UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

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

For the quarterly period ended March 31, 2022

or

☐ **TRANSITION REPORTS 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**

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 is a shell company (as defined in Exchange Act Rule 12b-2) Yes ☐ No ☒

As of May 10, 2022, the number of outstanding shares of the registrant's common stock was 147,114,006.

ACELRX PHARMACEUTICALS, INC.

QUARTERLY REPORT ON FORM 10-Q FOR THE QUARTER ENDED MARCH 31, 2022

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Unless the context indicates otherwise, the terms "AcelRx," "AcelRx Pharmaceuticals," "we," "us" and "our" refer to AcelRx Pharmaceuticals, Inc., and its consolidated subsidiaries. "DZUVEO" and "Niyad" are trademarks, and "ACELRX," "DSUVIA" 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.

Forward-Looking Statements

This Quarterly Report on Form 10-Q, or Form 10-Q, contains "forward-looking statements" within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, which are subject to the "safe harbor" created by that section. The forward-looking statements in this Form 10-Q are contained principally under "Part I. Financial Information - Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Part II. Other Information - Item 1A. Risk Factors". 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 statements involve risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Form 10-Q, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain. Many important factors affect our ability to achieve our objectives, including:

- the accuracy of our estimates regarding the sufficiency of our cash resources, future revenues, expenses, capital requirements and needs for additional financing, and our ability to obtain additional financing;
- the uncertainties and impact arising from the worldwide COVID-19 pandemic, including restrictions on the ability of our sales force to contact and communicate with target customers and resulting delays and challenges to our commercial sales of DSUVIA® (sufentanil sublingual tablet, 30 mcg);
- our success in commercializing DSUVIA in the United States, including the marketing, sales, and distribution of the product, whether alone or with contract sales organizations and other collaborators;
- our ability to satisfactorily comply with FDA regulations concerning the advertising and promotion of DSUVIA;
- the size and growth potential of the markets for DSUVIA, and, if approved, Zalviso® (sufentanil sublingual tablet system) and our other product candidates in the United States, and our ability to serve those markets;
- our ability to maintain regulatory approval of DSUVIA in the United States, including effective management of and compliance with the DSUVIA Risk Evaluation and Mitigation Strategies, or REMS, program;
- acceptance of DSUVIA by physicians, patients and the healthcare community, including the acceptance of pricing and placement of DSUVIA on payers' formularies;
- our ability to realize the expected benefits and potential value created by the acquisition of Lowell Therapeutics, Inc., or Lowell, pursuant to the Agreement and Plan of Merger, or Merger Agreement, for our stockholders, on a timely basis or at all;
- our ability to develop and commercialize products and product candidates that we in-license;
- our ability to develop sales and marketing capabilities in a timely fashion, whether alone through recruiting qualified employees, by engaging a contract sales organization, or with potential future collaborators;
- successfully establishing and maintaining commercial manufacturing with third parties;
- our ability to manage effectively, and the impact of any costs associated with, potential governmental investigations, inquiries, regulatory actions or lawsuits that may be, or have been, brought against us;
- continued demonstration of an acceptable safety profile of DSUVIA;
- effectively competing with other medications for the treatment of moderate-to-severe acute pain in medically supervised settings, including IV-opioids and any subsequently approved products;
- our ability to manufacture and supply DZUVEO® to Laboratoire Aguettant, or Aguettant, in accordance with their forecasts and the License and Commercialization Agreement, or DZUVEO Agreement, with Aguettant;
- the status of the DZUVEO Agreement or any other future potential collaborations, including potential milestones and revenue share payments under the DZUVEO Agreement;
- our, or Aguettant's, ability to maintain regulatory approval of DZUVEO in the European Union, or EU;
- our ability to fulfill our obligations under the Purchase and Sale Agreement with SWK Funding, LLC, or SWK, (assignee of PDL BioPharma, Inc., or PDL) including our obligation to use commercially reasonable efforts to negotiate a replacement license agreement for Zalviso with a third party;
- our ability to successfully execute the pathway towards a resubmission of the Zalviso New Drug Application, or NDA, and subsequently obtain and maintain regulatory approval of Zalviso in the United States and comply with any related restrictions, limitations, and/or warnings in the label of Zalviso if approved;

- the outcome of any potential FDA Advisory Committee meeting held for Zalviso;
- our ability to successfully commercialize Zalviso, if approved in the United States;
- the rate and degree of market acceptance of Zalviso, if approved in the United States;
- our ability to obtain adequate government or third-party payer reimbursement;
- our ability to attract additional collaborators with development, regulatory and commercialization expertise;
- our ability to successfully retain our key commercial, scientific, engineering, medical or management personnel and hire new personnel as needed;
- regulatory developments in the United States and foreign countries;
- the performance of our third-party suppliers and manufacturers, including any supply chain impacts or work limitations resulting from shelter-in-place orders related to COVID-19;
- the success of competing therapies that are or become available;
- our liquidity and capital resources; and
- our ability to obtain and maintain intellectual property protection for our approved products and product candidates.

In addition, you should refer to "Part II. Other Information - Item 1A. Risk Factors" in this Form 10-Q for a discussion of these and other important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Form 10-Q will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. Also, forward-looking statements represent our estimates and assumptions only as of the date of this Form 10-Q. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

PART I. FINANCIAL INFORMATION

Item 1. Financial Statements

AcelRx Pharmaceuticals, Inc.

Condensed Consolidated Balance Sheets
(In thousands, except share data)

	March 31, 2022 (unaudited)	December 31, 2021[1]
Assets		
Current Assets:		
Cash and cash equivalents	$ 21,822	$ 12,663
Short-term investments	17,527	38,967
Accounts receivable, net	184	160
Inventories, net	1,045	1,111
Prepaid expenses and other current assets	2,233	2,588
Total current assets	42,811	55,489
Operating lease right-of-use assets	4,147	4,302
Property and equipment, net	15,933	15,928
In-process research and development asset	8,819	—
Other assets	261	2,174
Total Assets	$ 71,971	$ 77,893
Liabilities and Stockholders' Deficit		
Current Liabilities:		
Accounts payable	$ 2,715	$ 2,121
Accrued and other liabilities	4,321	6,524
Long-term debt, current portion	8,813	8,796
Operating lease liabilities, current portion	1,184	1,068
Total current liabilities	17,033	18,509
Long-term debt, net of current portion	3,041	5,007
Deferred revenue, net of current portion	1,122	1,151
Operating lease liabilities, net of current portion	3,578	3,750
Liability related to the sale of future royalties	84,615	85,288
Other long-term liabilities	855	81
Total liabilities	110,244	113,786
Commitments and Contingencies		
Stockholders' Deficit:		
Common stock, $0.001 par value—200,000,000 shares authorized as of March 31, 2022 and December 31, 2021; 147,109,007 and 136,819,647 shares issued and outstanding as of March 31, 2022 and December 31, 2021, respectively	147	137
Additional paid-in capital	443,838	437,554
Accumulated deficit	(482,258)	(473,584)
Total stockholders' deficit	(38,273)	(35,893)
Total Liabilities and Stockholders' Deficit	$ 71,971	$ 77,893

[1] The condensed consolidated balance sheet as of December 31, 2021 has been derived from the audited financial statements as of that date included in the Company's Annual Report on Form 10-K for the year ended December 31, 2021.

See notes to condensed consolidated financial statements.

AcelRx Pharmaceuticals, Inc.

Condensed Consolidated Statements of Operations
(Unaudited)
(In thousands, except share and per share data)

	Three Months Ended March 31,	
	2022	**2021**
Revenue:		
Product sales	$ 442	$ 451
Contract and other collaboration	—	60
Total revenue	442	511
Operating costs and expenses:		
Cost of goods sold	784	1,040
Research and development	1,315	969
Selling, general and administrative	7,338	7,644
Total operating costs and expenses	9,437	9,653
Loss from operations	(8,995)	(9,142)
Other income:		
Interest expense	(390)	(672)
Interest income and other income, net	38	76
Non-cash interest income on liability related to future sale of royalties	673	782
Total other income	321	186
Net loss	$ (8,674)	$ (8,956)
Net loss per share of common stock, basic and diluted	$ (0.06)	$ (0.08)
Shares used in computing net loss per share of common stock, basic and diluted – See Note 11	145,623,751	113,256,550

See notes to condensed consolidated financial statements.

AcelRx Pharmaceuticals, Inc.

Condensed Consolidated Statements of Stockholders' Deficit
(Unaudited)
(in thousands, except share data)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount			
Balance as of December 31, 2021	136,819,647	$ 137	$ 437,554	$ (473,584)	$ (35,893)
Stock-based compensation	—	—	783	—	783
Issuance of common stock upon vesting of restricted stock units, net of shares withheld for employee taxes	515,393	—	(58)	—	(58)
Issuance of common stock in connection with asset acquisition	9,620,532	10	5,501	—	5,511
Issuance of common stock upon ESPP purchase	153,435	—	58	—	58
Net loss	—	—	—	(8,674)	(8,674)
Balance as of March 31, 2022	147,109,007	$ 147	$ 443,838	$ (482,258)	$ (38,273)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount			
Balance as of December 31, 2020	98,812,008	$ 98	$ 382,637	$ (438,485)	$ (55,750)
Stock-based compensation	—	—	1,089	—	1,089
Issuance of common stock upon vesting of restricted stock units, net of shares withheld for employee taxes	404,172	—	(249)	—	(249)
Net proceeds from issuance of common stock in connection with equity financings	19,701,562	20	36,340	—	36,360
Issuance of common stock upon ESPP purchase	183,132	—	192	—	192
Issuance of common stock upon exercise of stock options	2,125	—	2	—	2
Net loss	—	—	—	(8,956)	(8,956)
Balance as of March 31, 2021	119,102,999	$ 118	$ 420,011	$ (447,441)	$ (27,312)

See notes to condensed consolidated financial statements.

AcelRx Pharmaceuticals, Inc.

Condensed Consolidated Statements of Cash Flows
(Unaudited)
(In thousands)

	Three Months Ended March 31,	
	2022	**2021**
Cash flows from operating activities:		
Net loss	$ (8,674)	$ (8,956)
Adjustments to reconcile net loss to net cash used in operating activities:		
Non-cash royalty revenue related to royalty monetization	—	(45)
Non-cash interest income on liability related to royalty monetization	(673)	(782)
Depreciation and amortization	420	450
Non-cash interest expense related to debt financing	134	222
Stock-based compensation	783	1,089
Gain on lease termination	—	(522)
Other	2	68
Changes in operating assets and liabilities:		
Accounts receivable	(24)	(23)
Inventories	57	105
Prepaid expenses and other assets	360	361
Accounts payable	249	313
Accrued liabilities	(1,512)	(1,698)
Operating lease liabilities	(56)	(241)
Deferred revenue	—	(49)
Net cash used in operating activities	(8,934)	(9,708)
Cash flows from investing activities:		
Purchase of property and equipment	(89)	(24)
Purchase of investments	(6,175)	(24,441)
Cash paid for asset acquisition, net of cash acquired	(1,156)	—
Proceeds from maturities of investments	27,596	7,040
Net cash provided by (used in) investing activities	20,176	(17,425)
Cash flows from financing activities:		
Payment of long-term debt	(2,083)	(2,083)
Net proceeds from issuance of common stock in connection with equity financings	—	36,360
Net proceeds from issuance of common stock through equity plans	58	194
Payment of employee tax obligations related to vesting of restricted stock units	(58)	(249)
Net cash (used in) provided by financing activities	(2,083)	34,222
Net increase in cash and cash equivalents	9,159	7,089
Cash and cash equivalents—Beginning of period	12,663	27,274
Cash and cash equivalents—End of period	$ 21,822	$ 34,363
NONCASH INVESTING ACTIVITIES:		
Purchases of property and equipment in accounts payable and accrued liabilities	1,275	1,678
Asset acquisition costs in accounts payable and accrued liabilities	531	—
Liability for hold back shares in connection with asset acquisition in other long-term liabilities	800	—
Issuance of common stock in connection with asset acquisition	5,511	—

See notes to condensed 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) and Zalviso® are both focused on the treatment of acute pain, and each utilize 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. AcelRx is further developing a distribution capability and commercial organization to continue to market and sell DSUVIA in the United States. In geographies where AcelRx decides not to commercialize products by itself, the Company may seek to out-license commercialization rights. The Company currently intends to commercialize and promote DSUVIA/DZUVEO outside the United States with one or more strategic partners, and, in July 2021, 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. The timing of the resubmission of the Zalviso new drug application, or NDA, is in part dependent upon the finalization of the FDA's new opioid approval guidelines and process. AcelRx intends to seek regulatory approval for Zalviso in the United States and, if successful, potentially promote Zalviso either by itself or with strategic partners. Zalviso is approved in Europe and was commercialized by Grünenthal GmbH, or Grünenthal, through May 12, 2021 (see *Termination of Grünenthal Agreements* below). In July 2021, the Company also entered into a separate License and Commercialization 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. On January 7, 2022, the Company closed the definitive merger agreement dated as of November 14, 2021, or the Merger Agreement, to acquire Lowell Therapeutics, Inc., or Lowell, a privately held company (see Note 4. "Asset Acquisition" below). As a result of the Merger Agreement, the Company acquired Niyad, a regional anticoagulant for the dialysis circuit during continuous renal replacement therapy for acute kidney injury patients in the hospital, that the Company plans to study under an investigational device exemption, or IDE, and which has received Breakthrough Device Designation status from the FDA. While not approved for commercial use in the U.S., 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, with anticoagulant, anti-inflammatory, and potential anti-viral activities. The second intended indication for Niyad is as a regional anticoagulant for the dialysis circuit for chronic kidney disease patients undergoing intermittent hemodialysis in dialysis centers. 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.

The Company has incurred recurring operating losses and negative cash flows from operating activities since inception. As of March 31, 2022, the Company had cash, cash equivalents and short-term investments of $39.3 million. Based on the Company's current operating plans and projections, the Company expects that its existing cash, cash equivalents and short-term investments will be sufficient to fund operations for at least one year from the date this Quarterly Report on Form 10-Q is filed with the United States Securities and Exchange Commission, or SEC. Although Zalviso was approved for sale in Europe on September 18, 2015, the Company sold the majority of the royalty rights and certain commercial sales milestones it is entitled to receive under the Amended License Agreement (defined below) 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. In consideration of the termination of the Amended License Agreement, under the Royalty Monetization, the Company must use commercially reasonable efforts to negotiate a replacement license agreement, or New Arrangement, with a third party.

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 the Zalviso PCA system, or the Product, in the 28 European Union, or EU, member states, at the time of the agreement, plus Switzerland, Liechtenstein, Iceland, Norway and Australia (collectively, the Zalviso Territory) for human use in pain treatment within, or dispensed by, hospitals, hospices, nursing homes and other medically supervised settings, (collectively, the Field). In September 2015, the EC granted marketing approval for the marketing authorization application, or MAA, previously submitted to the EMA, 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, and together with the License Agreement, the Agreements. Under the MSA, the Company exclusively manufactured and supplied the Product to Grünenthal for the Field in the Zalviso Territory. On July 22, 2015, the Company and Grünenthal amended the MSA, or the Amended MSA, effective as of July 17, 2015. The Amended MSA and the Amended License Agreement are referred to as the Grünenthal Agreements.

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.

Principles of Consolidation

The Condensed Consolidated Financial Statements include the accounts of the Company and its wholly-owned subsidiaries. All intercompany accounts and transactions have been eliminated in consolidation.

Basis of Presentation

The accompanying unaudited Condensed Consolidated Financial Statements have been prepared in accordance with accounting principles generally accepted in the United States for interim financial information and the rules and regulations of the United States. Securities and Exchange Commission, or SEC. Accordingly, they do not include all of the information and footnotes required by accounting principles generally accepted in the United States for complete financial statements. In the opinion of management, all adjustments (consisting of normal recurring adjustments) considered necessary for a fair presentation have been included.

