agreement, or the Purchase Agreement, with an institutional investor, or the Purchaser, relating to the issuance and sale, or the Offering, of (i) 748,744 shares of its common stock (see Note 14, "Stockholders' Equity (Deficit)"), par value $0.001 per share, (ii) pre-funded warrants to purchase 2,632,898 shares of common stock, or the 2022 Pre-Funded Warrants, and (iii) common warrants to purchase an aggregate of 4,227,052 shares of common stock, or the 2022 Warrants, and collectively, the December 2022 Financing.

The 2022 Pre-Funded Warrants were exercisable immediately following the closing date of the Offering, or December 29, 2022, and have an unlimited term and an exercise price of $0.0001 per share. The 2022 Warrants will be exercisable following the six-month anniversary of the closing date of the Offering and have a six-year term and an exercise price of $2.07 per share. The combined offering price is $2.22625 per share of common stock and accompanying 2022 Warrant, or in the case of 2022 Pre-Funded Warrants, $2.22615 per 2022 Pre-Funded Warrant and accompanying 2022 Warrant. The December 2022 Financing resulted in aggregate gross proceeds of $7.5 million, before $1.7 million of transaction costs, $0.8 million of which were non-cash issuance costs.

The 2022 Warrants include full ratchet anti-dilutive adjustment rights in the event the Company issues shares of common stock or common stock equivalents in the future with a value less than the then effective exercise price of such common warrants subject to certain customary exceptions, and further subject to a minimum exercise price of $1.00 per share.

In the event of certain fundamental transactions involving the Company, the holder of the 2022 Warrants may require the Company to make a payment based on a Black-Scholes valuation, using specified inputs. The 2022 Pre-Funded Warrants do not provide similar rights to the Purchaser. Therefore, the Company accounted for the 2022 Warrants as a liability, while the 2022 Pre-Funded Warrants met the permanent equity criteria classification. The 2022 Pre-Funded Warrants are classified as a component of permanent equity, or APIC, because they are freestanding financial instruments that are legally detachable and separately exercisable from the shares of common stock with which they were issued, are immediately exercisable, do not embody an obligation for the Company to repurchase its shares, and permit the holders to receive a fixed number of shares of common stock upon exercise. In addition, the 2022 Pre-Funded Warrants do not provide any guarantee of value or return. The December 2022 Warrants were valued at approximately $7.1 million, using the Black-Scholes option pricing model as follows: exercise price of $2.07 per share, stock price of $2.13 per share, expected life of 6 years, volatility of 95.44%, a risk-free rate of 3.93% and 0% expected dividend yield. Accordingly, the Company allocated the fair value of $7.1 million of the gross proceeds received to Warrant liability on it consolidated balance sheets. The aggregate remaining gross proceeds of $0.4 million were allocated to the two remaining securities using the relative fair value method, resulting in the common stock and the 2022 Pre-Funded Warrants being allocated values of $95,000 and $335,000, respectively, and such amount being recorded to stockholders' equity (deficit). The change in fair value of the Warrant liability from the date of issuance to December 31, 2022 was immaterial. The 2022 Warrants meet the definition of participating securities; however, there is no contractual obligation on the part of the warrantholders to participate in the Company's losses.

As of December 31, 2022, the 2,632,898 pre-funded warrants and the 4,227,052 common warrants remained outstanding.

August 2022 LPC Warrant

On August 3, 2022, the Company entered into a securities purchase agreement with Lincoln Park Capital Fund, LLC, or LPC, pursuant to which the Company, in a private placement transaction, sold (i) an aggregate of 3,000 shares of the Company's Series A Redeemable Convertible Preferred Stock, and (ii) warrants to purchase up to an aggregate of 81,150 shares of common stock, for an aggregate purchase price of $0.3 million (see Note 14, "Stockholders' Equity (Deficit)"). In November 2022, the Company filed a resale registration statement to permit LPC to sell the shares of common stock issuable upon conversion of the Series A Redeemable Convertible Preferred Stock and upon exercise of the warrant.

The August 2022 LPC Warrant had an exercise price of $4.07 per share (subject to adjustment for stock splits, reverse stock splits and similar recapitalization events), became immediately exercisable and has a term ending on February 3, 2028. The August 2022 LPC Warrant provides for proportional adjustment of the number and kind of securities purchasable upon exercise of the August 2022 LPC Warrant and the per share exercise price upon the occurrence of certain events such as stock splits, combinations, reverse stock splits and similar events. In addition, until August 3, 2023, if the Company issues or sells (or is deemed to have issued or sold) any common stock, convertible securities or options (as defined in the August 2022 LPC Warrant), for a consideration per share, or the New Issuance Price, less than a price equal to the exercise price in effect immediately prior to such issue or sale or deemed issuance or sale, each of the foregoing, a dilutive issuance, then immediately after such dilutive issuance, the exercise price then in effect for the August 2022 LPC Warrant shall be reduced to an amount equal to the New Issuance Price, or the Down Round Feature.

In December 2022, the Down Round Feature was triggered due to the price per share received from the issuance of common stock and warrants in connection with the December 2022 Financing. The Company calculated the value of the effect of the Down Round Feature measured as the difference between the warrants' fair value, using the Black-Scholes option-pricing model, before and after the Down Round Feature was triggered using the original exercise price, $4.07, and the new exercise price, $2.07. The difference in fair value of the effect of the Down Round Feature was immaterial and had no impact on net loss per share in the periods presented. The exercise price will continue to be adjusted in the event the Company issues additional shares of common stock below the current exercise price, in accordance with the terms of the 2022 LPC Warrant.

The August 2022 LPC Warrant was valued at approximately $0.3 million using the Black-Scholes option pricing model as follows: exercise price of $4.07 per share, stock price of $4.44 per share, expected life of 5.5 years, volatility of 89.94%, a risk-free rate of 2.86% and 0% expected dividend yield. The Series A Redeemable Convertible Preferred Stock and the August 2022 LPC Warrant were issued in a unit structure with the August 2022 LPC Warrant eligible to be classified in stockholders' equity, therefore the aggregate net proceeds of $0.2 million were allocated to the two securities using the relative fair value method, resulting in the Series A Redeemable Convertible Preferred Stock and the August 2022 LPC Warrant being allocated values of $129,000 and $110,000, respectively, and recorded to stockholders' equity (deficit).

As of December 31, 2022, the August 2022 LPC Warrant had not been exercised and was still outstanding.

November 2021 Financing Warrants

On November 15, 2021, the Company entered into a securities purchase agreement with certain investors pursuant to which the Company, in a registered direct offering, sold (i) an aggregate of 875,000 shares of the Company's common stock, and (ii) warrants to purchase up to an aggregate of 875,000 shares of common stock, for an aggregate purchase price of $14.0 million (see Note 14, "Stockholders' Equity (Deficit)"). The November 2021 Financing Warrants meet the definition of participating securities; however, there is no contractual obligation on the part of the warrantholders to participate in the Company's losses.