Operating results for the three months ended March 31, 2022, are not necessarily indicative of the results that may be expected for the year ending December 31, 2022, or any future period. The Condensed Consolidated Balance Sheet as of December 31, 2021, was derived from the Company's audited financial statements as of December 31, 2021, included in the Company's Annual Report on Form 10-K filed with the SEC on March 10, 2022. These financial statements should be read in conjunction with the Company's Annual Report on Form 10-K for the year ended December 31, 2021, which includes a broader discussion of the Company's business and the risks inherent therein.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the amounts reported in the Consolidated Financial Statements and accompanying notes. 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.

Significant Accounting Policies

The Company's significant accounting policies are detailed in its Annual Report on Form 10-K for the year ended December 31, 2021. There have been no significant changes to the Company's significant accounting policies during the three months ended March 31, 2022, from those previously disclosed in its 2021 Annual Report on Form 10-K, except as follows:

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 ("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.

Recently Issued Accounting Pronouncements

In June 2016, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or 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 is currently assessing the date of adoption and the impact ASU 2016-13 and ASU 2019-05 will have on the Company, but it 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.

In March 2020, the FASB issued ASU 2020-04, "*Reference Rate Reform (Topic 848): Facilitation of the Effects of Reference Rate Reform on Financial Reporting,*" which provides elective amendments for entities that have contracts, hedging relationships and other transactions that reference LIBOR or another reference rate expected to be discontinued because of reference rate reform. These amendments are effective immediately and may be applied prospectively to contract modifications made and hedging relationships entered into or evaluated on or before December 31, 2022. In January 2021, the FASB issued ASU 2021-01, "*Reference Rate Reform (Topic 848),*" to expand and clarify the scope of Topic 848 to include derivative instruments on discounting transactions. The amendments in this ASU are effective in the same timeframe as ASU 2020-04. The Company is currently evaluating the impact this guidance will have on its Consolidated Financial Statements.

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 table below summarizes the Company's cash, cash equivalents and short-term investments (in thousands):

	As of March 31, 2022			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash	$ 2,621	$ —	$ —	$ 2,621
Money market funds	562	—	—	562
Commercial paper	18,639	—	—	18,639
Total cash and cash equivalents	21,822	—	—	21,822
Short-term investments:				
Commercial paper	13,557	—	—	13,557
Corporate debt securities	3,970	—	—	3,970
Total short-term investments	17,527	—	—	17,527
Total cash, cash equivalents and short-term investments	$ 39,349	$ —	$ —	$ 39,349

	As of December 31, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash	$ 1,443	$ —	$ —	$ 1,443
Money market funds	2,822	—	—	2,822
Commercial paper	8,398	—	—	8,398
Total cash and cash equivalents	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 and short-term investments	$ 51,630	$ —	$ —	$ 51,630

There were no other-than-temporary impairments for these securities at March 31, 2022 or December 31, 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 three months ended March 31, 2022 and 2021.

As of March 31, 2022, and December 31, 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 and Level III liabilities. 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 March 31, 2022, and December 31, 2021, the Company held, in addition to Level II assets, a contingent put option liability associated with the Loan Agreement with Oxford. See Note 6 "Long-Term Debt" for further description. The Company's estimate of fair value of the contingent put option liability 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. The resulting difference between the two estimated fair values is the estimated fair value of the default provisions, or the contingent put option, which is included under other long-term liabilities on the Condensed Consolidated Balance Sheets. Changes to the estimated fair value of this liability is recorded in interest income and other income, net in the Condensed Consolidated Statements of Operations. The fair value of the underlying debt facility is estimated by calculating the expected cash flows in consideration of an estimated probability of default and expected recovery rate in default and discounting such cash flows back to the reporting date using a risk-free rate.

The following table sets forth the fair value of the Company's financial assets and liabilities by level within the fair value hierarchy (in thousands):

	As of March 31, 2022			
	Fair Value	Level I	Level II	Level III
Assets				
Money market funds	$ 562	$ 562	$ —	$ —
Commercial paper	32,196	—	32,196	—
Corporate debt securities	3,970	—	3,970	—
Total assets measured at fair value	$ 36,728	$ 562	$ 36,166	$ —
Liabilities				
Contingent put option liability	$ 55	$ —	$ —	$ 55
Total liabilities measured at fair value	$ 55	$ —	$ —	$ 55

	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	$ —
Liabilities				
Contingent put option liability	$ 81	$ —	$ —	$ 81
Total liabilities measured at fair value	$ 81	$ —	$ —	$ 81

The following tables set forth a summary of the changes in the fair value of the Company's Level III financial liabilities for the three months ended March 31, 2022 and 2021 (in thousands):

	Three Months Ended March 31, 2022
Fair value—beginning of period	$ 81
Change in fair value of contingent put option associated with the Loan Agreement	(26)
Fair value—end of period	$ 55

	Three Months Ended March 31, 2021
Fair value—beginning of period	$ 246
Change in fair value of contingent put option associated with the Loan Agreement	(65)
Fair value—end of period	$ 181

There were no transfers between Level I, Level II or Level III of the fair value hierarchy during the three months ended March 31, 2022 and the year ended December 31, 2021.

3. Inventories, net

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

	Balance as of	
	March 31, 2022	December 31, 2021
Raw materials	$ 651	$ 722
Work-in-process	35	159
Finished goods	359	230
Total	$ 1,045	$ 1,111

The Company did not record any inventory impairment charges for the three months ended March 31, 2022. The Company recorded inventory impairment charges of $0.1 million, primarily related to Zalviso component parts inventory, for the three months ended March 31, 2021.

4. Asset Acquisition

On January 7, 2022, the Company closed the Merger Agreement with Lowell. Under the terms of the agreement, the Company 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. Pursuant to the terms of the Merger Agreement, 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) 9,009,538 shares of AcelRx common stock issued at a five day daily volume weighted average price of $0.57284 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) 1,396,526 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 pursuant to the Merger Agreement were issued in private placements 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 Agreement 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 hold 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 March 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 1,396,526 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 Condensed Consolidated Balance Sheets.

[2] Recorded as In-process research and development asset in the Condensed Consolidated Balance Sheets.

The IPR&D asset will be treated initially 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.

5. Revenue from Contracts with Customers

The following table summarizes revenue from contracts with customers for the three months ended March 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):

	Three Months Ended March 31,	
	2022	2021
Product sales:		
DSUVIA	$ 442	$ 181
Zalviso	—	270
Total product sales	442	451
Contract and other collaboration:		
Non-cash royalty revenue related to Royalty Monetization (See Note 8)	—	45
Royalty revenue	—	15
Total revenues from contract and other collaboration	—	60
Total revenue	$ 442	$ 511

For additional details 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" in the Company's Annual Report on Form 10-K for the year ended December 31, 2021.

Product Sales

The Company's commercial launch of DSUVIA in the United States occurred in the first quarter of 2019. Zalviso was sold in Europe by the Company's collaboration partner, Grünenthal, through May 12, 2021. DZUVEO sales in Europe by the Company's collaboration partner, Aguettant, have not commenced as of March 31, 2022.

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 three months ended March 31, 2022, the Company did not record any contract and other collaboration revenue.

Contract Liabilities

A contract liability of $1.2 million was recorded on the Condensed Consolidated Balance Sheets as deferred revenue as of March 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. The material right contract liability will be recognized over the period the discount on future product supply is made available.

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

Balance at January 1, 2022	$	1,237
Deductions for performance obligations satisfied:		
In current period		—
Balance at March 31, 2022	$	1,237
Balance at January 1, 2021	$	49
Deductions for performance obligations satisfied:		
In current period		(49)
Balance at March 31, 2021	$	—

6. Long-Term Debt

Loan Agreement with Oxford

On May 30, 2019, the Company entered into the Loan Agreement with Oxford Finance LLC, or 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.

In connection with the Loan Agreement, on May 30, 2019, the Company issued warrants to the Lender and its affiliates, or the Warrants, which are exercisable for an aggregate of 176,679 shares of the Company's common stock with a per share exercise price of $2.83. The Warrants have been classified within stockholders' deficit and accounted for as a discount to the loan by allocating the gross proceeds on a relative fair value basis.

As of March 31, 2022 and December 31, 2021, the accrued balance due under the Loan Agreement with Oxford was $11.4 million and $13.3 million, respectively. Interest expense related to the Loan Agreement was $0.4 million, $0.1 million of which represented amortization of the debt discount, for the three months ended March 31, 2022, and was $0.6 million, $0.2 million of which represented amortization of the debt discount, for the three months ended March 31, 2021.

Non-Interest Bearing Payments for the Construction of Leasehold Improvements

In August 2019, the Company entered into a Site Readiness Agreement, or SRA, with Catalent Pharma Solutions, LLC, or Catalent, 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 Catalent's production facility in Kansas City. 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 installments of $0.5 million through July 2022. As of March 31, 2022 and December 31, 2021, the accrued balance under the SRA was $0.5 million, and $1.7 million of these leasehold improvements had been capitalized. The effective interest rate related to the payments at March 31, 2022 was 14.4%. The leasehold improvements are recorded as property and equipment, net, in our Condensed Consolidated Balance Sheets.

7. Leases

Office Lease

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

The Company has entered into commercial supply manufacturing services agreements related to Zalviso and DSUVIA containing fixed fees which it has determined are in-substance lease payments. For additional information on these agreements, refer to Note 9 "Leases" in the Company's Annual Report on Form 10-K for the year ended December 31, 2021.

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

	Three Months Ended March 31,	
	2022	2021
Operating lease costs	$ 343	$ 340
Gain on derecognition of operating lease	—	(522)
Sublease income	—	(150)
Net lease costs	$ 343	$ (332)

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

	March 31, 2022	March 31, 2021
Weighted-average remaining lease term – operating leases (in years)	4.74	0.57
Weighted-average remaining discount rate – operating leases	12.8%	12.03%

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

Year:	
2022	$ 1,363
2023	1,294
2024	1,040
2025	1,040
2026	1,040
Thereafter	415
Total future minimum lease payments	6,192
Less imputed interest	(1,430)
Total	$ 4,762
Reported as:	
Operating lease liabilities	$ 4,762
Operating lease liabilities, current portion	(1,184)
Operating lease liabilities, net of current portion	$ 3,578

8. 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 assesses the expected royalty and milestone payments using a combination of historical results, internal projections and forecasts from external sources. To the extent such payments are greater or less than the Company's initial estimates or the timing of such payments is materially different than its original estimates, the Company will prospectively adjust the amortization of the liability and the effective interest rate. During the three months ended June 30, 2020, Grünenthal notified the Company that it was terminating the Amended License Agreement, 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. The rights to market and sell Zalviso in the Zalviso Territory reverted back to the Company on May 12, 2021. There is a continuing obligation on the Company's part, through the term of the Royalty Monetization with SWK (assignee of PDL), to use commercially reasonable efforts to negotiate a replacement license agreement, or New Arrangement. If the Company is unable to find a New Arrangement, a contingent gain of up to approximately $64 million may be recognized when it is realized upon expiration of the liability at the end of the Royalty Monetization term. Due to the significant judgments and factors related to the estimates of future payments under the Royalty Monetization, there are significant uncertainties surrounding the amount and timing of future payments and the probability of realization of the estimated contingent gain.

The effective interest rate over the life of the liability will be 0% as the Company records interest income over the remaining term of the arrangement as an offset to the interest expense that was recognized in prior periods. The effective interest income rate for the three months ended March 31, 2022 and 2021, was approximately 3.2% and 3.6%, respectively.

The following table shows the activity within the liability account for the three months ended and the period from inception on September 18, 2015 to March 31, 2022 (in thousands):

	Three months ended March 31, 2022	Period from inception to March 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	(673)	24,514
Liability related to sale of future royalties as of March 31, 2022	$ 84,615	$ 84,615

As royalties are remitted to SWK from ARPI LLC, as described in Note 1 "Organization and Summary of Significant Accounting Policies - Non-Cash Interest Income (Expense) on Liability Related to Sale of Future Royalties" in the Company's Annual Report on Form 10-K for the year ended December 31, 2021, the balance of the liability will be effectively repaid over the life of the agreement. The Company will record non-cash royalty revenues and non-cash interest (income) expense within its Condensed Consolidated Statements of Operations over the term of the Royalty Monetization.

9. 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 alleges 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 seeks 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 names the Company and three of its officers and continues 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 complaint also alleges a violation of Section 20A of the Exchange Act against the individual defendants for alleged insider trading. Defendants' motion to dismiss the amended complaint is due May 6, 2022.

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 shareholder 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 shareholder 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.

10. Stock-Based Compensation

The Company recorded total stock-based compensation expense for stock options, restricted stock units, or RSUs, and the Amended and Restated 2011 Employee Stock Purchase Plan, or the Amended ESPP, as follows (in thousands):

	March 31, 2022	March 31, 2021
Cost of goods sold	$ 19	$ 22
Research and development	174	181
Selling, general and administrative	590	886
Total	$ 783	$ 1,089

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, 2022	1,774,376	$ 1.71
Granted	1,061,826	0.40
Vested	(657,359)	1.92
Forfeited	(145,838)	1.56
Restricted stock units outstanding, March 31, 2022	2,033,005	$ 0.97

Upon vesting, certain of the Company's RSUs may be settled on a net-exercise basis to cover any required withholding tax with the remaining amount converted into an equivalent number of shares of common stock. There were 141,966 shares of common stock underlying vested RSUs that were withheld during the quarter ended March 31, 2022, based on the value of the RSUs as determined by the Company's closing stock price on the applicable vesting date.

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)
January 1, 2022	14,284,050	$ 2.99		
Granted	2,123,650	0.40		
Forfeited	(248,334)	1.72		
Expired	(517,902)	3.20		
Exercised	—	—		
March 31, 2022	15,641,464	$ 2.65	6.2	$ —
Vested and exercisable options—March 31, 2022	10,426,287	$ 3.36	4.8	$ —
Vested and expected to vest—March 31, 2022	15,641,464	$ 2.65	6.2	$ —

The per-share weighted average grant date fair value of the options granted during the quarter ended March 31, 2022 was estimated at $0.30 per share on the date of grant using the Black-Scholes option-pricing model with the following weighted average assumptions:

	Three months ended March 31, 2022
Expected term (in years)	6.3
Risk-free interest rate	1.6% - 2.2%
Expected volatility	88%
Expected dividend rate	0%

As of March 31, 2022, there were 5,585,531 shares available for grant under the Company's equity incentive plans and 4,302,929 shares available for grant under the Amended ESPP.

11. Net Loss per Share of Common Stock

The Company's basic net loss per share of common stock is calculated by dividing the net loss by the weighted average number of shares of common stock outstanding for the period. The diluted net loss per share of common stock is computed by giving effect to all potential common stock equivalents outstanding for the period determined using the treasury stock 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. 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.

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

	Three Months Ended March 31,	
	2022	2021
ESPP, RSUs and stock options to purchase common stock	17,864,469	16,789,212
Common stock warrants	17,676,679	176,679

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 loss per share of common stock for the periods presented because the contingencies for issuance of these shares have not been met.

12. Subsequent Event

In May 2022, the Company initiated a reorganization that will eliminate approximately 40% of its employees for which the Company estimates that it will incur aggregate severance and related charges of approximately $0.5 million, all of which it expects to recognize in the second quarter of 2022. These

estimates are subject to a number of assumptions, and actual results may differ. The Company may also incur additional costs not currently contemplated due to events that may occur as a result of, or that are associated with, the reduction.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion and analysis should be read in conjunction with the unaudited financial statements and notes thereto included in Part I, Item 1 of this Quarterly Report on Form 10-Q, or Form 10-Q, and with the audited Consolidated Financial Statements and related notes thereto included as part of our Annual Report on Form 10-K for the year ended December 31, 2021, or Annual Report.

About AcelRx Pharmaceuticals, Inc.

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 of products and product candidates consists of sufentanil sublingual products and product candidates, pre-filled syringe product candidates, and nafamostat product candidates as further described below.

Sufentanil Sublingual Products/Product Candidates

Product/Product Candidate	Description	Target Use	Status
DSUVIA®	Sufentanil sublingual tablet, 30 mcg	Moderate-to-severe acute pain in a medically supervised setting, administered by a healthcare professional	Received U.S. Food and Drug Administration, or FDA, approval in November 2018; commercial launch began first quarter of 2019.
DZUVEO®	Sufentanil sublingual tablet, 30 mcg	Moderate-to-severe acute pain in a medically monitored setting, administered by a healthcare professional	Granted European Commission, or EC, marketing approval in June 2018. Sunset date extended to December 31, 2022 by EC. To be commercialized in Europe by Laboratoire Aguettant, or Aguettant.
Zalviso®	Sufentanil sublingual tablet system, 15 mcg	Moderate-to-severe acute pain in the hospital setting, administered by the patient as needed	In the U.S., positive results from Phase 3 trial, IAP312, announced in August 2017. Currently evaluating the timing of the resubmission of the New Drug Application, or NDA, which is in part dependent on the finalization of the FDA's new opioid approval guidelines and process. Approved in the European Union, where it was marketed commercially by Grünenthal GmbH, or Grünenthal, through May 12, 2021.
ARX-02	Higher Strength Sufentanil Sublingual Tablet	Cancer breakthrough pain in opioid-tolerant patients	Phase 2 clinical trial and End of Phase 2 meeting completed. Investigational New Drug, or IND, application was inactivated. Future development contingent upon identification of corporate partnership resources.
ARX-03	Combination Sufentanil/Triazolam Sublingual Tablet	Mild sedation and pain relief during painful procedures in a physician's office	Phase 2 clinical trial and End of Phase 2 meeting completed. IND application was inactivated. Future development contingent upon identification of corporate partnership resources.

Pre-filled Syringe Product Candidates

Product/Product Candidate	Description	Target Use	Status
Ephedrine	Ephedrine pre-filled syringe, containing 10 ml of a solution of 3 mg/ml ephedrine hydrochloride for injection	Clinically important hypotension occurring in the setting of anesthesia	Product candidate licensed Aguettant; preparing 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 hydrochloride 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.

Nafamostat Product Candidates

Product/Product Candidate	Description	Target Use	Status
Niyad	Lyophilized vial 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.
LTX-608	Lyophilized vial 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 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 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 for injection	IV infusion for acute pancreatitis	IND to be submitted following toxicology evaluation to enable Phase 2 study

General Trends and Outlook

COVID-19-related

Government-mandated orders and related safety policies on account of the COVID-19 pandemic continue to prevent us from operating our business in the normal course. Beginning in early 2020, state and local officials issued orders in response to the pandemic which included, among other things, requirements for residents to shelter in place and for non-essential businesses to cease activities at facilities within certain cities, counties, and states. State and local officials have taken different approaches to these orders, and some have not issued any such orders. Once issued, the orders have been relaxed and then tightened, depending on the rate of COVID-19 cases. As a result of these orders, we implemented a work from home policy for our California-based employees and 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. We expect our near-term sales volumes to continue to be adversely impacted as long as access to healthcare facilities by our commercial and medical affairs personnel continues to be limited, especially in light of the rise in COVID-19 cases associated with the emerging variants. We will continue to evaluate the impact on our revenues and related metrics and operating expenses during this period and assess the need to adjust our expenses and expectations.

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 our DSUVIA fully automated packaging line, and subsequent FDA approval, has been delayed. Based on our best estimate, now that the line has been installed, we expect FDA approval in the first half of 2023.

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 impacts 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.

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 the next four years for the purchase of DSUVIA to support a DoD-sponsored study to aid the development of clinical practice guidelines. We believe that study will initiate clinically in 2022. 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.

Recent Developments

On January 7, 2022, we acquired Lowell Therapeutics, Inc., or 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" in the accompanying notes to the Condensed Consolidated Financial Statements.

On March 28, 2022, we received a close-out letter from the Office of Prescription Drug Promotion, or ODPD, of the U.S. Food and Drug Administration, or the FDA, to the Warning Letter we received on February 11, 2021 relating to certain DSUVIA-related promotional materials we used in 2019. The close-out letter indicated that the FDA had concluded its evaluation of our corrective actions in response to the Warning Letter and that we had addressed the issues raised by the Warning Letter.

Financial Overview

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 of Zalviso by any replacement partner, and fund any future research and development activities needed to support the FDA regulatory review of our product candidates.

We will incur capital expenditures related to our fully automated packaging line for DSUVIA, which has now been installed, and for which we expect FDA approval in the first half of 2023. We anticipate that the fully automated line for DSUVIA will contribute to a significant decrease in costs of goods sold in 2023 and beyond.

Our net loss for the three months ended March 31, 2022 and 2021 was $8.7 million and $9.0 million, respectively. As of March 31, 2022, we had an accumulated deficit of $482.3 million. As of March 31, 2022, we had cash, cash equivalents and short-term investments totaling $39.3 million compared to $51.6 million as of December 31, 2021.

AcelRx is realigning its cost structure from a focus on commercialization to a focus on advancing our late-stage development pipeline. We believe that the uptake of DSUVIA will be maximized through a larger commercial infrastructure and, as such, we are in active discussions with potential partners that can execute a more robust commercial plan to support DSUVIA sales expansion, while further reducing AcelRx's operating costs. The ultimate structure of a potential transaction with a third party may take multiple forms and is not known at this time. Accordingly, we are initiating a reorganization that will eliminate approximately 40% of our employees, resulting in an estimated $9 million in annual savings, and an estimated $0.5 million in a restructuring charge in our Condensed Consolidated Statement of Operations for the three months ended June 30, 2022.

Critical Accounting Estimates

The accompanying discussion and analysis of our financial condition and results of operations are based upon our unaudited Condensed 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. Our critical accounting policies and estimates are detailed in our Annual Report.

There have been no significant changes to our critical accounting policies or significant judgements and estimates for the three months ended March 31, 2022, from those previously disclosed in our Annual Report, as follows:

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 ("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.

Results of Operations

Our results of operations have fluctuated from period to period and may continue to fluctuate in the future, based upon the progress of our commercial launch of DSUVIA, our research and development efforts, variations in the level of expenditures related to commercial launch, 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. In particular, to the extent our commercial and medical affairs personnel continue to be subject to varying levels of restriction on accessing hospitals and ambulatory surgical centers due to COVID-19, and to the extent government authorities and certain healthcare providers are continuing to limit elective surgeries, we expect our sales volume to be adversely affected.

Three Months Ended March 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 three months ended March 31, 2022 and 2021, was as follows (in thousands, except percentages):

	Three Months Ended March 31,		$ Change	% Change
	2022	2021	2022 vs. 2021	2022 vs. 2021
DSUVIA	$ 442	$ 181	$ 261	144%
Zalviso	—	270	(270)	(100)%
Total product sales revenue	$ 442	$ 451	$ (9)	(2)

The increase in DSUVIA product sales revenue for the three months ended March 31, 2022, as compared to the three months ended March 31, 2021, was primarily the result of increased sales volume for DSUVIA. For the three months ended March 31, 2021, there was $0.3 million in product sales revenue of Zalviso by Grünenthal GmbH, or 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.

Contract and Other Collaboration Revenue

Contract and other collaboration revenue, prior to May 13, 2021, 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 under the Grünenthal Agreements to SWK Funding, LLC, or SWK, (assignee of PDL BioPharma, Inc., or PDL), in a transaction referred to as the Royalty Monetization, and royalty revenue for sales of Zalviso in Europe.

Contract and other collaboration revenue for the three months ended March 31, 2022 and 2021, was as follows (in thousands, except percentages):

	Three Months Ended March 31,		$ Change	% Change
	2022	2021	2022 vs. 2021	2022 vs. 2021
Non-cash royalty revenue related to Royalty Monetization (See Note 8)	$ —	$ 45	$ (45)	(100)%
Royalty revenue	—	15	(15)	(100)%
Total contract and other collaboration revenue	$ —	$ 60	$ (60)	(100)%

On July 14, 2021, we granted Aguettant the license rights to DZUVEO in the European Union under the DZUVEO Agreement. As of March 31, 2022 and December 31, 2021, we had current and non-current portions of deferred revenue under the DZUVEO Agreement of $0.1 million and $1.1 million, respectively.

Cost of Goods Sold

Total cost of goods sold for the three months ended March 31, 2022 and 2021, was as follows (in thousands, except percentages):

	Three Months Ended March 31,		$ Change	% Change
	2022	2021	2022 vs. 2021	2022 vs. 2021
Direct costs	$ 153	$ 311	$ (158)	(51)%
Indirect costs	631	729	(98)	(13)%
Total cost of goods sold	$ 784	$ 1,040	$ (256)	(25)%

Direct costs from contract manufacturers for DSUVIA totaled $0.2 million for the three months ended March 31, 2022, and totaled $0.3 million for DSUVIA and Zalviso for the three months ended March 31, 2021. We recorded inventory impairment charges of $0.1 million, primarily related to Zalviso component parts inventory, for the three months ended March 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.

The indirect costs to manufacture DSUVIA totaled $0.6 million for the three months ended March 31, 2022, and totaled $0.7 million for DSUVIA and Zalviso for the three months ended March 31, 2021. Indirect costs include internal personnel and related costs for purchasing, supply chain, quality assurance, depreciation and related expenses.

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. The timing of the resubmission of the Zalviso NDA is in part dependent on the finalization of the FDA's new opioid approval guidelines and process.

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 during the three months ended March 31, 2022 and 2021 (in thousands, except percentages):

	Three Months Ended March 31,		$ Change	% Change
	2022	2021	2022 vs. 2021	2022 vs. 2021
DSUVIA	$ 392	$ 162	$ 230	142%
Zalviso	8	6	2	33%
PFS	57	—	57	100%
Overhead	858	801	57	7%
Total research and development expenses	$ 1,315	$ 969	$ 346	36%

Research and development expenses for the three months ended March 31, 2022 increased as compared to the three months ended March 31, 2021, primarily due to increased DSUVIA manufacturing-related 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 three months ended March 31, 2022 and 2021, were as follows (in thousands, except percentages):

	Three Months Ended March 31,		$ Change	% Change
	2022	2021	2022 vs. 2021	2022 vs. 2021
Selling, general and administrative expenses	$ 7,338	$ 7,644	$ (306)	(4)%

Selling, general and administrative expenses decreased by $0.3 million during the three months ended March 31, 2022, as compared to the three months ended March 31, 2021. The decrease is primarily due to net decreases in selling, general and administrative expenses including a $0.5 million reduction in personnel-related costs, a $0.3 million reduction in non-cash stock-based compensation expense, partially offset by an increase in facilities-related expenses in the first quarter of 2022 due to the $0.5 million gain related to the lease termination in the first quarter of 2021.

Other Income

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

	Three Months Ended March 31,		$ Change	% Change
	2022	2021	2022 vs. 2021	2022 vs. 2021
Interest expense	$ (390)	$ (672)	$ 282	(42)%
Interest income and other income, net	38	76	(38)	(50)%
Non-cash interest income on liability related to sale of future royalties	673	782	(109)	(14)%
Total other income	$ 321	$ 186	$ 135	73%

Interest expense consisted primarily of interest accrued or paid on our debt obligation agreements and amortization of debt discounts. Interest expense decreased for the three months ended March 31, 2022, as compared to the three months ended March 31, 2021, primarily as a result of a lower average outstanding loan balance. As of March 31, 2022, the outstanding balance due under the Loan Agreement with Oxford was $11.4 million. Refer to Note 6 “Long-Term Debt” in the accompanying notes to the Condensed Consolidated Financial Statements for additional information.

Interest income and other income, net, for the three months ended March 31, 2022 and 2021, primarily consisted of the change in the fair value of our contingent put option and interest earned on our investments.

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 8 “Liability Related to Sale of Future Royalties”, the Royalty Monetization has been recorded as debt under the applicable accounting guidance. We periodically assess the expected royalty and milestone payments using a combination of historical results, internal projections and forecasts from external sources. To the extent such payments are greater or less than our initial estimates or the timing of such payments is materially different than our original estimates, we will prospectively adjust the amortization of the liability and the interest rate.

The effective interest income rate for each of the three months ended March 31, 2022 and 2021, was approximately 3.2% and 3.6%, respectively. We anticipate that we will record approximately $3 million in non-cash interest income related to the Royalty Monetization for the year ending December 31, 2022.

Liquidity and Capital Resources

Liquidity

We have incurred losses and generated negative cash flows from operations since inception. We expect to continue to incur significant losses in 2022 and may incur significant losses and negative cash flows from operations in the future. 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 March 31, 2022, we had cash, cash equivalents and investments totaling $39.3 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, as we continued our commercialization activities for DSUVIA, including installation of our fully automated packaging line for DSUVIA, and business development activities. We anticipate that our existing capital resources will permit us to meet our capital and operational requirements for at least the next twelve months; however, our expectations may change depending on a number of factors including the extent and magnitude of the impact from the COVID-19 pandemic, in particular the negative impact on sales volumes as our sales force is limited in its access to potential customers, our expenditures related to the development of our product candidates and the United States commercial launch of DSUVIA, and the timing of business development activities. 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.

On November 17, 2021, we completed a registered direct offering in which we issued and sold 17,500,000 shares of our common stock at a price of $0.80 per share and warrants exercisable for an aggregate of 17,500,000 shares of our common stock at a price of $1.00 per share. The total net proceeds from this offering were approximately $13.9 million. As of December 31, 2021, the 17,500,000 warrants remain outstanding and will be exercisable following the six-month anniversary of the closing date of this offering and expire on November 15, 2026.

On January 22, 2021, we completed an underwritten public offering in which we issued and sold 14,500,000 shares of our common stock to the underwriter at a price of $1.7625 per share. On January 27, 2021, the underwriters exercised their option in full and purchased an additional 2,175,000 shares at a price of $1.7625 per share. The total net proceeds from this offering of an aggregate 16,675,000 shares were approximately $28.9 million.

We entered into a Controlled Equity Offering℠ Sales Agreement, or 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. There were no sales under the ATM Agreement for the three months ended March 31, 2022. For the three months ended March 31, 2021, we issued and sold approximately 3.0 million shares of common stock and received net proceeds of approximately $7.5 million, after deducting fees and expenses, under the ATM Agreement. As of March 31, 2022, we have the ability to sell approximately $36.1 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 March 31, 2022, the outstanding balance under the Loan Agreement was $11.4 million. For more information, see Note 6 “Long-Term Debt” in the accompanying notes to the Condensed Consolidated Financial Statements.

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

The following is a summary of our cash flows for the periods indicated and has been derived from our Condensed Consolidated Financial Statements which are included elsewhere in this Form 10-Q (in thousands):

	Three Months Ended March 31,	
	2022	**2021**
Net cash used in operating activities	$ (8,934)	$ (9,708)
Net cash provided by (used in) investing activities	20,176	(17,425)
Net cash (used in) provided by financing activities	(2,083)	34,222

Cash Flows from Operating Activities

The primary use of cash for our operating activities during these periods was to fund commercial activities for our approved product, 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 $8.9 million during the three months ended March 31, 2022, reflected a net loss of $8.7 million, partially offset by aggregate non-cash charges of $0.7 million and included an approximate $0.9 million net change in our operating assets and liabilities. Non-cash charges included $0.8 million in stock-based compensation expense, $0.7 million in interest income on the liability related to the Royalty Monetization, and $0.4 million in depreciation expense. The net change in our operating assets and liabilities included a $1.5 million decrease in accrued liabilities.