The November 2021 Financing Warrants have an exercise price of $20.00 per share and become exercisable, if the holder's post-exercise beneficial ownership is less than or equal to 9.99%, 6 months after their issuance date and have a five-year term through November 15, 2026. All common stock issuable under the issued warrants, were added to the Company's effective registration statement on November 15, 2021.

The November 2021 Financing warrants were valued at approximately $8.6 million using the Black-Scholes option pricing model as follows: exercise price of $20.00 per share, stock price of $14.92 per share, expected life of five years, volatility of 91.77%, a risk-free rate of 1.26% and 0% expected dividend yield. The common stock and warrants were issued in a unit structure; therefore, in accordance with ASC Topic 815, the aggregate gross proceeds of $14.0 million were allocated to the two securities using the relative fair value method, resulting in the common stock and warrants being allocated values of $8.4 million and $5.6 million, respectively, and recorded to stockholders' equity (deficit).

Upon the closing of the December 2022 Financing, 750,000 of the 875,000 November 2021 Financing Warrants were modified, to reduce the exercise price for the warrants from $20.00 per share to $2.07 per share and to extend the expiration date to December 29, 2028. The modification of these November 2021 Financing Warrants lowered the exercise price to the price per share in the December 2022 Financing. These November 2021 Financing Warrants remained a freestanding equity-classified instrument following the modification. The Company concluded that the modification of these November 2021 Financing Warrants provided more favorable terms to the Purchaser with the purpose of inducing the Purchaser to complete the December 2022 Financing. Pursuant to ASU 2021-04, the Company remeasured the fair value of the November 2021 Financing Warrants as of the modification date based on the modified terms and recorded the increase in fair value of $0.8 million as equity issuance costs, $0.7 million of which was allocated to selling, general and administrative expenses and $0.1 million of which was allocated to additional paid in capital, based on the relative fair values of the 2022 Warrants, classified as liabilities, and the Common Stock and Pre-funded Warrants, classified in equity, respectively. The fair value assumptions related to the modification of these 750,000 November 2021 Financing Warrants as of December 29, 2022 were as follows: exercise price of $2.07 per share, stock price of $2.13 per share, expected life of six years, volatility of 95.44%, a risk-free rate of 3.93% and 0% expected dividend yield.

The remaining warrants issued in the November 17, 2021 registered direct offering for 125,000 shares of the Company's common stock remain outstanding at December 31, 2022, are currently exercisable at a price of $20.00 per share and expire on November 15, 2026.

Loan Agreement Warrants

In connection with the Loan Agreement, on May 30, 2019, the Company issued warrants to the Lender and its affiliates, which are exercisable for an aggregate of 8,833 shares of the Company's common stock with a per share exercise price of $56.60, or the Loan Agreement Warrants. The Loan Agreement Warrants may be exercised on a cashless basis. The Loan Agreement Warrants are exercisable for a term beginning on the date of issuance and ending on the earlier to occur of ten years from the date of issuance or the consummation of certain acquisitions of the Company as set forth in the Loan Agreement Warrants. The number of shares for which the Loan Agreement Warrants are exercisable and the associated exercise price are subject to certain proportional adjustments as set forth in the Loan Agreement Warrants.

The Company estimated the fair value of these Loan Agreement Warrants as of the issuance date to be $0.4 million, which was used in estimating the fair value of the debt instrument and was recorded as equity. The fair value of the Loan Agreement Warrants was calculated using the Black-Scholes option-valuation model, and was based on the strike price of $56.60, the stock price at issuance of $53.20, the ten-year contractual term of the warrants, a risk-free interest rate of 2.22%, expected volatility of 80.22% and 0% expected dividend yield.

As of December 31, 2022, Loan Agreement Warrants to purchase 8,833 shares of common stock issued to the Lender and its affiliates had not been exercised and were still outstanding. These warrants expire in May 2029.

13. Commitments and Contingencies

Litigation

On June 8, 2021, a securities class action complaint was filed in the U.S. District Court for the Northern District of California against the Company and two of its officers. The plaintiff is a purported stockholder of the Company. The complaint alleged that defendants violated Sections 10(b) and 20(a) of the Exchange Act and SEC Rule 10b-5 by making false and misleading statements and omissions of material fact about the Company's disclosure controls and procedures with respect to its marketing of DSUVIA. The complaint sought unspecified damages, interest, attorneys' fees, and other costs. On December 16, 2021, the Court appointed co-lead plaintiffs. Plaintiffs' amended complaint was filed on March 7, 2022. The amended complaint named the Company and three of its officers and continued to allege that defendants violated Sections 10(b) and 20(a) of the Exchange Act and SEC Rule 10b-5 by making false and misleading statements and omissions of material fact about the Company's disclosure controls and procedures with respect to its marketing of DSUVIA. The amended complaint also asserted a violation of Section 20A of the Exchange Act against the individual defendants for alleged insider trading. The amended complaint sought unspecified damages, interest, attorneys' fees, and other costs. On September 1, 2022, the Court held oral hearings on the Company's motion to dismiss the amended complaint with prejudice that was filed on July 21, 2022. On September 28, 2022, the Court issued a formal written opinion dismissing all of plaintiffs' claims against the Company and the named defendants with leave to amend, and on November 28, 2022, plaintiffs filed a second amended complaint naming the Company and three of its officers and asserting violations under Sections 10(b) and 20(a) of the Exchange Act on the same grounds as in the amended complaint and seeking unspecified damages, interest, attorneys' fees, and other costs. On January 30, 2023, the Company filed a motion to dismiss the second amended complaint with prejudice and on March 16, 2023, plaintiffs filed their opposition to the motion to dismiss the second amended complaint, The Company has an April 17, 2023 deadline to file its reply in support of the motion to dismiss the second amended complaint.

On July 6, 2021, a purported shareholder derivative complaint was filed in the U.S. District Court for the Northern District of California. The complaint names ten of the Company's officers and directors and asserts state and federal claims based on the same alleged misstatements as the securities class action complaint. On September 30, 2021, October 26, 2021, and November 17, 2021, three additional purported shareholder derivative complaints were filed in the U.S. District Court for the Northern District of California. The complaints name nine of the Company's officers and directors and also assert state and federal claims based on the same alleged misstatements as the securities class action complaint. All four complaints seek unspecified damages, attorneys' fees, and other costs. On December 6, 2021, the Court entered an order consolidating all four actions and staying the consolidated action pending the outcome of any motion to dismiss the securities class action. Please see "Part II., Item 1A. Risk Factors—Risks of a General Nature—Litigation may substantially increase our costs and harm our business."

The Company believes that these lawsuits are without merit and intends to vigorously defend against them. Given the uncertainty of litigation, the preliminary stage of the cases, and the legal standards that must be met for, among other things, class certification and success on the merits, the Company cannot estimate the reasonably possible loss or range of loss that may result from these actions.

14. Stockholders' Equity (Deficit)

Reverse Stock Split

On September 23, 2022, at a special meeting of stockholders, the Company's stockholders authorized the Company's Board of Directors to effect the Reverse Stock Split of all outstanding shares of common stock in a range of 1-for-10 to 1-for-30 shares. The Board of Directors subsequently approved the Reverse Stock Split at a ratio of 1-for-20. The Reverse Stock Split became effective at 5:01 p.m. Eastern Time on October 25, 2022. The Company's common stock began trading on the Nasdaq Global Market on a split-adjusted basis on October 26, 2022. The Reverse Stock Split was primarily intended to bring the Company into compliance with the minimum bid price requirements for maintaining its listing on the Nasdaq Global Market.

Preferred Stock

On August 3, 2022, the Company entered into a securities purchase agreement with LPC, or the Purchaser, pursuant to which the Company issued, in a private placement transaction, 3,000 shares of Series A Redeemable Convertible Preferred Stock, par value $0.001 per share, with $100 per share stated value, together with a warrant to purchase up to an aggregate of 81,150 shares of common stock at an exercise price of $4.07 per share, for $0.3 million. Upon the closing of the December 29, 2022 registered direct offering, the Company agreed to amend the August 2022 LPC Warrant to reduce the exercise price to $2.07 per share (see Note 12, "Warrants"). The transaction price of $0.3 million was allocated to the Series A Redeemable Convertible Preferred Stock and warrants based on their relative fair values. The Series A Redeemable Convertible Preferred Stock was initially recorded at $0.1 million separately from stockholders' equity in the Company's consolidated balance sheets due to the shares being redeemable based on contingent events outside of the Company's control.

The Series A Redeemable Convertible Preferred Stock was convertible, at the option of the holders, into shares of common stock at a conversion price of approximately $3.70 per share, subject to adjustment and beneficial ownership limitations set forth in the Certificate of Designation. The Company had the option to redeem the Series A Redeemable Convertible Preferred Stock for cash at 105% of the Stated Value on the date of and for 15 days following the Reverse Stock Split, subject to the Purchaser's right to convert the shares prior to such redemption. The Purchaser had the right to require the Company to redeem the shares of Series A Redeemable Convertible Preferred Stock for cash at 110% of the Stated Value of such shares commencing after the Company's right to redeem expired. The Series A Redeemable Convertible Preferred Stock was required to redeemed for cash at 110% of the Stated Value upon a delisting event. As a result, the Series A Redeemable Convertible Preferred Stock was recorded separately from stockholders' equity because it was redeemable upon the occurrence of redemption events that were considered not solely withing the Company's control. As such, during the year ended December 31, 2022, the Company recognized approximately $0.2 million in deemed dividends related to the Series A Redeemable Convertible Preferred Stock in the consolidated statements of operations and the consolidated statements of changes in redeemable convertible preferred stock and stockholders' equity (deficit).

The holders of the Series A Redeemable Convertible Preferred Stock were entitled to certain registration rights, rights for approval of increases in the authorized shares of such series, and to dividends paid on common stock on an as-if converted basis. The Series A Redeemable Convertible Preferred stock had no voting rights, other than the right to (i) vote exclusively on the Reverse Stock Split and any proposal to adjourn any meeting of stockholders called for the purpose of voting on the Reverse Stock Split and (ii) to 1,000,000 votes per each share of Series A Redeemable Convertible Preferred Stock, to vote together with the common stock, as a single class; to the extent cast on the Reverse Stock Split in the same proportion as shares of common stock. In addition, in the event of any liquidation, dissolution, or winding-up of the Company, the holders of the Series A Redeemable Convertible Preferred Stock were entitled to receive 110% the preferred stock's Stated Value plus any declared but unpaid dividends before any payment was made to holders of common stock.

On October 11, 2022, the Company and LPC entered into the Securities Redemption Agreement whereby on October 12, 2022, the Company redeemed for cash at a price equal to 105% of the Stated Value per share all 3,000 outstanding shares of Series A Redeemable Convertible Preferred Stock for $0.3 million. As a result, all shares of such series were retired and are no longer outstanding. On October 25, 2022, the Company filed a certificate of elimination to its amended and restated certificate of incorporation which (i) eliminated the previous designation of 3,000 shares of Series A Redeemable Convertible Preferred Stock from the Company's amended and restated certificate of incorporation and (ii) caused such shares of Series A Redeemable Convertible Preferred Stock to resume their status as authorized but unissued and non-designated shares of preferred stock.

Common Stock

2022 Registered Direct Offering

On December 29, 2022, the Company completed the December 2022 Financing in which it issued (i) 748,744 shares of its common stock, par value $0.001 per share, (ii) the 2022 Pre-Funded Warrants to purchase 2,632,898 shares of common stock, and (iii) the 2022 Warrants, which will accompany the common stock and 2022 Pre-Funded Warrants, to purchase an aggregate of 4,227,052 shares of common stock (see Note 12, "Warrants"). The shares of common stock and accompanying 2022 Warrants were sold at a combined offering price of $2.22625 per share and accompanying common warrant, and the 2022 Pre-Funded Warrants and accompanying 2022 Warrants were sold at a combined offering price of $2.22615 per 2022 Pre-Funded Warrant and accompanying 2022 Warrant. Total net proceeds from the offering were approximately $6.6 million, after deducting fees payable to the placement agent and other estimated offering expenses payable by the Company, excluding the proceeds, if any, from the exercise of the 2022 Pre-Funded Warrants and the 2022 Warrants. The common stock was allocated $0.1 million of the gross proceeds received based on its relative fair value to the other instruments issued (see Note 12, "Warrants").

2021 Underwritten Public Offering

On January 22, 2021, the Company completed an underwritten public offering in which the Company issued and sold 725,000 shares of its common stock to the underwriter at a price of $35.25 per share. On January 27, 2021, the underwriters exercised their option in full and purchased an additional 108,750 shares at a price of $35.25 per share. The total net proceeds from this offering of an aggregate 833,750 shares were approximately $28.9 million.