Cash used in operating activities of $9.7 million during the three months ended March 31, 2021, reflected a net loss of $9.0 million, partially offset by aggregate non-cash charges of $0.5 million and included an approximate $1.2 million net change in our operating assets and liabilities. Non-cash charges included $1.1 million for stock-based compensation expense, $0.8 million in non-cash interest income on the liability related to the Royalty Monetization, $0.5 million in depreciation expense and $0.5 million gain on our lease termination. The net change in our operating assets and liabilities included a $1.7 million decrease in accrued liabilities.

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 three months ended March 31, 2022, cash provided by investing activities of $20.2 million was primarily the net result $27.6 million in proceeds from maturity of investments partially offset by $6.2 million for purchases of investments and $1.2 million in cash paid for the Lowell asset acquisition, net of cash acquired. During the three months ended March 31, 2021, cash used investing activities of $17.4 million was primarily the net result of $24.4 million for purchases of investments offset by $7.0 million in proceeds from 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 three months ended March 31, 2022, cash used in financing activities of $2.1 million was primarily due to long-term debt payments under the Loan Agreement with Oxford. During the three months ended March 31, 2021, cash provided by financing activities of $34.2 million was primarily due to $36.4 million in net proceeds received in connection with equity financings, and $0.2 million in net proceeds received through our equity plans, partially offset by $2.1 million used for payment of long-term debt and $0.2 million used for payment of employee tax obligations relating to the vesting of restricted stock units.

Capital Commitments and Capital Resources

Our current operating plan includes expenditures related to the development of our product candidates and the continued launch of DSUVIA in the United States. 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” in the accompanying notes to the Condensed Consolidated Financial Statements Our operating plan includes an assumption that COVID-19 related restrictions will not increase considerably, and includes anticipated activities required to resubmit the Zalviso NDA 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 product candidates from Aguettant. These assumptions may change as a result of many factors. We will continue to evaluate the work necessary to successfully launch DSUVIA and gain approval of our product candidates in the United States and intend to update our cash forecasts accordingly. Our forecast that our existing capital resources will permit us to meet our capital and operational requirements through at least the next twelve months is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially.

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

- the impact and timing of COVID-19 on our operations, our sales representatives’ access to hospitals or other healthcare facilities, and our level of sales;
- expenditures related to the launch of DSUVIA and potential commercialization of our product candidates, if approved;
- future manufacturing, selling and marketing costs related to DSUVIA and our product candidates, if approved, including our contractual obligations to Aguettant under the DZUVEO Agreement;
- costs associated with business development activities and licensing transactions;
- the outcome, timing and cost 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 DSUVIA, or 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, including the DZUVEO Agreement;
- 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 and commercial supplies of DSUVIA and our product candidates, if approved;
- 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 6 "Long-Term Debt"), contract manufacturing services and office rent (as described in Note 7 "Leases" in the accompanying notes to the Consolidated Financial Statements) and the Royalty Monetization that we completed in September 2015 (as described in Note 8 "Liability Related to Sale of Future Royalties").

Item 3. 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 4. 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. As required by Rule 13a-15(b) under the Exchange Act, we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures as of the end of the period covered by this Quarterly Report on Form 10-Q. In accordance with guidance issued by the SEC, companies are permitted to exclude acquisitions from their final assessment of internal control over financial reporting for the fiscal year in which the acquisition occurred while integrating the acquired operations; our management's evaluation of internal control over financial reporting excluded the internal control activities of Lowell which are included in our consolidated financial statements. Based on the foregoing, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in internal control over financial reporting. There have been no changes in our internal control over financial reporting during our most recent fiscal quarter that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

Item 1. 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 I. Financial Information —Item 1. Financial Statements—Note 9, Commitments and Contingencies—Litigation."

Item 1A. Risk Factors

This Quarterly Report on Form 10-Q contains forward-looking information based on our current expectations. Because our actual results may differ materially from any forward-looking statements made by or on behalf of us, this section includes a discussion of important factors that could affect our actual future results, including, but not limited to, our revenues, expenses, net loss and loss per share. You should carefully consider these risk factors, together with all of the other information included in this Quarterly Report on Form 10-Q as well as our other publicly available filings with the U.S. Securities and Exchange Commission, or SEC.

Summary 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 business is being adversely impacted by the COVID-19 pandemic.
- We have incurred significant losses since our inception, anticipate that we will continue to incur significant losses in 2022 and may continue to incur losses in the future.
- We have not yet generated significant product revenue and may never be profitable.
- We will require additional capital and may be unable to raise capital, which would force us to delay, reduce or eliminate our commercialization efforts and product development programs and could cause us to cease operations.
- Positive clinical results obtained to date for Zalviso may be disputed in FDA review, do not guarantee regulatory approval and may not be obtained from future clinical trials.
- Existing and future legislation may increase the difficulty and cost for us to commercialize our products and affect the prices we may obtain.
- Guidelines and recommendations published by government agencies, as well as non-governmental organizations, and existing laws and regulations can reduce the use of DSUVIA, and Zalviso, if approved in the United States.
- Zalviso may cause adverse effects or have other properties that could delay or prevent regulatory approval or limit the scope of any approved label or market acceptance. DSUVIA may cause adverse effects or have other properties that could limit market acceptance.
- Although we have obtained regulatory approval for DSUVIA, and even if we obtain regulatory approval for our other product candidates in the United States, we and our collaborators face extensive regulatory requirements, and our products may face future development and regulatory difficulties.
- The commercial success of DSUVIA and, if approved, Zalviso and our other product candidates in the United States, as well as DZUVEO and Zalviso in Europe, will depend upon the acceptance of these products by the medical community, including physicians, nurses, patients, and pharmacy and therapeutics committees.
- If we are unable to maintain or grow our sales and marketing capabilities or enter into agreements with third parties to market and sell our products and, if approved, our product candidates, we may be unable to generate sufficient product revenue.
- The success of our merger agreement with Lowell Therapeutics, Inc, or Lowell, depends on our ability to realize the expected benefits and potential value creation related to the acquisition;
- 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.
- 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.
- The market price of our common stock may be highly volatile.
- Nasdaq may delist our securities from trading on its exchange, which could limit investors' ability to make transactions in our securities and subject us to additional trading restrictions.
- Litigation may substantially increase our costs and harm our business.
- Our involvement in securities-related class action litigation could divert our resources and management's attention and harm our business.

Risks Related to COVID-19 Pandemic

Our business is being adversely impacted by the COVID-19 pandemic.

Our business has been adversely affected by the COVID-19 outbreak. Federal, state, local and foreign government orders on account of the COVID-19 pandemic are preventing us from conducting certain activities. Following local and state government orders in California, where our corporate office is located and many of our employees live, we implemented work from home policies, which are limiting certain of our operations. If the COVID-19 outbreak continues, we may need to limit operations further and implement additional limitations, such as extending our work from home policies.

In response to the COVID-19 pandemic, some hospitals, ambulatory surgery centers and other healthcare facilities have barred visitors that are not caregivers or mission-critical and we have no visibility as to when these restrictions on access will be lifted for all of our customers. As a result, our commercial and medical affairs teams' educational and promotional efforts have been reduced, and in some cases, stopped. Furthermore, some governments, hospitals and doctors, as a measure to combat the further spread of COVID-19, reduced the number of procedures in which DSUVIA is administered as part of the pain treatment program, and temporarily halted performing elective surgeries, which adversely impacted the level of our sales relating to such procedures. We expect our near-term sales volumes to be adversely impacted for as long as access to healthcare facilities by our commercial and medical affairs personnel and the number of procedures in which DSUVIA is administered continues to be limited. The ultimate impact of the COVID-19 outbreak remains highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, healthcare systems or the global economy as a whole. However, these effects could have a material impact on our operations, and we will continue to monitor the COVID-19 situation closely.

Risks Related to Commercialization

Our success is highly dependent on our ability to successfully commercialize DSUVIA.

We invested a significant portion of our efforts and financial resources to develop and gain regulatory approval for DSUVIA and expect to continue making significant investments to commercialize DSUVIA. We believe our success is highly dependent on, and a significant portion of the value of our company relates to, our ability to successfully commercialize DSUVIA in the United States. The commercial success of DSUVIA depends heavily on numerous factors, including:

- our ability to market, sell, and distribute DSUVIA;
- our ability to establish and maintain commercial manufacturing with third parties;
- acceptance by the medical community, including physicians, nurses, patients and pharmacy and therapeutics committees;
- acceptance of pricing and placement on payers' formularies;
- our 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
- our ability to obtain, maintain, enforce, and defend our intellectual property rights and claims.

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

The commercial success of DSUVIA and, if approved, Zalviso and our other product candidates in the United States, as well as DZUVEO and Zalviso in Europe, will depend upon the acceptance of these products by the medical community, including physicians, nurses, patients, and pharmacy and therapeutics committees.

The degree of market acceptance of DSUVIA and, if approved, Zalviso and our other product candidates in the United States, as well as DZUVEO and Zalviso in Europe, by the medical community will depend on a number of factors, including:

- demonstration of clinical safety and efficacy compared to other products;
- the relative convenience, ease of administration and acceptance by physicians, patients and health care payers;
- the use of our approved products by a healthcare professional for patient types that were not specifically studied in clinical trials;
- the prevalence and severity of any adverse events, or AEs, or serious adverse events, or SAEs;
- overcoming any perceptions of sufentanil as a potentially unsafe drug due to its high potency opioid status;

- limitations or warnings contained in the U.S. Food and Drug Administration, or FDA, -approved label for DSUVIA and, if approved, our other product candidates, or the European Medicines Agency, or EMA,-approved label for DZUVEO or Zalviso;
- restrictions or limitations placed on DSUVIA due to the REMS program or, if approved, on our product candidates;
- availability of alternative treatments;
- existing capital investment by hospitals in IV PCA technology;
- pricing and cost-effectiveness;
- the effectiveness of our current or any future collaborators' sales and marketing strategies;
- our ability to obtain formulary approvals; and
- our ability to obtain and maintain sufficient third-party coverage and reimbursement.

If our approved products do not achieve an adequate level of acceptance by the medical community, including physicians, nurses, patients and pharmacy and therapeutics committees, we may not generate sufficient revenue and become or remain profitable.

If we are unable to maintain or grow our sales and marketing capabilities or enter into agreements with third parties to market and sell our products and, if approved, our product candidates, we may be unable to generate sufficient product revenue.

In order to commercialize DSUVIA and, if approved, our product candidates in the United States, we must maintain or grow internal sales, marketing, distribution, managerial and other capabilities or make arrangements with third parties to perform these services. We have entered into agreements with third parties for the distribution of DSUVIA and may enter into such agreements for our product candidates, if approved, in the United States, including the product candidates we in-licensed from Laboratoire Aguettant, or Aguettant, in July 2021 pursuant to a License and Commercialization Agreement, or the PFS Agreement, and the product candidates we acquired through our acquisition of Lowell; however, if these third parties do not perform as expected or there are delays in establishing such relationships, our ability to effectively distribute products would suffer.

We have entered into strategic partnerships with third parties to commercialize our products outside of the United States. For example, in 2013 we entered into a collaboration with Grünenthal GmbH, or Grünenthal, for the commercialization of Zalviso in Europe and Australia, and in July 2021, we entered a License and Commercialization Agreement, or the DZUVEO Agreement, with Aguettant for the commercialization of DZUVEO in the European Union, Norway, Iceland, Liechtenstein, Andorra, Vatican City, Monaco, Switzerland and the United Kingdom, or the DZUVEO Territory. Grünenthal ceased commercializing Zalviso on May 12, 2021 and the rights to market and sell Zalviso reverted back to us. We intend to enter into additional strategic partnerships with third parties to commercialize our products outside of the United States, including a replacement license agreement for Zalviso in Europe. Per the terms of the royalty monetization arrangement with SWK Funding, LLC, or SWK (assignee of PDL BioPharma, Inc., or PDL), or the Royalty Monetization, we are obligated to use commercially reasonable efforts to negotiate a replacement license agreement, or New Arrangement. Accordingly, even if we are able to enter into a New Arrangement, and that licensee is successful in commercializing Zalviso in Europe, we will receive only a portion of any royalties until the capped amount owing to SWK is reached.

We face significant competition in seeking appropriate strategic partners, and these strategic partnerships can be intricate and time consuming to negotiate and document. We may not be able to negotiate future strategic partnerships on acceptable terms, or at all. We are unable to predict when, if ever, we will enter into any new strategic partnerships because of the numerous risks and uncertainties associated with establishing strategic partnerships. Our current or future collaboration partners, if any, may not dedicate sufficient resources to the commercialization of our products and product candidates, if approved, or may otherwise fail in their commercialization due to factors beyond our control. If we are unable to establish effective collaborations to enable the sale of our products to healthcare professionals and in geographical regions that will not be covered by our own marketing and sales force, or if our potential future collaboration partners do not successfully commercialize our products, our ability to generate revenues from product sales will be adversely affected.

If we are unable to maintain or grow adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate sufficient product revenue and become profitable. We compete with many companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

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 force majeure notices 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, 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. For example, we have a continuing obligation, through the term of the Royalty Monetization with SWK, to use commercially reasonable efforts to negotiate a New Arrangement following Grünenthal's termination of our collaboration agreement for the commercialization of Zalviso in Europe. More generally, 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, including our continued commercialization of DSUVIA.

We need to retain and maintain our existing sales, managerial, operational, finance and other personnel and resources in order to continue the commercialization of DSUVIA 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 33% of our workforce in March 2020 in connection with a strategic transaction, may be disruptive to our operations, may negatively affect our productivity, and may constrain our commercialization activities. For example, a 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 successfully commercializing DSUVIA 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.

Guidelines and recommendations published by government agencies, as well as non-governmental organizations, and existing laws and regulations can reduce the use of DSUVIA, and Zalviso, if approved in the United States.

Government agencies and non-governmental organizations promulgate regulations and guidelines applicable to certain drug classes that may include DSUVIA and Zalviso, if approved in the United States. Recommendations of government agencies or non-governmental organizations may relate to such matters as maximum quantities dispensed to patients, dosage, route of administration, and use of concomitant therapies. Government agencies and non-governmental organizations have offered commentary and guidelines on the use of opioid-containing products. We are uncertain how these activities and guidelines may impact DSUVIA and our ability to gain marketing approval of Zalviso in the United States. Regulations or guidelines suggesting the reduced use of certain drug classes that may include DSUVIA or Zalviso, or the use of competitive or alternative products as the standard-of-care to be followed by patients and healthcare providers, could result in decreased use of DSUVIA or Zalviso, if approved, or negatively impact our ability to gain market acceptance and market share. The U.S. government and state legislatures have prioritized combatting the growing misuse and addiction to opioids and opioid overdose deaths and have enacted legislation and regulations as well as other measures intended to fight the opioid epidemic. Addressing opioid drug abuse is a priority for the current U.S. administration and the FDA and is part of a broader initiative led by the U.S. Department of Health and Human Services, or HHS. Overall, there is greater scrutiny of entities involved in the manufacture, sale and distribution of opioids. These initiatives, existing laws and regulations, and any negative publicity related to opioids may have a material impact on our business and our ability to manufacture opioid products.

Governmental investigations, inquiries, and regulatory actions and lawsuits brought against us by government agencies and private parties with respect to our commercialization of opioids could adversely affect our business, financial condition, results of operations and cash flows.

As a result of greater public awareness of the public health issue of opioid abuse, there has been increased scrutiny of, and investigation into, the commercial practices of opioid manufacturers by state and federal agencies. As a result of our manufacturing and commercial sale of DSUVIA in the United States and Zalviso in Europe, we could become the subject of federal, state and foreign government investigations and enforcement actions, focused on the misuse and abuse of opioid medications.