2021 Registered Direct Offering

On November 17, 2021, the Company completed a registered direct offering in which the Company issued and sold 875,000 shares of its common stock at a price of $16.00 per share and warrants exercisable for an aggregate of 875,000 shares of its common stock at a price of $20.00 per share (see Note 12, "Warrants"). The total net proceeds from this offering were approximately $13.9 million. The November 2021 issued shares were valued at approximately $13.1 million based on the closing stock price of $14.92 per share on November 15, 2021. The common stock and warrants were issued in a unit structure; therefore, in accordance with ASC Topic 815, the aggregate gross proceeds of $14.0 million were allocated to the two securities using the relative fair value method, resulting in the common stock and warrants being allocated values of $8.4 million and $5.6 million, respectively.

ATM Agreement

On June 21, 2016, the Company entered into a Controlled Equity Offering℠ Sales Agreement, or the ATM Agreement, with Cantor Fitzgerald & Co., or Cantor, as agent, pursuant to which the Company may offer and sell, from time to time through Cantor, shares of the Company's common stock, or the Common Stock having an aggregate offering price of up to $40.0 million, or the Shares. On May 9, 2019, the Company increased the aggregate offering price of shares of the Company's common stock which may be offered and sold under the ATM Agreement by $40.0 million, for a total of $80.0 million, or the Shares. The offering of Shares pursuant to the ATM Agreement will terminate upon the earlier of (a) the sale of all of the Shares subject to the ATM Agreement or (b) the termination of the ATM Agreement by Cantor or the Company, as permitted therein. The Company will pay Cantor a commission rate in the low single digits on the aggregate gross proceeds from each sale of Shares and has agreed to provide Cantor with customary indemnification and contribution rights.

The Company issued and sold approximately 0.1 million shares of common stock pursuant to the ATM Agreement and received net proceeds of $0.5 million, after deducting fees and expenses, during the year ended December 31, 2022. During the year ended December 31, 2021, the Company issued and sold approximately 0.2 million shares of common stock pursuant to the ATM Agreement, and received net proceeds of approximately $7.5 million, after deducting fees and expenses.

As of December 31, 2022, the Company had the ability to offer and sell shares of the Company's common stock having an aggregate offering price of up to $35.6 million under the ATM Agreement.

Stock Plans

2011 Equity Incentive Plan

In January 2011, the Board of Directors adopted, and the Company's stockholders approved, the 2011 Equity Incentive Plan, or 2011 EIP. The initial aggregate number of shares of the Company's common stock that were issuable pursuant to stock awards under the 2011 EIP was approximately 0.1 million shares. The number of shares of common stock reserved for issuance under the 2011 EIP automatically increased on January 1 of each year, starting on January 1, 2012 and continuing through January 1, 2020, by 4% of the total number of shares of the Company's common stock outstanding on December 31 of the preceding calendar year, or such lesser number of shares of common stock as determined by the Board of Directors.

As of June 16, 2020, no more awards may be granted under the 2011 Equity Incentive Plan, or the 2011 EIP, although all outstanding stock options and other stock awards previously granted under the 2011 EIP will continue to remain subject to the terms of the 2011 EIP.

Amended 2020 Plan

On June 16, 2020, at the 2020 Annual Meeting of Stockholders of the Company, the Company's stockholders, upon the recommendation of the Company's Board of Directors, approved the Company's 2020 Equity Incentive Plan, or the 2020 EIP.

The initial aggregate number of shares of the Company's common stock issuable pursuant to stock awards under the 2020 EIP was approximately 0.3 million shares. In addition, the share reserve will be increased by the number of returning shares, if any, as such shares become available from time to time under the 2011 EIP, for an additional number of shares not to exceed approximately 0.7 million shares. The term of any option granted under the 2020 EIP is determined on the date of grant but shall not be longer than 10 years. The Company issues new shares for settlement of vested restricted stock units and exercises of stock options. The Company does not have a policy of purchasing its shares relating to its stock-based programs.

On June 17, 2021, at the 2021 Annual Meeting of Stockholders of the Company, upon the recommendation of the Company's Board of Directors, the Company's stockholders approved an amendment and restatement of the Company's 2020 Equity Incentive Plan, or 2020 Plan, or as amended and restated, the Amended 2020 Plan, to increase the number of authorized shares reserved for issuance thereunder by approximately 0.2 million shares, subject to adjustment for certain changes in the Company's capitalization. The aggregate number of shares of the Company's common stock that may be issued under the Amended 2020 Plan will not exceed the sum of (i) approximately 0.2 million shares approved in connection with the adoption of the Amended 2020 Plan, (ii) approximately 0.3 million shares approved in connection with the original adoption of the 2020 Plan, and (iii) certain shares subject to outstanding awards granted under the 2011 Equity Incentive Plan that may become available for issuance under the 2020 Plan and Amended 2020 Plan, as such shares become available from time to time.

Amended and Restated 2011 Employee Stock Purchase Plan

Additionally, on June 16, 2020, the Company's stockholders, upon the recommendation of the Company's Board of Directors, approved the Amended and Restated 2011 Employee Stock Purchase Plan, or the Amended ESPP, which increased the aggregate number of shares of the Company's common stock reserved for issuance under the 2011 Employee Stock Purchase Plan, or ESPP, to approximately 0.2 million shares, subject to adjustment for certain changes in the Company's capitalization, and removed the "evergreen" provision from the ESPP.

In the year ended December 31, 2022, there were 10,941 shares issued under the Amended ESPP. The weighted average fair value of shares issued under the Amended ESPP in 2022 and 2021 was $6.82 and $20.23 per share, respectively. As of December 31, 2022, there were 211,876 shares available for future grant under the Amended ESPP.

15. Stock-Based Compensation

The Company recorded total stock-based compensation expense for stock options, stock awards and the Amended ESPP as follows (in thousands):

	December 31, 2022	December 31, 2021
Cost of goods sold	$ 62	$ 92
Research and development	570	813
Selling, general and administrative	2,257	3,704
Total	$ 2,889	$ 4,609

The following table summarizes restricted stock unit activity under the Company's Equity Incentive Plans:

	Number of Restricted Stock Units	Weighted Average Grant Date Fair Value
Restricted stock units outstanding, January 1, 2021	69,890	$ 35.75
Granted	57,448	33.65
Vested	(29,338)	37.75
Forfeited	(9,289)	31.56
Restricted stock units outstanding, December 31, 2021	88,711	$ 34.16
Granted	58,502	7.75
Vested	(44,744)	35.46
Forfeited	(19,691)	25.00
Restricted stock units outstanding, December 31, 2022	82,778	$ 16.97

The following table summarizes stock option activity under the Company's Equity Incentive Plans:

	Number of Stock Options Outstanding	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (Years)	Aggregate Intrinsic Value (in thousands)
December 31, 2021	714,085	$ 59.79		
Granted	117,022	7.75		
Forfeited	(35,645)	26.46		
Expired	(69,839)	60.42		
Exercised	—	—		
December 31, 2022	725,623	$ 52.98	5.3	$ —
Vested and exercisable options—December 31, 2022	515,933	$ 65.76	3.9	$ —
Vested and expected to vest—December 31, 2022	725,623	$ 52.80	5.3	$ —

As of December 31, 2022, there were 342,827 shares available for future grant under the 2020 EIP.

Additional information regarding the Company's stock options outstanding and vested and exercisable as of December 31, 2022 is summarized below:

	Options Outstanding			Options Vested and Exercisable	
Exercise Prices	Number of Stock Options Outstanding	Weighted-Average Remaining Contractual Life (Years)	Weighted-Average Exercise Price per Share	Shares Subject to Stock Options	Weighted-Average Exercise Price per Share
$4.62 - $8.03	88,096	9.2	$ 7.54	—	$ —
$8.36 - $12.54	19,046	9.1	$ 8.43	—	$ —
$14.40 - $21.60	20,941	6.9	$ 16.93	13,643	$ 16.84
$22.40 - $33.60	11,700	8.1	$ 28.62	10,774	$ 28.58
$34.40 - $51.60	311,695	6.0	$ 41.16	217,425	$ 42.75
$52.00 - $78.00	168,275	3.5	$ 62.66	168,221	$ 62.66
$78.40 - $117.60	62,756	1.0	$ 97.95	62,756	$ 97.95
$132.00 - $198.00	20,520	1.6	$ 133.16	20,520	$ 133.16
$204.40 - $306.60	22,594	1.0	$ 206.96	22,594	$ 206.96
	725,623	5.3	$ 52.98	515,933	$ 65.76

The weighted average grant-date fair value of options granted during the years ended December 31, 2022 and 2021 was $5.80 and $24.74 per share, respectively. As of December 31, 2022, total stock-based compensation expense related to unvested options to be recognized in future periods was $1.8 million which is expected to be recognized over a weighted-average period of 1.8 years. The grant date fair value of shares vested during the years ended December 31, 2022 and 2021 was $1.7 million and $2.4 million, respectively. The total intrinsic value of options exercised during the years ended December 31, 2021 and 2020 was $0 and $5.7 thousand, respectively.

On March 3, 2021, the Company granted 1.27 million performance-based stock options to certain of its executive officers, which are included in the stock option tables and associated disclosures above. The awards were granted under the 2020 EIP with an exercise price of $1.88 per share, the closing sales price as reported on the Nasdaq on the date of grant. The performance-based stock options are eligible to vest subject to the satisfaction of the service-based vesting requirements and attainment of share price target goals, a market-based condition. No performance-based stock options vested during the years ended December 31, 2022 and 2021.

The Company uses the Monte Carlo Simulation model to evaluate the derived service period and fair value of awards with market conditions, including assumptions of historical volatility and risk-free interest rate commensurate with the vesting term.

The Company used the following assumptions to calculate the fair value of each performance-based stock option:

	Year Ended December 31,	
	2022	2021
Derived service period (in years)	—	2.3 – 2.6
Risk-free interest rate	—	1.5%
Expected volatility	—	90%
Expected dividend rate	—	0%

The Company used the following assumptions to calculate the fair value of each time-based stock option:

	Year Ended December 31,	
	2022	2021
Expected term (in years)	6.3	6.0 – 6.2
Risk-free interest rate	1.6% - 3.0%	0.9% - 1.3%
Expected volatility	88%	90%
Expected dividend rate	0%	0%

16. Net Income (Loss) per Share of Common Stock

The Company applies the two-class method to compute basic net income (loss) per share by dividing the net income (loss) allocable to common shareholders by the weighted average number of shares of common stock outstanding for the period. The diluted net income (loss) per share of common stock is computed by giving effect to all potential common stock equivalents outstanding for the period determined using the more dilutive of the 1) treasury stock method, if-converted method, or contingently issuable share method, as applicable, or 2) the two-class method. For purposes of this calculation, options to purchase common stock, RSUs, and warrants to purchase common stock were considered to be common stock equivalents. During 2022, the Company presents diluted EPS using the two-class method as it was more dilutive. The Company's participating securities do not have a contractual obligation to share in the Company's losses, therefore, net loss for the year ended December 31, 2021 was attributed entirely to common stockholders. In periods with a reported net loss, common stock equivalents are excluded from the calculation of diluted net loss per share of common stock if their effect is antidilutive. Potential common shares that are issuable for little or no cash consideration, such as the Company's pre-funded warrants issued in December 2022 with a de minimis exercise price of $0.0001 per share, are considered outstanding common shares which are included in the calculation of basic and diluted net income (loss) per share in all circumstances.

The following table sets forth the computation of the Company's basic and diluted net income (loss) per share of common stock during the years ended December 31, 2022 and 2021 (in thousands, except for share and per share amounts):

	Year ended December 31,	
	2022	2021
	(in thousands, except share and per share amounts)	
Basic net income (loss) per common share:		
Net income (loss)	$ 47,755	$ (35,099)
Less: deemed dividend related to Series A Redeemable Convertible Preferred Stock	(186)	—
Less: income allocated to participating securities	(5,240)	—
Net income (loss) attributable to common shareholders	$ 42,329	$ (35,099)
Weighted average shares outstanding — basic	7,385,348	5,993,013
Net income (loss) — basic	$ 5.73	$ (5.86)

	Year ended December 31,	
	2022	2021
	(in thousands, except share and per share amounts)	
Diluted net income (loss) per common share:		
Net income (loss)	$ 47,755	$ (35,099)
Less: deemed dividend related to Series A Redeemable Convertible Preferred Stock	(186)	—
Less: income allocated to participating securities	(5,227)	—
Net income (loss) attributable to common shareholders	$ 42,342	$ (35,099)
Weighted average shares outstanding — basic	7,385,348	5,993,013
Dilutive effect of warrants	20,285	—
Dilutive effect of RSUs	1,353	—
Weighted average shares outstanding — diluted	7,406,986	5,993,013
Net income (loss) — diluted	$ 5.72	$ (5.86)

The following outstanding shares of common stock equivalents were excluded from the computation of diluted net income (loss) per share of common stock for the periods presented because including them would have been antidilutive:

	Year Ended December 31,	
	2022	2021
ESPP, RSUs and stock options to purchase common stock	815,710	816,421
Common stock warrants	133,833	883,833

In addition, the shares held back and contingently issuable in connection with the Lowell Merger, as described in Note 4 above, have also been excluded from the computation of diluted net income (loss) per share of common stock for the periods presented because the contingencies for issuance of these shares have not been met.