In addition, a significant number of lawsuits have been filed against opioid manufacturers, distributors, and others in the supply chain by cities, counties, state Attorney's General and private persons seeking to hold them accountable for opioid misuse and abuse. The lawsuits assert a variety of claims, including, but not limited to, public nuisance, negligence, civil conspiracy, fraud, violations of the Racketeer Influenced and Corrupt Organizations Act, or RICO, or similar state laws, violations of state Controlled Substance Acts or state False Claims Acts, product liability, consumer fraud, unfair or deceptive trade practices, false advertising, insurance fraud, unjust enrichment and other common law and statutory claims arising from defendants' manufacturing, distribution, marketing and promotion of opioids and seek restitution, damages, injunctive and other relief and attorneys' fees and costs. The claims generally are based on alleged misrepresentations and/or omissions in connection with the sale and marketing of prescription opioid medications and/or an alleged failure to take adequate steps to prevent abuse and diversion. While DSUVIA is designed for use solely in certified medically supervised healthcare settings and administered only by a healthcare professional in these settings, and is not distributed or available at retail pharmacies to patients by prescription, we can provide no assurance that parties will not file lawsuits of this type against us in the future. In addition, current public perceptions of the public health issue of opioid abuse may present challenges to favorable resolution of any potential claims. Accordingly, we cannot predict whether we may become subject to these kinds of investigations and lawsuits in the future, and if we were to be named as a defendant in such actions, we cannot predict the ultimate outcome. Any allegations against us may negatively affect our business in various ways, including through harm to our reputation.

If we were required to defend ourselves in these matters, we would likely incur significant legal costs and could in the future be required to pay significant amounts as a result of fines, penalties, settlements or judgments. It is unlikely that our current product liability insurance would fully cover these potential liabilities, if at all. Moreover, we may be unable to maintain insurance in the future on acceptable terms or with adequate coverage against potential liabilities or other losses. For more information about our product liability insurance and exclusions therefrom, please see the risk factor entitled "We face potential product liability claims, and, if such claims are successful, we may incur substantial liability" elsewhere in this section. The resolution of one or more of these matters could have a material adverse effect on our business, financial condition, results of operations and cash flows.

Furthermore, in the current climate, stories regarding prescription drug abuse and the diversion of opioids and other controlled substances are frequently in the media or advocated by public interest groups. Unfavorable publicity regarding the use or misuse of opioid drugs, the limitations of abuse-deterrent formulations, the ability of drug abusers to discover previously unknown ways to abuse opioid products, public inquiries and investigations into prescription drug abuse, litigation, or regulatory activity regarding sales, marketing, distribution or storage of opioids could have a material adverse effect on our reputation and impact on the results of litigation.

Finally, various government entities, including Congress, state legislatures or other policy-making bodies, or public interest groups have in the past and may in the future hold hearings, conduct investigations and/or issue reports calling attention to the opioid crisis, and may mention or criticize the perceived role of manufacturers, including us, in the opioid crisis. Similarly, press organizations have and likely will continue to report on these issues, and such reporting may result in adverse publicity for us, resulting in reputational harm.

Approval of Zalviso and DZUVEO in Europe has resulted in a variety of risks associated with international operations that could materially adversely affect our business.

Our collaborations with international partners, including Grünenthal and Aguettant, have required, and will require, us to supply product to support the commercialization of our products in Europe and it is likely that any New Arrangement would also include such a requirement. Entering into international business relationships subjects us to additional risks including:

- multiple, conflicting, and changing laws and regulations such as privacy and data regulations, transparency regulations, tax laws, export and import restrictions, employment laws, regulatory requirements, including for drug approvals, and other governmental approvals, permits, and licenses;
- EMA "sunset clause" requirements, which apply to DZUVEO, providing that the marketing authorization of a medicine will cease to be valid if it is not placed on the market within three years of the authorization being granted or if it is removed from the market for three consecutive years; however, the European Commission has extended this date to December 31, 2022 for DZUVEO;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- different payer reimbursement regimes, governmental payers, patient self-pay systems and price controls;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from pandemics, geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

Any of these factors could have a material adverse effect on our business.

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. DSUVIA competes, and our product candidates, if approved in the U.S., will compete, 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. Zalviso, if approved in the U.S., may compete with a number of opioid-based treatment options, including IV PCA pumps, oral PCA devices, and transdermal opioid PCAs. 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 achieving widespread market acceptance. Our competitors' drugs 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 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.

Hospital or other health care facility formulary approvals for DSUVIA or our product candidates, if approved, in the United States may not be achieved, or could be subject to certain restrictions, which could make it difficult for us to sell our products.

Obtaining hospital or other health care facility formulary approvals can be an expensive and time-consuming process. We cannot be certain if and when we will obtain formulary approvals to allow us to sell our products into our target markets. In particular, the COVID-19-related restrictions on our commercial and medical affairs teams' access to hospitals and other health care facilities has adversely impacted the number of formulary approvals we achieved to date, and for as long as these restrictions remain in place, or new restrictions are implemented, we may have limited visibility or difficulties in obtaining these formulary approvals. Failure to obtain timely formulary approvals will limit our commercial success. In order to obtain formulary approvals, we often are required to complete evaluation programs whereby DSUVIA, or our product candidates, if approved, are used on a limited basis for certain patient types. The evaluation period may last several months and there can be no assurance that use during the evaluation period will lead to formulary approvals of DSUVIA, or our product candidates, if approved. Further, even successful formulary approvals are subject to certain restrictions based on patient type or hospital protocol. Failure to obtain timely formulary approvals for DSUVIA, or our product candidates, if approved, would materially adversely affect our ability to attain or sustain profitable operations.

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

Our ability to commercialize DSUVIA or our product candidates, if approved, in the United States, including Zalviso, and any collaboration partner's ability to commercialize DZUVEO or Zalviso in Europe successfully 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 to provide scientific and clinical support for the use of our 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 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 ability to sell our 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 DSUVIA or Zalviso, if approved, in the United States, and DSUVIA/DZUVEO and Zalviso in Europe and elsewhere. The application of user fees to generic drug products may expedite the approval of additional pain medication generic drugs. We expect to experience pricing pressures in connection with our sales of DSUVIA and Zalviso, if approved, in the United States, and future product sales of Zalviso and DZUVEO in Europe, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. If we fail to successfully secure and maintain reimbursement coverage for our products or are significantly delayed in doing so, we will have 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 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 DZUVEO or Zalviso in Europe. Also, reimbursement amounts may reduce the demand for, or the price of, our products. For example, studies of DZUVEO 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 may not be able to successfully commercialize DSUVIA or our product candidates, if approved, in the United States, or DZUVEO or Zalviso in Europe.

Additionally, the regulations that govern marketing approvals, pricing, coverage and reimbursement for new drugs 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 any future collaboration partners' ability to market and successfully commercialize our products in the 27 member states of the European Union. Adverse pricing limitations may hinder our ability to recoup our investment in DSUVIA in the United States, or our 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, including DSUVIA or our product candidates, if approved, 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 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. While we have received marketing approval for DSUVIA for our proposed indication, physicians may nevertheless use our products for their patients in a manner that is inconsistent with the approved label, if the physicians personally believe in their professional medical judgment it could be used in such manner. However, if the FDA determines that our promotional materials or training constitutes promotion of an off-label use, it could request that we modify our training or promotional materials or subject us 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 promotional or training materials to constitute promotion of an 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 our operations, any of which could adversely affect our ability to operate 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 DSUVIA or 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 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 products have relationships with group purchasing organizations, or GPOs, whereby such GPOs provide such end-users access to a broad range of pharmaceutical products from multiple suppliers at competitive prices and, in certain cases, exercise considerable influence over the drug 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 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.

We intend to rely on a limited number of distributors and pharmaceutical wholesalers to distribute DSUVIA and our product candidates, if approved, in the United States.

We intend to rely primarily upon distributors and pharmaceutical wholesalers in connection with the distribution of DSUVIA and our product candidates, if approved, in the United States. As part of the DSUVIA REMS program, we monitor distribution and audit wholesalers' data and will monitor such data from other distributors. If our distributors and wholesalers do not comply with the DSUVIA REMS requirements, or if we are unable to establish or maintain our business relationships with these distributors and pharmaceutical wholesalers on commercially acceptable terms, or if our distributors and wholesalers are unable to distribute our drugs for regulatory, compliance or any other reason, it could have a material adverse effect on our sales and may prevent us from achieving profitability.

Risks Related to Clinical Development and Regulatory Approval

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 hydrochloride for injection. Aguettant will supply us with the products for use in commercialization, if they are approved in the U.S. Our current expectation is that the PFS products will be approvable by the FDA without additional manufacturing, nonclinical or clinical development, but we have not yet received FDA feedback on the available data to support the planned NDA filings for the PFS products. If, after receiving the FDA written feedback, we determine that additional development work will be needed for U.S. approval, we would incur additional expense and be delayed in obtaining any revenue from the PFS products.

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 has received Breakthrough Device Designation from the FDA for regional anticoagulant for injection into the extracorporeal circuit. Niyad 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 filing of a PMA; the Breakthrough Designation allows for more frequent and informal FDA communication regarding development plans, and allows for priority review once the marketing application is submitted.

The active drug component of Niyad, nafamostat, is also being developed for drug indications for which we expect to submit Investigational New Drug applications.

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 and some foreign jurisdictions, the legislative landscape continues to evolve, including changes to the regulation of opioid-containing products. There have been a number of legislative and regulatory changes and proposed changes regarding healthcare systems that could prevent or delay marketing approval of Zalviso outside of Europe. These changes will restrict or regulate post-approval activities for DSUVIA, DZUVEO and Zalviso, and affect our ability to profitably sell any products for which we obtain marketing approval. For example, in February 2016, the FDA announced a comprehensive action plan to take concrete steps towards reducing the impact of opioid abuse on American families and communities. As part of this plan, the FDA announced that it intended to review product and labeling decisions and re-examine the risk-benefit paradigm for opioids. In June 2019, the FDA issued draft guidance related to a new benefit/risk framework for new opioid analgesic products, which proposes that the new product candidate show some benefit over an existing product. In September 2019, the FDA held a public hearing to receive stakeholder input on the approval process for new opioids. In January 2020, FDA's Anesthetic and Analgesic Drug Products Advisory Committee recommended against the approval of a new opioid analgesic, oxycodegol, the NDA for which was subsequently withdrawn by its sponsor. The timing of the resubmission of the Zalviso NDA is in part dependent upon the finalization of the FDA's new opioid approval guidelines and process.

In the European Union, or EU, the pricing of prescription drugs is subject to government control. The EU also 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. In addition, the EMA has a "sunset clause" which provides that the marketing authorization of a medicine will cease to be valid if it is not placed on the market within three years of the authorization being granted or if it is removed from the market for three consecutive years; however, the European Commission has extended this date to December 31, 2022 for DZUVEO.

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. Aspects of the Affordable Care Act that may impact our business include:

- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- expansion of eligibility criteria for Medicaid programs, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of healthcare fraud and abuse laws, including the federal False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for non-compliance; and
- a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

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. While Congress has not passed comprehensive repeal legislation, several bills affecting the implementation of certain taxes under the Affordable Care Act have been signed into law. The Tax Cuts and Jobs Act of 2017 includes a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". 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. Thus, the Affordable Care Act will remain in effect in its current form. Moreover, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace, which began on February 15, 2021 and remained open through August 15, 2021. The executive order instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the Affordable Care Act. 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 through 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 3% 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. Congress is also considering additional health reform measures.

Moreover, the Drug Supply Chain Security Act of 2013 imposes additional obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing. Among the requirements of this legislation, manufacturers are required to 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.

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, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, President Trump announced several executive orders related to prescription drug pricing that attempt to implement several of the administration's proposals. The FDA concurrently released a final rule and guidance in September 2020, implementing a portion of the importation executive order providing pathways for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which has also been delayed until January 1, 2023. Further, on November 20, 2020, the Centers for Medicare & Medicaid Services, or CMS, issued an interim final rule implementing President Trump's Most Favored Nation, or MFN, executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. As a result of litigation challenging the MFN model, on December 27, 2021, CMS published a final rule that rescinds the MFN Model interim final rule. 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. 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 Zalviso and DZUVEO 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. For instance, it is possible that additional governmental action is taken in response to the COVID-19 pandemic. 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 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.

We may experience market resistance, delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy regarding opioids generally, and sufentanil specifically.

In February 2016, the FDA announced a comprehensive action plan to take concrete steps towards reducing the impact of opioid abuse on American families and communities. As part of this plan, the FDA announced that it intended to review product and labeling decisions and re-examine the risk-benefit paradigm for opioids. In June 2019, the FDA issued draft guidance related to a new benefit/risk framework for new opioid analgesic products, which proposes that the new product candidate show some benefit over an existing product. In September 2019, the FDA held a public hearing to receive stakeholder input on the approval process for new opioids. The timing of the resubmission of the Zalviso NDA is in part dependent upon the finalization of the FDA's new opioid approval guidelines and process.

In May 2017, an Opioid Policy Steering Committee was established to address and advise regulators on opioid use. The Committee was charged with three initial questions: (i) should the FDA require mandatory education for healthcare professionals, or HCPs, who prescribe opioids; (ii) should the FDA take steps to ensure the number of prescribed opioid doses is more closely tailored to the medical indication; and (iii) is the FDA properly considering the risk of abuse and misuse of opioids during its drug review process. Zalviso has not been designed with an abuse-deterrent formulation and is not tamper-resistant. As a result, Zalviso has not undergone testing for tamper-resistance or abuse deterrence.

The FDA can delay, limit or deny marketing approval for many reasons, including:

- a product candidate may not be considered safe or effective;
- the manufacturing processes or facilities we have selected may not meet the applicable requirements; and
- changes in their approval policies or adoption of new regulations may require additional work on our part.

Part of the regulatory approval process includes compliance inspections of manufacturing facilities to ensure adherence to applicable regulations and guidelines. The regulatory agency may delay, limit or deny marketing approval of our product candidate, Zalviso, as a result of such inspections. We, our contract manufacturers, and their vendors, are all subject to preapproval and post-approval inspections at any time. The results of these inspections could impact our ability to obtain FDA approval for Zalviso and, if approved, our ability to launch and successfully commercialize Zalviso in the United States. In addition, results of FDA inspections could impact our ability to maintain FDA approval of DSUVIA, and our ability to expand and sustain commercial sales of DSUVIA in the United States.

Any delay in, or failure to receive or maintain, approval for Zalviso in the United States could prevent us from generating meaningful revenues or achieving profitability. Zalviso may not be approved even if we believe it has achieved its endpoints in clinical trials. Regulatory agencies, including the FDA, or their advisors, may disagree with our trial design and our interpretations of data from preclinical studies and clinical trials. Regulatory agencies may change requirements for approval even after a clinical trial design has been approved. The FDA exercises significant discretion over the regulation of combination products, including the discretion to require separate marketing applications for the drug and device components in a combination product. Zalviso is being regulated as a drug product under the NDA process administered by the FDA. The FDA could in the future require additional regulation of Zalviso, or DSUVIA, under the medical device provisions of the Federal Food, Drug and Cosmetic Act, or FDCA. We must comply with the Quality Systems Regulation, or QSR, which sets forth the FDA's current good manufacturing practice, or cGMP, requirements for medical devices, and other applicable government regulations and corresponding foreign standards for drug cGMPs. If we fail to comply with these regulations, it could have a material adverse effect on our business and financial condition.