17. Accrued Liabilities

Accrued liabilities consist of the following (in thousands):

	December 31,	
	2022	2021
Accrued compensation and employee benefits	$ 1,944	$ 2,974
Accrued professional services	625	1,523
Accrued product returns and sales allowances	315	775
Deferred revenue	115	86
Other accrued liabilities	1,267	1,166
Total accrued liabilities	$ 4,266	$ 6,524

18. 401(k) Plan

The Company sponsors a 401(k) plan that stipulates that eligible employees can elect to contribute to the 401(k) plan, subject to certain limitations. Pursuant to the 401(k) plan, the Company makes a matching contribution of up to 4% of the related compensation. Under the vesting schedule, employees have ownership in the matching employer contributions based on the number of years of vesting service completed. Company contributions were $0.3 million and $0.4 million for the years ended December 31, 2022 and 2021, respectively.

19. Income Taxes

The Company recorded a provision for income taxes of $13 thousand and $5 thousand for the years ended December 31, 2022 and 2021, respectively.

Net deferred tax assets as of December 31, 2022 and 2021 consist of the following (in thousands):

	December 31, 2022	December 31, 2021
Deferred tax assets:		
Accruals and other	$ 1,738	$ 3,989
Research credits	7,392	7,275
Net operating loss carryforward	84,325	75,452
Section 59(e) R&D expenditures	3,496	5,070
Section 174 R&D expenditures	981	—
Deferred revenue	—	19,666
Total deferred tax assets	97,932	111,452
Valuation allowance	(97,932)	(111,452)
Net deferred tax assets	$ —	$ —

Reconciliations of the statutory federal income tax to the Company's effective tax during the years ended December 31, 2022 and 2021 are as follows (in thousands):

	Year Ended December 31,	
	2022	2021
Tax at statutory federal rate	$ 10,031	$ (7,370)
State tax—net of federal benefit	823	231
Acquired assets	1,728	—
Stock options	611	718
Other	340	(20)
Change in valuation allowance	(13,520)	6,446
Provision for income taxes	$ 13	$ 5

ASC 740 requires that the tax benefit of net operating losses, temporary differences and credit carryforwards be recorded as an asset to the extent that management assesses that realization is "more likely than not." Realization of deferred tax assets is dependent on future taxable income, if any, the timing and the amount of which are uncertain. Accordingly, the deferred tax assets have been fully offset by a valuation allowance. The valuation allowance decreased by $13.5 million and increased by $6.4 million during the years ended December 31, 2022 and 2021, respectively.

As of December 31, 2022, the Company had federal net operating loss carryforwards of $346.4 million, of which $114.9 million federal net operating losses generated before January 1, 2018 will begin to expire in 2029. Federal net operating losses of $231.5 million generated from 2018 to 2022 will carryforward indefinitely but are subject to the 80% taxable income limitation. As of December 31, 2022, the Company had state net operating loss carryforwards of $167.9 million, which begin to expire in 2028.

As of December 31, 2022, the Company had federal research credit carryovers of $6.6 million, which begin to expire in 2026. As of December 31, 2022, the Company had state research credit carryovers of $4.1 million, which will carryforward indefinitely.

Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes, such as research credits, to offset its post-change income may be limited. Based on an analysis performed by the Company as of December 31, 2013, it was determined that two ownership changes have occurred since inception of the Company. The first ownership change occurred in 2006 at the time of the Series A financing and, as a result of the change, $1.4 million in federal and state net operating loss carryforwards will expire unutilized. In addition, $26 thousand in federal and state research and development credits will expire unutilized. The second ownership change occurred in July 2013 at the time of the underwritten public offering; however, the Company believes the resulting annual imposed limitation on use of pre-change tax attributes is sufficiently high that the limit itself will not result in unutilized pre-change tax attributes.

Uncertain Tax Positions

A reconciliation of the beginning and ending balances of the unrecognized tax benefits during the years ended December 31, 2022 and 2021 is as follows (in thousands):

	Year Ended December 31,	
	2022	**2021**
Unrecognized benefit—beginning of period	$ 2,635	$ 2,635
Gross increases—prior period tax positions	—	—
Gross increases—current period tax positions	43	—
Unrecognized benefit—end of period	$ 2,678	$ 2,635

The entire amount of the unrecognized tax benefits would not impact the Company's effective tax rate if recognized.

There were no accrued interest or penalties related to unrecognized tax benefits in the years ended December 31, 2022 and 2021. The Company files income tax returns in the United States, California, and other states. The tax years 2005 through 2014, and 2016 through 2022, remain open in all jurisdictions. The Company is not currently under examination by income tax authorities in U.S. federal, state or foreign jurisdictions. The Company does not anticipate any significant changes within 12 months of this reporting date of its uncertain tax positions.

In March 2020, the Coronavirus Aid, Relief and Economic Security, or CARES, Act was signed into law. The CARES Act included several tax changes as part of its economic package. These changes principally related to expanded net operating loss carryback periods, increases to interest deductibility limitations, and accelerated alternative minimum tax refunds. The Company has evaluated these items and determined that the items do not have a material effect on the Company's financial statements as of December 31, 2021 or 2022. Additionally, the CARES Act enacted the Employee Retention Credit, or ERC, to incentivize companies to retain employees, which was subsequently modified by extension of the CARES Act. Under the provisions of the CARES Act and its subsequent extension, the Company was eligible for ERCs, subject to certain criteria. Accordingly, the Company recorded a reduction in payroll taxes related to ERCs claimed for $1.4 million in the year ended December 31, 2021. These credits were recorded in the consolidated statements of operations as an offset to the related payroll expenses in the respective operating costs and expenses line item and are disclosed within prepaid expenses and other current assets on the Company’s consolidated balance sheets at December 31, 2022.

20. Subsequent Events

Asset Purchase Agreement

On March 12, 2023, the Company, or AcelRx, entered into an Asset Purchase Agreement, or the Purchase Agreement, with Vertical Pharmaceuticals, LLC, a wholly owned subsidiary of Alora Pharmaceuticals, LLC, or the Buyer, pursuant to which Buyer agreed to acquire certain assets and assume certain liabilities of AcelRx relating to its sufentanil sublingual tablet product referred to as DSUVIA or DZUVEO, or any other single-dose pharmaceutical product for use in medically supervised settings containing a sublingual tablet that includes sufentanil as the sole active ingredient, as a 30 mcg tablet or other dosage form or strength as reasonably necessary for lifecycle management, or the Product. The Product expressly excludes the pharmaceutical product referred to as Zalviso (sufentanil sublingual tablets, each 15 mcg), any other multi-dose administration system containing sufentanil sublingual tablets (whether as the sole active ingredient or in combination with other active ingredients), and any single-dose formulation of sufentanil for use outside of a medically supervised setting. Subject to consummation of the transactions contemplated by the Purchase Agreement, or the Closing, AcelRx will be entitled to receive (a) up to $116.5 million in sales-based milestones, (b) quarterly payments in an amount equal to 15% of net sales based on sales of Product to all customers, other than sales to the United States Department of Defense, or DoD, under the Marketing Agreement (as defined below), pursuant to which the Buyer will pay AcelRx 75% of Product net sales to the DoD, and sales by or on behalf of Laboratoire Aguettant, or Aguettant, and (c) 20% of any consideration, excluding royalty payments based on sales of Product and subject to customary exclusions, received by Buyer or its affiliates in connection with a grant to any third party of a license related to Product, or by Buyer or its affiliates or equityholders in connection with a sale or transfer to any third party of an ownership interest in any assets acquired by Buyer under the Purchase Agreement.