Regulatory agencies also may approve a product candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post-marketing trials. For example, DSUVIA is subject to a deferred post-marketing requirement for study in the pediatric population ages 6-17 years. As required in the DSUVIA FDA approval letter, a final protocol for this trial was submitted to the FDA in August 2020, in conjunction with a previously FDA approved request to defer initiation of pediatric studies until additional post-market safety data is obtained in adult patients using DSUVIA. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. For example, we intend to seek approval of Zalviso for the management of moderate-to-severe acute pain in adult patients in the hospital setting; however, our clinical trial data was generated exclusively from the post-operative segment of this population, and the FDA may restrict any approval to post-operative patients only, which would reduce the size of the commercial opportunity.

The success of Zalviso relies, in part, on obtaining regulatory approval in the United States.

The success of Zalviso relies, in part, upon our ability to develop and receive regulatory approval of this product candidate in the United States for the management of moderate-to-severe acute pain in adult patients in the hospital setting. Our Phase 3 program for Zalviso initially consisted of three Phase 3 clinical trials. We reported positive top-line data from each of these trials and submitted an NDA for Zalviso to the FDA in September 2013, which the FDA then accepted for filing in December 2013. In July 2014, the FDA issued a Complete Response Letter, or CRL, for our NDA for Zalviso, or the Zalviso CRL. The Zalviso CRL contained requests for additional information on the Zalviso System to ensure proper use of the device. The requests include submission of data demonstrating a reduction in the incidence of device errors, changes to address inadvertent dosing, among other items, and submission of additional data to support the shelf life of the product. Furthermore, in March 2015, we received correspondence from the FDA stating that in addition to the bench testing and two Human Factors studies we had performed in response to the issues identified in the Zalviso CRL, a clinical trial was needed to assess the risk of inadvertent dispensing and overall risk of dispensing failures. Based on the results of our Type C meeting with the FDA in September 2015, we completed the protocol review with the FDA and initiated this study, IAP312, in September 2016.

IAP312 was a Phase 3 study in post-operative patients designed to evaluate the effectiveness of changes made to the functionality and usability of the Zalviso device and to take into account comments from the FDA on the study protocol. The IAP312 study was designed to rule out a 5% device failure rate. The study design required a minimum of 315 patients. In the IAP312 study, sites proactively looked for tablets that were dispensed by the patient but failed to be placed under the tongue, known as dropped tablets. The FDA refers to dropped tablets as inadvertent dispensing. Correspondence from the FDA suggests that they may include the rate of inadvertent dispensing along with the device failures to calculate a total error rate. The IAP312 study evaluated all incidents of misplaced tablets; however, per the protocol, the error rate calculation does not include the rate of inadvertent dispensing. If the FDA includes the rate of inadvertent dispensing along with the device failures to calculate a total error rate, the resulting error rate may be unacceptable to the FDA. Further, the correspondence from the FDA suggests that we may need to modify the REMS program for Zalviso to address dropped tablets. The IAP312 results will supplement the three Phase 3 trials already completed in the Zalviso NDA resubmission. The timing of the resubmission of the Zalviso NDA is in part dependent upon the finalization of the FDA's new opioid approval guidelines and process.

There is no guarantee that the additional work we performed related to Zalviso, including the IAP312 trial, will result in our successfully obtaining FDA approval of Zalviso in a timely fashion, if at all. Although we believe the IAP312 study met safety, satisfaction and device usability expectations, there is no guarantee the IAP312 trial results will address the issues raised by the FDA. For example, the FDA may include the rate of inadvertent dispensing along with the device failures to calculate a total error rate and the resulting error rate may be unacceptable to the FDA, or the FDA may still have concerns regarding the performance of the device, inadvertent dosing (dropped tablets), or other issues. At any future point in time, the FDA could require us to complete further clinical, Human Factors, pharmaceutical, reprocessing or other studies, which could delay or preclude any NDA resubmission or approval of the NDA and could require us to obtain significant additional funding. We may not be able to identify appropriate remediations to issues that the FDA may raise, and we may not have sufficient time or financial resources to conduct future activities to remediate issues raised by the FDA. We intend to seek a label indication for Zalviso for the management of moderate-to-severe acute pain in adult patients in the hospital setting. However, our clinical trial data was generated exclusively from the post-operative segment of this population, and the FDA may restrict any approval to post-operative patients only, which would reduce our commercial opportunity.

Upon resubmission of the Zalviso NDA, the FDA may hold an advisory committee meeting to obtain committee input on the safety and efficacy of Zalviso. Typically, advisory committees will provide responses to specific questions asked by the FDA, including the committee's view on the approvability of the drug under review. Advisory committee decisions are not binding, but an adverse decision at the advisory committee may have a negative impact on the regulatory review of Zalviso. Additionally, we may choose to engage in the dispute resolution process with the FDA.

Our proposed trade name of Zalviso has been approved by the EMA and is currently being used in Europe. It has also been conditionally approved by the FDA, which must approve all drug trade names to avoid medication errors and misbranding. However, the FDA may withdraw this approval in which case any brand recognition or goodwill that we establish with the name Zalviso prior to commercialization may be worthless.

Any delay in approval by the FDA of the Zalviso NDA, once it is resubmitted, may negatively impact our stock price and harm our business operations. Any delay in obtaining, or inability to obtain, regulatory approval would prevent us from commercializing Zalviso in the United States, generating revenues and potentially achieving profitability. If any of these events occur, we may be forced to delay or abandon our development efforts for Zalviso, which would have a material adverse effect on our business.

Positive clinical results obtained to date for Zalviso may be disputed in FDA review, do not guarantee regulatory approval and may not be obtained from future clinical trials.

We have reported positive top-line data from each of our four Zalviso Phase 3 clinical trials completed to date, as well as our Phase 2 clinical trials for Zalviso. However, even if we believe that the data obtained from clinical trials is positive, the FDA has, and in the future could, determine that the data from our trials was negative or inconclusive or could reach a different conclusion than we did on that same data. Negative or inconclusive results of a clinical trial or difference of opinion could cause the FDA to require us to repeat the trial or conduct additional clinical trials prior to obtaining approval for commercialization, and there is no guarantee that additional trials would achieve positive results or that the FDA will agree with our interpretation of the results. If the FDA were to require any additional clinical trials for Zalviso, our development efforts would be further delayed, which would have a material adverse effect on our business. Any such determination by the FDA would delay the timing of our commercialization plan for Zalviso and adversely affect our business operations.

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. While we have completed four Phase 3 clinical trials and several Phase 2 clinical trials for Zalviso, future clinical trials may not begin on time, have an effective design, enroll a sufficient number of patients or be completed on schedule, if at all. For example, we postponed the start of IAP312, originally planned for the first quarter of 2016, to September 2016. The postponement was due to a delay in the receipt and testing of final clinical supplies for this trial. As a result, the development timeline for Zalviso was further extended.

Our post-approval clinical trials for DSUVIA, or any future FDA-required clinical trials for Zalviso, could be delayed for a variety of reasons, including:

- inability to raise funding necessary to initiate or continue a trial;
- 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 to participate in a trial;
- delays in the testing, validation, manufacture and delivery of the tablets and device components of DSUVIA or Zalviso;
- 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 Zalviso could be delayed, our ability to commercialize and commence sales of Zalviso could be materially harmed, and our ability to maintain FDA approval of DSUVIA could be jeopardized, which could have a material adverse effect on our business.

Zalviso may cause adverse effects or have other properties that could delay or prevent regulatory approval or limit the scope of any approved label or market acceptance. DSUVIA may cause adverse effects or have other properties that could limit market acceptance.

Adverse events, or AEs, caused by Zalviso could cause us, other reviewing entities, clinical trial sites or regulatory authorities to interrupt, delay or halt any future FDA-required clinical trials and could result in the denial of regulatory approval. Phase 2 clinical trials we conducted with Zalviso did generate some AEs, but no significant adverse events, or SAEs, related to the trial drug. In our Phase 3 active-comparator clinical trial (IAP309), 8% of Zalviso-treated patients dropped out of the trial prematurely due to an AE (11% in the IV patient-controlled morphine group), and we observed three SAEs that were assessed as possibly or probably related to study drug (one- respiratory depression in the Zalviso group and two- abdominal distension and ileus in the IV patient-controlled morphine group). In our Phase 3, double-blind, placebo-controlled, abdominal surgery trial (IAP310), 6% of Zalviso-treated patients dropped out of the trial prematurely due to an AE (9% in placebo group). There were no SAEs determined to be related to study drug. In our Phase 3, double-blind, placebo-controlled, orthopedic surgery trial (IAP311), 7% of Zalviso-treated patients dropped out of the trial prematurely due to an AE (7% in placebo group). Four patients (three in the Zalviso group and one in the placebo group) experienced an SAE considered possibly or probably related to the trial drug by the investigator. The SAEs possibly or probably attributed to Zalviso were severe oxygen saturation decrease, sinus tachycardia and confusional state. In our Phase 3 multicenter, open-label study of Zalviso (IAP312), 3% of patients dropped out prematurely due to an AE. Five patients experienced SAEs in the IAP312 study and none of these were considered possibly or probably related to the study drug by the investigator.

In our Phase 2 DSUVIA placebo-controlled bunionectomy study (SAP202), two patients in the DSUVIA 30 mcg group (5%) discontinued treatment due to an AE, one unrelated to study drug and the other probably related to study drug. There were no SAEs deemed related to study drug. In our Phase 3 placebo-controlled abdominal surgery study (SAP301), one DSUVIA-treated patient (1%) dropped out of the trial prematurely due to an AE (4% in placebo group). There were two SAEs determined to be related to study drug in the placebo-treated group and no related SAEs in the DSUVIA group. In our Phase 3 open-label, single-arm emergency room study (SAP302), no DSUVIA-treated patients dropped out of the trial prematurely due to an AE. One patient had an SAE – angina pectoris – possibly related to study drug. In our post-operative study in patients aged 40 years or older (SAP303), 3% of DSUVIA-treated patients dropped out of the trial prematurely due to an AE. There were no SAEs deemed related to study drug.

If DSUVIA or, if approved, Zalviso cause serious or unexpected side effects after receiving marketing approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product or impose restrictions on its distribution in the form of a modified REMS program;
- regulatory authorities may require the addition of labeling statements, such as warnings or contraindications;
- we may be required to change the way the product is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; or
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of DSUVIA or, if approved, Zalviso, and could substantially increase the costs of commercializing our products.

Additional time may be required to obtain U.S. regulatory approval for Zalviso because it is a drug/device combination product candidate.

DSUVIA and Zalviso are combination products with both drug and device components. The FDA requires both the drug and device components of combination product candidates to be reviewed as part of an NDA submission. There are very few examples of the FDA approval process for drug/device combination products such as DSUVIA and Zalviso. As a result, we experienced delays in the development and commercialization of DSUVIA, and may experience future delays in the development and commercialization of Zalviso, due to regulatory uncertainties in the product development and approval process, in particular as it relates to a drug/device combination product approval under an NDA.

The process for obtaining approval of an 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 an 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 Human Factors 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 candidate, Zalviso, and would have a material adverse effect on our business and financial condition. In addition, an NDA may not be approved, or approval may be delayed, as a result of changes in FDA policies for drug 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. More generally, the FDA's comprehensive action plan to take concrete steps towards reducing the impact of opioid abuse on American families and communities may result in delays and challenges in obtaining NDA approval. Any significant delay in the acceptance, review or approval of an NDA 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.

Although we have obtained regulatory approval for DSUVIA, and even if we obtain regulatory approval for our product candidates in the United States, we and our collaborators face extensive regulatory requirements, and our products may face future development and regulatory difficulties.

Although we have obtained regulatory approval for DSUVIA, and even if we obtain regulatory approval for our product candidates in the United States, the FDA may impose significant restrictions on the indicated uses or marketing of our products or impose ongoing requirements for potentially costly post-approval trials or post-market surveillance. For example, DSUVIA is subject to a deferred post-marketing requirement for study in the pediatric population ages 6-17 years. A final protocol for this trial was submitted to the FDA in August 2020, in conjunction with a previously FDA approved request to defer initiation of pediatric studies until additional post-market safety data is obtained in adult patients using DSUVIA. Additionally, the labeling approved for DSUVIA includes restrictions on use due to the opioid nature of sufentanil. If approved, the labeling for Zalviso will likely include similar restrictions on use.

DSUVIA in the United States is also subject to ongoing FDA requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, record-keeping and reporting of safety and other post-market information. The holder of an approved NDA is obligated to monitor and report AEs and any failure of a product to meet the specifications in the NDA. The holder of an approved NDA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process.

Advertising and promotional materials must comply with FDA rules concerning the advertising and promotion of DSUVIA and are subject to FDA review, in addition to other potentially applicable federal and state laws. Failure to comply with these regulations can result in the receipt of Warning Letters and further liability if off-label promotion is involved. For example, on February 11, 2021, we received a Warning Letter from the Office of Prescription Drug Promotion, or OPDP, of the FDA relating to a banner advertisement we submitted to the OPDP on December 6, 2019, and a tabletop display we submitted on February 28, 2020, and resubmitted to the OPDP at its request on September 23, 2020. We submitted the materials to the OPDP pursuant to the FDA requirement that sponsors submit all promotional materials to the FDA at the time of their initial dissemination or publication. The FDA's concerns identified in the letter include its view that the promotional material makes misleading claims and representations about the risks and efficacy of DSUVIA because the material does not reveal facts that are material in light of the representations made. As a result, we conducted a review of our marketing materials to identify any potential revisions in light of the letter. We responded to the FDA within the timeframe requested in the letter and, on March 23, 2021, held a teleconference with OPDP to seek guidance and clarification on the concerns raised in the letter. Following our meeting with OPDP, we conducted a further review of our marketing materials to identify any potential revisions in light of the letter and OPDP's guidance. We submitted a second response to FDA on April 7, 2021, and on June 17, 2021 we announced that the FDA agreed with our proposed plan to update certain promotional materials, including providing a letter to healthcare professionals, or the DHCP letter, explaining the corrections to the discontinued promotional materials. We included this DHCP letter on the DSUVIA.com website for a period of eight months. On February 18, 2022, in agreement with OPDP, the link to the corrective DCHP letter was removed from the DSUVIA.com website. Although we believe we have updated all promotional materials currently in use by our commercial team to address the FDA's concerns and we received a close-out Letter to the Warning Letter in March 2022, we cannot give any assurances that we will not receive additional FDA Warning Letters in the future. If approved, our product candidates will be subject to these same requirements.

We must also register and obtain various state prescription drug distribution licenses and controlled substance permits, and any delay or failure to obtain or maintain these licenses or permits may limit our market and materially impact our business. In certain states we cannot apply for a license until a drug is approved by the FDA. The state licensing process may take several months which would delay commercialization in those states. In addition, manufacturers of drug products and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMPs and adherence to commitments made in the NDA. If we, or a regulatory agency, discover previously unknown problems with a product, such as AEs of unanticipated severity or frequency, or problems with the facilities where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facilities, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of our products, a regulatory agency may:

- issue a Warning Letter asserting that we are in violation of the law;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending NDA or supplements to an NDA submitted by us;
- seize product; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize DSUVIA, or, if approved, our product candidates, and generate revenues.

Except for Zalviso and DZUVEO, which are both approved in Europe, we may never obtain additional regulatory approvals for our products and product candidates outside of the United States, which would limit our ability to realize their full market potential.

In order to market any products outside of the United States, we or our commercial partners, must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. On September 22, 2015, we announced that the EC had granted marketing approval for Grünenthal's MAA for Zalviso for the management of acute moderate-to-severe post-operative pain in adult patients. In April 2016, Grünenthal completed the first commercial sale of Zalviso. Grünenthal terminated the collaboration, 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. Grünenthal's rights to market and sell Zalviso reverted back to us on May 12, 2021. We have not yet negotiated a New Arrangement and there can be no assurance that we will successfully enter into a New Arrangement. In June 2018, we announced that the EC had granted marketing approval of DZUVEO for the treatment of patients with moderate-to-severe acute pain in medically monitored settings. In July 2021, we entered into the DZUVEO Agreement with Aguettant.