The Purchase Agreement contains customary representations, warranties, and covenants by each party. Buyer agreed not to, after the Closing, practice, license or otherwise exploit any of the intellectual property rights acquired by it under the Purchase Agreement to manufacture, develop or commercialize any product (other than Product) that is or has been commercialized by AcelRx or its affiliate as of the date of the Purchase Agreement, or any product that is competitive with any such product. In addition, after the Closing, Buyer will use commercially reasonable efforts to maintain regulatory approvals for and commercialize Product in the United States. If the Buyer (together with other relevant parties, taken as a whole) fails to commercialize, sell and distribute Product within the six-month period beginning on July 1, 2023, then all rights granted to Buyer pursuant to the Purchase Agreement will, upon AcelRx’s written notice, revert back to AcelRx. The Purchase Agreement also contains indemnification rights for each of AcelRx and Buyer for breaches of representations, warranties, and covenants, as well as certain other matters, subject to certain specified limitations.

The Closing is subject to customary conditions (including, the accuracy of representations and warranties, performance of covenants, and no occurrence of a material adverse effect) and the execution of the Amended DZUVEO Agreement (as defined below) and the Amended and Restated Supply Agreement (as defined below) between AcelRx and Aguettant, as well as certain ancillary agreements between AcelRx and Buyer. Such ancillary agreements include (a) an intellectual property agreement, pursuant to which Buyer will grant fully-paid, royalty-free and perpetual licenses to AcelRx under certain specified intellectual property rights acquired by Buyer under the Purchase Agreement for, among other things, the development, manufacture, commercialization and exploitation of certain products, including Zalviso, (b) a transition services agreement, pursuant to which, during the period specified therein, AcelRx will be paid to provide certain services (including, manufacturing technology transfer, supply chain, regulatory, and medical affairs services) to Buyer, and distribute, on behalf of Buyer, certain inventory of Product transferred to Buyer under the Purchase Agreement, and (c) a marketing agreement, or the Marketing Agreement, pursuant to which AcelRx will have the exclusive right to market and offer Product for sale to DoD and Buyer will pay to AcelRx 75% of net sales of Product sold to DoD, subject to adjustment in certain circumstances.

Amendments to Certain Agreements Between AcelRx and Aguettant

AcelRx and Aguettant are parties to (a) the License and Commercialization Agreement, dated July 14, 2021, pursuant to which Aguettant obtained the exclusive right to develop and commercialize DZUVEO in certain European countries for the management of acute moderate to severe pain in adults in medically monitored settings, or the DZUVEO Agreement, and (b) the supply agreement, dated December 6, 2021, with respect to the manufacture and supply of DZUVEO in form of bulk product by AcelRx to Aguettant, or the Supply Agreement. Pursuant to the Purchase Agreement, as a condition of the Closing, AcelRx and Aguettant will enter into an amendment to the DZUVEO Agreement, or the Amended DZUVEO Agreement, and an amendment and restatement to the Supply Agreement, or the Amended and Restated Supply Agreement, in each case, in a form reasonably acceptable to Buyer.

Pursuant to the Amended DZUVEO Agreement, upon execution thereof, (a) Aguettant’s obligations to make sales-based milestone payments and to achieve certain levels of minimum sales will terminate, (b) before Aguettant has established a semi-automated packaging line for Product, AcelRx will manufacture and supply DZUVEO in the form of bulk products (*i.e.*, products that are pre-packaged in labeled pouches and packed in bright stock cartons for shipment) to Aguettant or its affiliates or sublicensees, and Aguettant will be responsible for manufacturing finished products from bulk products, and (c) after Aguettant has established such semi-automated packaging line, AcelRx will cause DZUVEO to be manufactured and supplied in the form of bulk tablets (*i.e.*, products in tablet forms supplied in bulk (not packaged) quantities) to Aguettant or its affiliates or sublicensees, and Aguettant will be responsible for manufacturing finished products from bulk tablets. The Amended and Restated Supply Agreement will govern the manufacture and supply of DZUVEO in the form of bulk products or bulk tablets, and contain customary terms, including those with respect to manufacturing requirements, forecast, delivery, and post-delivery inspection.

Pursuant to the Purchase Agreement, AcelRx will assign the Amended DZUVEO Agreement and the Amended and Restated Supply Agreement to Buyer at the Closing.

In addition, AcelRx and Aguettant are parties to the License and Commercialization Agreement, dated July 14, 2021, pursuant to which AcelRx obtained exclusive rights to develop and commercialize certain ephedrine pre-filled syringe and certain phenylephrine prefilled syringe in the United States, or the PFS Agreement. In connection with AcelRx's and Aguettant's agreement to enter into the Amended DZUVEO Agreement and the Amended and Restated Supply Agreement, the parties will enter into an amendment to the PFS Agreement, or the Amended PFS Agreement, pursuant to which, effective on the later of the Closing and April 1, 2023, (a) Aguettant will pay AcelRx a complementary payment in the amount of EUR 1,500,000, and (b) AcelRx's obligation to make a certain specified sales-milestone payment will terminate.

Termination Agreement and Mutual Release Between AcelRx and Catalent

On March 12, 2023, AcelRx and Catalent Pharma Solutions, LCC, or Catalent, entered into a termination agreement and mutual release, or the Termination Agreement, to terminate the Site Readiness Agreement with an effective date of August 15, 2019 and as amended on September 24, 2020, the SRA Agreement, and the commercial supply agreement with an effective date of March 31, 2021, the CSA Agreement. Pursuant to the Termination Agreement, as of the date on which AcelRx has removed and transported certain equipment from Catalent's site, the SRA Agreement and the CSA Agreement will terminate except with respect to certain specified provisions of such agreements.

2022 Pre-Funded Warrants

The 2022 Pre-Funded Warrants to purchase 2,632,898 shares of common stock were fully exercised in the first quarter of 2023.