Part of the foreign regulatory approval process includes compliance inspections of manufacturing facilities to ensure adherence to applicable regulations and guidelines. The foreign regulatory agency may delay, limit or deny marketing approval as a result of such inspections. We, our contract manufacturers, and their vendors, are all subject to preapproval and post-approval inspections at any time. The results of these inspections could impact our ability to obtain regulatory approval of DSUVIA and Zalviso in countries outside of the United States and Europe, or our ability to launch and successfully commercialize these products, once approved. In addition, results of EMA inspections could impact our ability to maintain EC approval of Zalviso and DZUVEO, and any future collaboration partner's ability to expand and sustain commercial sales of Zalviso or DZUVEO in Europe.

Outside of Europe, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and costs for us and require additional non-clinical trials or clinical trials, which could be costly and time consuming. Regulatory requirements can vary widely from country-to-country and could delay or prevent the introduction of our products in those countries. Our current clinical trial data may not be sufficient to support marketing approval or premium reimbursement in all territories. For example, we anticipate we may need comparator studies for DZUVEO in Europe to ensure premium reimbursement in certain countries. While we have obtained approval of DZUVEO in Europe, we will be substantially dependent on Aguettant to comply with regulatory requirements. If we, or our commercial partners, fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our products will be harmed.

DSUVIA requires, and, if approved, Zalviso will require, a REMS program.

DSUVIA was approved in the United States with a REMS program. If Zalviso is approved in the United States, it will also require a REMS program. The DSUVIA REMS program includes restrictions on product distribution and use only in certified medically supervised settings. Before DSUVIA is distributed, an authorized representative from each medically supervised setting must sign an attestation that they have the ability to manage acute opioid overdose and will train all relevant staff on administration of DSUVIA, including the importance of only dispensing the product in a medically supervised setting. Therefore, REMS-certification is a key gating item to generating product revenues for DSUVIA. In addition, the REMS program for DSUVIA may significantly increase our costs to commercialize this product. While we have received pre-clearance from the FDA regarding certain aspects of the proposed required REMS program for Zalviso, we cannot predict the final REMS program to be required as part of any FDA approval of Zalviso. Depending on the extent of the REMS requirements, any U.S. launch may be delayed, the costs to commercialize Zalviso may increase substantially and the potential commercial market could be restricted. Furthermore, risks of sufentanil that are not adequately addressed through the proposed REMS program for Zalviso may also prevent or delay its approval for commercialization.

Risks Related to Our Financial Condition and Need for Additional Capital

We have incurred significant losses since our inception, anticipate that we will continue to incur significant losses in 2022 and may continue to incur losses in the future.

We have incurred significant net losses in each year since our inception in July 2005, and as of March 31, 2022, we had an accumulated deficit of $482.3 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 commercialization activities for DSUVIA, manufacturing and supply activities for DZUVEO, and research and development activities for our product candidates, including the FDA regulatory review of the Zalviso NDA, once resubmitted. If DSUVIA is not successfully commercialized in the U.S., 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 have not yet generated significant product revenue and may never be profitable.

Our ability to generate revenue from commercial sales 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 will successfully commercialize DZUVEO. 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.

In September 2015, we consummated a monetization transaction with PDL pursuant to which we sold to PDL for $65.0 million 75% of the European royalties from sales of Zalviso and 80% of the first four commercial milestones under the Amended License Agreement, subject to a capped amount. PDL sold its royalty interest for Zalviso to SWK in 2020. As mentioned above, Grünenthal has terminated the Grünenthal Agreements and the rights reverted back to us on May 12, 2021. Per the terms of the Royalty Monetization, we are obligated to use commercially reasonable efforts to negotiate a New Arrangement. Accordingly, even if we are able to enter into a New Arrangement, and that licensee is successful in commercializing Zalviso in Europe, we will receive only a portion of any royalties until the capped amount owing under the Royalty Monetization is reached. 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 our 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 DSUVIA and 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 and Zalviso 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.

We anticipate continuing to incur significant costs associated with commercializing DSUVIA in the United States. Even if we are able to generate revenues from the sale of 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. 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. Even if we do generate revenue from such sales, 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. Our expectations about the timing and size of initial stocking orders for the SKOs and other orders by the DoD are based on our understanding of 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.

We have been substantially dependent on Grünenthal to successfully commercialize Zalviso in Europe and they have terminated their collaboration agreement with us.

Under our agreements with Grünenthal, we granted Grünenthal rights to commercialize Zalviso in Europe for human use in pain treatment within, or dispensed by, hospitals, hospices, nursing homes and other medically supervised settings. In September 2015, the EC granted marketing approval for Grünenthal's MAA for Zalviso for the management of acute moderate-to-severe post-operative pain in adult patients, and Grünenthal began its European launch of Zalviso with the first commercial sale occurring in April 2016. Grünenthal terminated the collaboration, 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. Grünenthal's rights to market and sell Zalviso reverted back to us on May 12, 2021.

During the pilot and launch phases in the various European countries, Grünenthal reported certain issues from HCPs with the initial set up of the Zalviso controllers before being given to patients for use. To address the issues, we assisted Grünenthal with implementing additional training for HCPs and revised the controller software. Controllers with the revised software, which were delivered in December 2016, underwent extensive bench testing and we believe we successfully addressed the issues presented. Additional devices were delivered beginning in early 2017. Controllers with the U.S. version of the revised software were also used in the IAP312 clinical study that was initiated in September 2016. There can be no assurance that the issues identified in the initial pilot and launch phases by Grünenthal will not have a material adverse impact on future sales of Zalviso in Europe under a New Arrangement. Further, if new issues occur, there may be a material adverse impact on the future sales of Zalviso in Europe under a New Arrangement which may have a negative impact on future revenues received and recognized by us.

We did not realize the expected benefits from our collaboration with Grünenthal, and may not realize the expected benefits from any New Arrangement, due to a number of important factors, including:

- The timing and amount of any payments we may receive under our agreements will depend on, among other things, the efforts, allocation of resources, and successful commercialization of Zalviso by any future collaboration partner in Europe;
- Grünenthal changed the focus of its commercialization efforts to pursue higher-priority programs and any future collaboration partner may do the same;
- Grünenthal stopped its commercialization efforts in countries where it had the sole right to commercialize Zalviso, requiring us to find another collaboration partner for Zalviso in Europe; and
- Grünenthal terminated its agreements with us, and any future collaboration partner may also terminate any future agreement with us, adversely affecting our potential revenue from Zalviso;

Any failures in commercialization of Zalviso outside the United States could have a material adverse impact on our business, including an adverse impact on the commercialization of DSUVIA or the development of Zalviso in the United States, if related to issues underlying the sufentanil sublingual tablet technology, safety or efficacy. Additionally, we agreed to certain representations and covenants relating to the Grünenthal Agreements under our agreements with PDL, and, if we breach those representations or covenants, we may become subject to indemnification claims by SWK (assignee of PDL) and liable to SWK for its indemnifiable losses relating to such breaches. The amount of such losses could be material and could have a material adverse impact on our business.

We will be substantially dependent on Aguettant to successfully commercialize DZUVEO in Europe.

In June 2018, the EC granted marketing approval for DZUVEO and in July 2021 we entered into the DZUVEO Agreement with Aguettant to commercialize DZUVEO in Europe. We will be substantially dependent on Aguettant to successfully commercialize DZUVEO in Europe. Any failures in the commercialization of DZUVEO in Europe could have a significant adverse impact on our revenues and operating results.

The DZUVEO Agreement requires us to support the manufacturing and supply of DZUVEO for Aguettant. In addition, we anticipate we may need comparator studies in Europe to ensure premium reimbursement in certain countries. Our inability to profitably manufacture and supply DZUVEO to Aguettant, or to successfully complete these additional comparator studies and obtain premium reimbursement in certain countries, may prevent, limit or delay commercialization and any associated future revenues from DZUVEO in Europe.

We have limited experience commercializing DSUVIA, which may make it difficult to predict our future performance or evaluate our business and prospects.

Since inception, our operations have been primarily focused on developing our technology and undertaking pharmaceutical development and clinical trials for DSUVIA and Zalviso, understanding the market potential for DSUVIA and Zalviso, and preparing for the commercialization of DSUVIA and the potential commercialization of Zalviso in the United States. We launched commercialization efforts for DSUVIA in February 2019. As a result of our limited commercialization experience, any predictions that are made about our future performance, or viability, or evaluation of our business and prospects, may not be accurate.

We will require additional capital and may be unable to raise capital, which would force us to delay, reduce or eliminate our commercialization efforts and product development programs and could cause us to 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 ongoing commercialization activities for DSUVIA, manufacturing and supply activities for DZUVEO, and research and development activities for our product candidates, including the FDA regulatory review of the Zalviso NDA, once resubmitted. While we believe we have sufficient capital resources to continue planned operations for at least the next twelve months, we will need additional capital to pursue full commercialization of DSUVIA and our product candidates, if approved.

Clinical trials, regulatory reviews, and the launch of 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 Sales Agreement with Cantor, and debt securities, monetize or securitize certain assets including future royalty streams and milestones, refinance our loan agreement, obtain a revolving credit facility, enter into product development, license or distribution agreements with third parties, or divest DSUVIA, DZUVEO, Zalviso in Europe, or any of our product candidates. Such arrangements may not be available on favorable terms, if at all.

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 commercial launch of DSUVIA, or the development 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 commercialize DSUVIA or 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:

- significantly scale back or discontinue the commercialization of DSUVIA, or the development of our product candidates;
- seek additional corporate partners for Zalviso on terms that might be less favorable than might otherwise be available;
- seek corporate partners for DSUVIA/DZUVEO 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.

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. Our primary uses of cash include operating costs such as costs to fund commercial activities for our approved product, DSUVIA. Our future capital requirements may vary materially from those currently planned and will depend on many factors (see *Operating Capital and Capital Expenditure Requirements* for a description of such factors). Uses of cash also include our recent acquisition of Lowell, see Note 4. "Asset Acquisition" in the accompanying notes to the Condensed Consolidated Financial Statements. In order to raise additional funds to support our operations, we may sell additional equity securities, including under the Controlled Equity Offering℠ Sales Agreement, or the ATM Agreement, with Cantor Fitzgerald & Co., or Cantor, as agent. 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.

In addition, worsening economic conditions and other adverse effects or developments relating to the ongoing COVID-19 pandemic may negatively affect the market price of our stock, regardless of our actual operating performance. The market price for our common stock is likely to continue to be volatile, particularly due to the ongoing COVID-19 pandemic, and subject to significant price and volume fluctuations in response to market, industry and other factors. If additional funding is not available on favorable terms, if at all, due to these factors, we may not be able to obtain sufficient additional funding to support our operations.

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 March 31, 2022, we had approximately $11.4 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, commercial supplies of Zalviso in Europe, and clinical supplies of Zalviso in the United States, and will rely on third party manufacturers to produce DZUVEO for Aguettant and on Aguettant to produce commercial supplies of our product candidates, if approved, in the United States. 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.

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.

In addition, the DZUVEO Agreement requires us to manufacture and supply DZUVEO to Aguettant. As mentioned above, we were obligated to manufacture and supply Zalviso under the Grünenthal Agreements for use in Europe and their other licensed territories and will likely be required to do so under any New Arrangement. If we are unable to establish a reliable commercial supply of DZUVEO for Aguettant, and, if a New Arrangement is entered into, Zalviso for Europe, we may be unable to satisfy our obligations under the DZUVEO Agreement or any New Arrangement in a timely manner or at all, and we may, as a result, be in breach of such agreements. If any such breach, or other breach, were to be material and remain uncured, it could result in termination of the agreement, which in turn could, in the case of a New Arrangement, result in us being responsible for indemnification of losses suffered by SWK under the Royalty Monetization. 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 DSUVIA and Zalviso and any disruption in the chain of supply may cause a delay in supplying DSUVIA and Zalviso.

Currently we only have one supplier qualified as a vendor for the manufacture of DSUVIA, known as DZUVEO in Europe, and Zalviso with the FDA and EMA, respectively. If supply from the approved vendor is interrupted, there could be a significant disruption in commercial supply. Any alternate vendor would need to be qualified through an NDA supplement and/or an MAA variation which could result in delays. The FDA or other regulatory agencies outside of the United States may also require additional trials if a new sufentanil supplier is relied upon for commercial production.

Manufacture of sufentanil sublingual tablets requires specialized equipment and expertise.

Ethanol, which is used in the manufacturing process for our sufentanil sublingual tablets, is flammable, and sufentanil is a highly potent, Schedule II controlled substance. These factors necessitate the use of specialized equipment and facilities for manufacture of sufentanil sublingual tablets. There are a limited number of facilities that can accommodate our manufacturing process and we or our partners need to use dedicated equipment throughout development and commercial manufacturing to avoid the possibility of cross-contamination. If our or our partners' equipment breaks down or needs to be repaired or replaced, it may cause significant disruption in clinical or commercial supply, which could result in delay in the process of obtaining approval for or sale of our products. Furthermore, we are using one manufacturer to produce our sufentanil sublingual tablets. Any problems with our or our partners' facilities or equipment may impair our ability to successfully commercialize DSUVIA or Zalviso, if approved, and to complete our clinical trials, and increase our cost.

Manufacturing issues may arise that could delay or increase costs related to commercialization, 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 DSUVIA single-dose applicator, or SDA, and Zalviso devices for the commercial marketplace. We currently outsource manufacturing and packaging of the DSUVIA SDA and the controller, dispenser and cartridge components of the Zalviso device to third parties and intend to continue to do so. Some of 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 of DSUVIA, DZUVEO or Zalviso devices with each of the third-party manufacturers or may be unable to do so on acceptable terms. In addition, we have encountered and may continue to 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 including scale-up and automating processes, which could adversely impact our ability to supply our customers with DSUVIA, Zalviso and DZUVEO in Europe, and, if approved, Zalviso in the U.S. and any other foreign territories.

As we scale up manufacturing of DSUVIA and Zalviso, if approved, 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 DSUVIA, increased scrutiny by regulatory agencies, delays in clinical program and regulatory approval, increases in our operating expenses, or failure to obtain approval for our product candidates in the United States.

We have built out a suite within our CMO's production facility in Cincinnati, Ohio that serves as a manufacturing facility for clinical and commercial supplies of sufentanil sublingual tablets. Late-stage development and manufacture of registration stability lots, which were utilized in clinical trials, were manufactured at this location. While we produced a number of commercial lots to support Grünenthal's launch in Europe, our experience is limited, which impacted our ability to deliver commercial supplies to Grünenthal on a timely basis, and may in the future impact our ability to deliver commercial supplies under any New Arrangement, if required, on a timely basis.

In January 2013, we entered into an agreement with a CMO to manufacture, supply, and provide certain validation and stability services with respect to Zalviso for potential sales in the United States, Canada, Mexico and other countries, subject to agreement by the parties to any additional fees for such other countries. On August 22, 2017, we entered into an amendment to this agreement to manufacture, supply, and provide certain validation and stability services with respect to DSUVIA for sales in the United States, and potential sales in Canada and Mexico, and other countries. There is no guarantee that our CMO's services will be satisfactory or that they will continue to meet the strict regulatory guidelines of the FDA or other foreign regulatory agencies. If our CMO cannot provide us with an adequate supply of sufentanil sublingual tablets, we may be required to pursue alternative sources of manufacturing capacity. Switching or adding commercial manufacturing capability can involve substantial cost and require extensive management time and focus, as well as additional regulatory filings which may result in significant delays. In addition, there is a natural transition period when a new manufacturing facility commences work. As a result, delays may occur, which can materially impact our ability to meet our desired commercial timelines, thereby increasing our costs and reducing our ability to generate revenue.