21. Restatement (Unaudited)

Restatement of Previously Issued Unaudited Interim Condensed Consolidated Financial Statements

In connection with the Company's year-end financial statement close and preparation of its Annual Report on Form 10-K for the year ended December 31, 2022, an error in the earnings per share calculations was identified in the interim financial statements (the "Prior Period Financial Statements") for the three and six months ended June 30, 2022 and nine months ended September 30, 2022 (the "Interim Periods"). The error in the earnings per share calculation was due to the Company not properly applying the two-class method of calculating earnings per share with respect to, or disclose that, the warrants issued in November 2021 are participating securities. The financial statements for the year ended December 31, 2021 and the three months ended March 31, 2022, did not require the application of the two-class method of calculating earnings per share, and therefore were not impacted by the issuance of the warrants in November 2021.

The error has no impact on the Company's cash balance, liquidity, revenues, operating expenses, or total net income. Further, there is no impact to the Company's balance sheet accounts or cash flows.

On March 30, 2023, the Company's management and the Audit Committee of the Company determined that the Company's Prior Period Financial Statements for the Interim Periods, should no longer be relied upon because of the error in the earnings per share calculations. The Company's management and the Audit Committee concluded that it is appropriate to restate the Prior Period Financial Statements for the Interim Periods noted above.

The following tables present the impact of the error on basic and diluted EPS for the three and six months ended June 30, 2022, and the nine months ended September 30, 2022 (amounts in thousands, except per share data, 1-for-20 reverse stock split adjusted).

	Three Months Ended June 30, 2022		
	As Previously Reported	Adjustment	As Restated
Basic net income per common share:			
Net income	$ 70,663	$ —	$ 70,663
Income allocated to participating securities	—	(7,511)	(7,511)
Net income attributable to Common Shareholders, basic	$ 70,663	$ (7,511)	$ 63,152
Net income attributable to Common Shareholders per share, basic	$ 9.60	$ (1.02)	$ 8.58
Shares used in computing net income attributable to Common Shareholders per share, basic	7,356,952	—	7,356,952
Diluted net income (loss) per common share:			
Net income	$ 70,663	$ —	$ 70,663
Income allocated to participating securities	—	(7,508)	(7,508)
Net income attributable to Common Shareholders, diluted	$ 70,663	$ (7,508)	$ 63,155
Net income attributable to Common Shareholders per share, diluted	$ 9.60	$ (1.02)	$ 8.58
Shares used in computing net income attributable to Common Shareholders per share, diluted	7,360,453	—	7,360,453

	Six Months Ended June 30, 2022		
	As Previously Reported	Adjustment	As Restated
Basic net income per common share:			
Net income	$ 61,989	$ —	$ 61,989
Income allocated to participating securities	—	(6,619)	(6,619)
Net income attributable to Common Shareholders, basic	$ 61,989	$ (6,619)	$ 55,370
Net income attributable to Common Shareholders per share, basic	$ 8.47	$ (0.91)	$ 7.56
Shares used in computing net income attributable to Common Shareholders per share, basic	7,319,279	—	7,319,279
Diluted net income per common share:			
Net income	$ 61,989	$ —	$ 61,989
Income allocated to participating securities	—	(6,618)	(6,618)
Net income attributable to Common Shareholders, diluted	$ 61,989	$ (6,618)	$ 55,371
Net income attributable to Common Shareholders per share, diluted	$ 8.47	$ (0.91)	$ 7.56
Shares used in computing net income attributable to Common Shareholders per share, diluted	7,321,022	—	7,321,022

	Nine Months Ended September 30, 2022		
	As Previously Reported	Adjustment	As Restated
Basic net income per common share:			
Net income	$ 55,239	$ —	$ 55,239
Deemed dividend related to Series A Redeemable Convertible Preferred Stock	(186)	—	(186)
Income allocated to participating securities	(129)	(5,851)	(5,980)
Net income attributable to Common Shareholders, basic	$ 54,924	$ (5,851)	$ 49,073
Net income attributable to Common Shareholders per share, basic	$ 7.48	$ (0.79)	$ 6.69
Shares used in computing net income attributable to Common Shareholders per share, basic	7,338,853	—	7,338,853
Diluted net income per common share:			
Net income	$ 55,239	$ —	$ 55,239
Deemed dividend related to Series A Redeemable Convertible Preferred Stock	(186)	—	(186)
Income allocated to participating securities	(129)	(5,846)	(5,975)
Net income attributable to Common Shareholders, diluted	$ 54,924	$ (5,846)	$ 49,078
Net income attributable to Common Shareholders per share, diluted	$ 7.46	$ (0.78)	$ 6.68
Shares used in computing net income attributable to Common Shareholders per share, diluted	7,367,293	(21,339)	7,345,954

SCHEDULE II: VALUATION AND QUALIFYING ACCOUNTS
(in thousands)

Description	Balance at Beginning of Period	Additions Charged as a Reduction to Revenue	Deductions*	Balance at End of Period
Sales & return allowances, discounts, chargebacks and rebates:				
Year ended December 31, 2022	$ 780	$ 521	$ (977)	$ 324
Year ended December 31, 2021	$ 668	$ 1,012	$ (900)	$ 780

* Deductions to sales discounts and allowances relate to discounts or allowances actually taken or paid.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (Nos. 333-268396, 333-264326, and 333-239156) and Form S-8 (Nos. 333-258896, 333-239213, 333-230139, 333-223535, 333-216492, 333-202709, 333-194634, 333-187206, 333-237195, 333-209998, 333-180334, and 333 172409) of AcelRx Pharmaceuticals, Inc. of our report dated March 31, 2023, which includes an explanatory paragraph relating to AcelRx Pharmaceuticals, Inc.'s ability to continue as a going concern, relating to the consolidated financial statements and schedule II, which appears in this Annual Report on Form 10 K.

/s/ WithumSmith+Brown, PC

San Francisco, California
March 31, 2023

Exhibit 31.1

CERTIFICATIONS

I, Vincent J. Angotti, certify that:

1. I have reviewed this annual report on Form 10-K of AcelRx Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's Board of Directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 31, 2023

/s/ Vincent J. Angotti
Vincent J. Angotti
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Raffi Asadorian, certify that:

1. I have reviewed this annual report on Form 10-K of AcelRx Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's Board of Directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 31, 2023

/s/ Raffi Asadorian
Raffi Asadorian
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Vincent J. Angotti, Chief Executive Officer of AcelRx Pharmaceuticals, Inc. (the "Company"), and Raffi Asadorian, Chief Financial Officer of the Company, each hereby certifies that, to the best of his or her knowledge:

1. The Company's Annual Report on Form 10-K for the period ended December 31, 2022, to which this Certification is attached as Exhibit 32.1 (the "Annual Report") fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act, and

2. The information contained in the Annual Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

In Witness Whereof, the undersigned have set their hands hereto as of the 31st day of March 2023.

/s/ Vincent J. Angotti	/s/ Raffi Asadorian
Vincent J. Angotti	Raffi Asadorian
Chief Executive Officer	Chief Financial Officer

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