The facilities of any of our future manufacturers of sufentanil-containing sublingual tablets must be approved by the FDA or the relevant foreign regulatory agency, such as the EMA, before commercial distribution from such manufacturers occurs. We do not fully control the manufacturing process of sufentanil sublingual tablets 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 process. 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. Although European inspectors have approved our tablet manufacturing site, our third-party manufacturing partner is responsible for maintaining compliance with the relevant foreign regulatory agency's requirements. If the FDA or the relevant foreign regulatory agency does not approve these facilities for the commercial manufacture of sufentanil sublingual tablets, we will need to find alternative suppliers, which would result in significant delays in obtaining FDA approval for Zalviso, and other foreign regulatory agency approval of DSUVIA/DZUVEO and Zalviso outside Europe. 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 sufentanil-containing sublingual tablets or device manufacture. 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, or in ISO 13485 accredited facilities, and subject to ongoing inspections by regulatory agencies. Failure by any of our suppliers to comply with applicable regulations may result in delays and interruptions to our product supply while we seek to secure another supplier that meets all regulatory requirements. In addition, if we are unable to establish a reliable commercial supply of Zalviso for Europe, we may be unable to satisfy our obligations under any New Arrangement, if required, in a timely manner or at all, and we may, as a result, be in breach of any New Arrangement.

For DSUVIA, we currently package the finished goods under a manual process and would package DZUVEO in the same manner. The capacity and cost to package the goods under this manual process are not optimal to support successful future sales of DSUVIA and DZUVEO. We have purchased and installed an automated filling and packaging line to support increased capacity packaging for DSUVIA and DZUVEO. We have experienced delays to final implementation of our automated line due to the impact of COVID-19, in addition to testing requirements of our vendor. While we have now completed the acquisition and installation of this line; there can be no assurance that we will be able to successfully complete the qualification and validation of this line and obtain the necessary regulatory approvals to manufacture commercial product on this line. Due to the recent strains on the global supply chain, the lead time 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 rely on 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 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 DSUVIA and 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 Zalviso, 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

Failure to receive required quotas of controlled substances or comply with the Drug Enforcement Agency regulations, or the cost of compliance with these regulations, may adversely affect our business.

Our sufentanil-based products are subject to extensive regulation by the DEA, due to their status as scheduled drugs. Sufentanil is classified as a Schedule II controlled substance, considered to present a high risk of abuse. The manufacture, shipment, storage, sale and use of controlled substances are subject to a high degree of regulation, including security, record-keeping and reporting obligations enforced by the DEA and also by comparable state agencies. In addition, our contract manufacturers are required to maintain relevant licenses and registrations. This high degree of regulation can result in significant compliance costs, which may have an adverse effect on the commercialization of DSUVIA and the development and commercialization of Zalviso, if approved.

The DEA limits the availability and production of all Schedule II controlled substances, including sufentanil, through a quota system. The DEA requires substantial evidence and documentation of expected legitimate medical and scientific needs before assigning quotas to manufacturers. Our contract manufacturers apply for quotas on our behalf. We will need significantly greater amounts of sufentanil to successfully commercialize DSUVIA, to support European commercialization of DZUVEO and Zalviso, and to commercialize Zalviso, if approved in the United States. Any delay by the DEA in establishing the procurement quota, reduction in our quota for sufentanil, failure to increase our quota over time to meet anticipated increases in demand, or refusal by the DEA to establish the procurement quota could delay or stop the commercial sale of our approved products or the clinical development of Zalviso in the United States. This, in turn, could have a material adverse effect on our business, results of operations, financial condition and prospects.

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 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.

In order to supply the Zalviso device to any future collaborator for commercial sales in Europe, we must maintain conformity of our quality system to applicable ISO standards and must comply with applicable European laws and directives.

We underwent a Conformité Européenne approval process for the Zalviso device, more commonly known as a CE Mark approval process. We received CE Mark approval in December 2014, which permits the commercial sale of the Zalviso device in Europe. In connection with the CE Mark approval, we were also granted International Standards Organization, or ISO, 13485:2003 certification of our quality management system in November 2014. This is an internationally recognized quality standard for medical devices. The CE Mark was originally issued by the British Standards Institution, or BSI, a Notified Body, or NB, located in the United Kingdom, or U.K., or BSI-U.K. The CE Mark file and certification has been transferred to the Netherlands NB of BSI, or BSI-NL, to mitigate the uncertainty with regards to Brexit. The ISO certification issued through BSI-U.K. was recently upgraded to the latest version of the standard, ISO 13485:2016 through BSI-U.K. and remains in effect. BSI ISO 13485:2016 certification recognizes that consistent quality policies and procedures are in place for the development, design and manufacturing of medical devices. The certification indicates that we have successfully implemented a quality system that conforms to ISO 13485 standards for medical devices. Certification to this standard is one of the key regulatory requirements for a CE Mark in the EU and European Economic Area (which includes the 27 EU member states as well as Norway, Iceland and Liechtenstein), or EEA, as well as to meet equivalent requirements in other international markets. The certification applies to the Hayward, California location which designs, manufactures and distributes finished medical devices, and includes critical suppliers. If we fail to remain in compliance with applicable European laws and directives, we would be unable to continue to affix the CE Mark to our Zalviso device, which would prevent any future collaboration partner from selling these devices within the EU and EEA.

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 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. 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 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.

The financial results of the combined company may be adversely affected by cash expenses and non-cash accounting charges incurred in connection with our integration of the business and operations of Lowell. The amount and timing of these possible charges are not yet known. Further, 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. The price of our common stock could decline to the extent the combined company's financial results are materially affected by any of these events.

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.

Commercial sales of DSUVIA and Zalviso 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.

Our insurance coverage included the sale of Zalviso to our former commercial partner, Grünenthal, and will likely include the sale of Zalviso by any future commercial partner. We intend to commercialize and promote DZUVEO in Europe with a strategic partner which may result in further expansion of our insurance coverage to include sales of DZUVEO in Europe. 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 March 31, 2022, we are the owner of record of 92 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, Zalviso, 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.

As we continue to develop our product candidates ephedrine, phenylephrine, Niyad and LTX-608, we expect to pursue 505(b)(2) NDA application pathways since all of the base pharmacological agents are not new chemical entities. As a result of this filing avenue, we will need to include patent certifications regarding the reference listed drugs that our 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 trademarks, or misappropriating other third-party intellectual property. Although we are not currently aware of litigation or other proceedings or third-party claims of intellectual property infringement related to DSUVIA or Zalviso, 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 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 ability to commercialize DSUVIA, DZUVEO and Zalviso in Europe or any of our ephedrine, 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 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. In early 2014, the FDA accepted the Zalviso mark and, in November 2018, the FDA accepted the DSUVIA mark. 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.

Risks Related to Ownership of Our Common Stock

The market price of our common stock may 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 $0.61 and $0.28 during the first quarter of 2022, and between $0.49 and $2.77 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 successfully commercialize DSUVIA in the United States 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;
- further delays in resubmitting the NDA for Zalviso, and any additional adverse developments or perceived adverse developments with respect to the FDA's review of the Zalviso NDA, upon resubmission;
- inability to enter into, or unfavorable terms associated with, a New Arrangement for the commercialization of Zalviso in Europe;
- 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 approvals for DZUVEO and Zalviso in the European Union, including ISO 13485 certification and CE Mark approval for Zalviso;
- 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; 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.

Our common stock may be delisted from The Nasdaq Global Market if we cannot regain compliance with Nasdaq's continued listing requirements.

In order to maintain our listing on Nasdaq, we are required to comply with the Nasdaq requirements, which includes maintaining a minimum bid price and a minimum public float. In particular, we are required to maintain a minimum bid price of $1.00 per share. On December 2, 2021, we received a notice from Nasdaq stating that we were not in compliance with Nasdaq Listing Rule 5450(a)(1) (the "Minimum Bid Price Rule") because our common stock failed to maintain a minimum closing bid price of $1.00 for 30 consecutive business days. This notice had no immediate effect on the Nasdaq listing or trading of our common stock.

We have a compliance period for the Minimum Bid Price Rule of 180 calendar days, or until May 31, 2022, in which to regain compliance, pursuant to Nasdaq Marketplace Rule 5810(c)(3)(A). If, at any time before that date the bid price of our common stock closes at $1.00 per share or more for a minimum of 10 consecutive business days, Nasdaq will notify us that we have achieved compliance with the Rule.

If we do not achieve compliance with the Minimum Bid Price Rule during the initial 180 calendar day period, we may be eligible for an additional 180 calendar day compliance period. To qualify, we would need to transfer the listing of our common stock to the Nasdaq Capital Market, provided that it meets the continued listing requirement for market value of publicly held shares and all other initial listing standards of the Nasdaq Capital Market, with the exception of the Minimum Bid Price Rule. In addition, the Company would also be required to notify Nasdaq of its intent to cure the minimum bid price deficiency, which may include, if necessary, implementing a reverse stock split. However, if it appears to Nasdaq that we will not be able to cure the deficiency, or if we do not meet the other listing standards, Nasdaq could provide notice that the common stock will become subject to delisting. In the event we receive notice that our common stock is being delisted, Nasdaq rules permit us to appeal any delisting determination by Nasdaq to a Hearings Panel (the "Panel"). We expect that our common stock would remain listed pending the Panel's decision. However, there can be no assurance that, if we do appeal the delisting determination by Nasdaq to the Panel, that such appeal would be successful, or that we will be able to regain compliance with the Minimum Bid Price Rule or maintain compliance with the other listing requirements.

If we fail to effect a reverse stock split, thus regaining compliance with the Minimum Bid Price Rule, our common stock may be delisted. Delisting from the Nasdaq Global Market or any Nasdaq market could make trading our common stock more difficult for investors, potentially leading to declines in our share price and liquidity. In addition, without a Nasdaq market listing, stockholders may have a difficult time getting a quote for the sale or purchase of our common stock, the sale or purchase of our common stock would likely be made more difficult and the trading volume and liquidity of our common stock could decline. Delisting from Nasdaq could also result in negative publicity and could also make it more difficult for us to raise additional capital. The absence of such a listing may adversely affect the acceptance of our common stock as currency or the value accorded by other parties. Further, if we are delisted, we would also incur additional costs under state blue sky laws in connection with any sales of our securities. These requirements could severely limit the market liquidity of our common stock and the ability of our stockholders to sell our common stock in the secondary market. If our common stock is delisted by Nasdaq, our common stock may be eligible to trade on an over-the-counter quotation system, such as the OTCQB market, where an investor may find it more difficult to sell our common stock or obtain accurate quotations as to the market value of our common stock. We cannot assure you that our common stock, if delisted from Nasdaq, will be listed on another national securities exchange or quoted on an over-the counter quotation system. If our common stock is delisted, it may come within the definition of "penny stock" as defined in the Exchange Act, and would be covered by Rule 15g-9 of the Exchange Act. That Rule imposes additional sales practice requirements on broker-dealers who sell securities to persons other than established customers and accredited investors. For transactions covered by Rule 15g-9, the broker-dealer must make a special suitability determination for the purchaser and receive the purchaser's written agreement to the transaction prior to the sale. Consequently, Rule 15g-9, if it were to become applicable, would affect the ability or willingness of broker-dealers to sell our securities, and accordingly would affect the ability of stockholders to sell their securities in the public market. These additional procedures could also limit our ability to raise additional capital in the future.

Sales of a substantial number of shares of our common stock in the public market by 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 $54.5 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. We may also issue 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.

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 9 to the Condensed Consolidated Financial Statements in this Quarterly Report on Form 10-Q 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 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 Note 9 to the Condensed Consolidated Financial Statements in this Quarterly Report on Form 10-Q 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, 2021, we had federal net operating loss carryforwards of $308.5 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 $193.6 million generated after January 1, 2018 will carryforward indefinitely but are subject to the 80% taxable income limitation. As of December 31, 2021, we had state net operating loss carryforwards of $154.7 million, which begin to expire in 2028. 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. Federal net operating losses generated prior to 2018 will continue to be governed by the net operating loss tax rules as they existed prior to the adoption of the Tax Cuts and Jobs Act of 2017, or Tax Act, which means that generally they will expire 20 years after they were generated if not used prior thereto. Many states have similar laws. Accordingly, our federal and state net operating losses could expire unused and be unavailable to offset future income tax liabilities. Under the newly enacted Tax Act as modified by CARES Act, federal net operating losses incurred in tax years beginning after December 31, 2017 and before January 1, 2021 may be carried back to each of the five tax years preceding such loss, and federal net operating losses arising in tax years beginning after December 31, 2020 may not be carried back. Moreover, federal net operating losses generated in tax years ending after December 31, 2017 may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited to 80% of current year taxable income for tax years beginning after December 31, 2020.

In addition, under Section 382 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 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. In addition, since we will need to raise substantial additional funding to finance our operations, we may undergo further ownership changes in the future. In the future, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset United States federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us.

Our effective tax rate may fluctuate, and we may incur obligations in tax jurisdictions in excess of accrued amounts.

We are subject to taxation in numerous U.S. states and territories. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each of such places. Nevertheless, our effective tax rate may be different than experienced in the past due to numerous factors, including passage of the newly enacted federal income tax law, changes in the mix of our profitability from state to state, 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 changes in tax laws. 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.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds

On January 7, 2022, pursuant to the terms of the Merger Agreement, 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 (i) the issuance of 9,009,538 shares of common stock, issued at a five day daily volume weighted average price of $0.57284 per share, valued at $5.2 million on closing, (ii) the holding back of 1,396,557 shares of common stock to satisfy any potential indemnification and other obligations of Lowell and its securityholders valued at $0.8 million and (iii) the reservation of up to $26.0 million of contingent consideration, at the Company's option, payable in cash or shares of common stock, upon the achievement of regulatory and sales-based milestones. The shares issued pursuant to the Merger Agreement were issued in private placements pursuant to the exemption from registration under Section 4(a)(2) of 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. Please see the matters under the caption "Part I. Financial Information—Item 1. Financial Statements—Note 4. Asset Acquisition" under the notes to the "Condensed Consolidated Financial Statements (unaudited)".

Item 3. Defaults Upon Senior Securities

None.

Item 4. Mine Safety Disclosures

Not applicable.

Item 5. Other Information

None.

Item 6. Exhibits

Exhibit Number	Exhibit Description	Incorporation By Reference			
		Form	SEC File No.	Exhibit	Filing Date
3.1	Amended and Restated Certificate of Incorporation of the Registrant.	8-K	001-35068	3.1	02/18/2011
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	Amended and Restated Bylaws of the Registrant.	S-1	333-170594	3.4	01/07/2011
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 and Accounting 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	Inline 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).				

* The certifications attached as Exhibit 32.1 accompany this Quarterly Report on Form 10-Q 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.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Date: May 16, 2022

AcelRx Pharmaceuticals, Inc.
(Registrant)

/s/ Raffi Asadorian

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

Exhibit 31.1

CERTIFICATION

I, Vincent J. Angotti, certify that:

1. I have reviewed this quarterly report on Form 10-Q 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: May 16, 2022

/s/ Vincent J. Angotti
Vincent J. Angotti
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

I, Raffi Asadorian, certify that:

1. I have reviewed this quarterly report on Form 10-Q 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: May 16, 2022

/s/ Raffi Asadorian
Raffi Asadorian
Chief Financial Officer
(Principal Financial and Accounting 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 knowledge:

1. The Company's Quarterly Report on Form 10-Q for the period ended March 31, 2022, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report") fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act, and

2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

In Witness Whereof, the undersigned has set his hands hereto as of the 16th day of May 2022.

/s/ Vincent J. Angotti
Vincent J. Angotti
Chief Executive Officer

/s/ Raffi Asadorian
Raffi Asadorian
Chief Financial Officer

This certification accompanies the Form 10-Q 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-Q), irrespective of any general incorporation language contained in such filing.