

**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**  
**WASHINGTON, DC 20549**

**FORM 10-Q**

(Mark One)

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

For the quarterly period ended **September 30, 2021**

OR

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

For the transition period from \_\_\_\_\_ to \_\_\_\_\_

Commission File Number: **001-38268**

**ALLENA PHARMACEUTICALS, INC.**

(Exact Name of Registrant as Specified in its Charter)

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

**Delaware**

(State or other jurisdiction of  
incorporation or organization)

**45-2729920**

(I.R.S. Employer  
Identification No.)

**One Newton Executive Park, Suite 202**

**Newton, Massachusetts**

(Address of principal executive offices)

**02462**

(Zip Code)

Registrant's telephone number, including area code: **(617) 467-4577**

Securities registered or to be registered pursuant to Section 12(b) of the Act.

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common Stock, par value \$0.001 per share	ALNA	The Nasdaq Global Select 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, 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  Small 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 Rule 12b-2 of the Exchange Act). Yes  No

As of November 5, 2021, the registrant had 82,571,078 shares of common stock, \$0.001 par value per share, outstanding.

## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements. These statements include all matters that are not related to present facts or current conditions or that are not historical facts, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth. The words “anticipate,” “believe,” “could,” “continue,” “should,” “predict,” “estimate,” “expect,” “intend,” “may,” “plan,” “potentially,” “will,” “may,” “would,” or the negative of these terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements.

We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions described in the section titled “Risk Factors” and elsewhere in this Quarterly Report on Form 10-Q, regarding, among other things:

- our estimates and expectations regarding our capital requirements, cash and expense levels, liquidity sources and our need for additional financing;
  - the design and conduct of our planned Phase 3 clinical program of reloxaliase (formerly ALLN-177) in enteric hyperoxaluria, including the timing and outcome of our planned interim analyses;
  - our ability to utilize the accelerated approval regulatory pathway for reloxaliase, including the timing of any Biologic License Application, or BLA, submission utilizing the accelerated approval regulatory pathway;
  - the number, designs, results and timing of our clinical trials, including our pivotal Phase 3 program for reloxaliase, our Phase 2 program for ALLN-346 and our preclinical studies and the timing of the availability of data from these trials and studies;
  - our ability to enroll a sufficient number of patients (including as a result of any delays arising from the recent global outbreak of the coronavirus, or the COVID-19 coronavirus, which originated in Wuhan, China) and the ability of subjects in our clinical trials to adhere to the protocol, including capsule and dietary regimen and urinary collection requirements;
  - the therapeutic benefits, effectiveness and safety of reloxaliase, ALLN-346 and our future product candidates;
  - our ability to receive regulatory approval for our product candidates in the United States, Europe and other geographies;
  - our expected regulatory approval pathway, and our ability to obtain, on satisfactory terms or at all, the financing required to support operations, development, clinical trials, and commercialization of products;
  - our reliance on third parties for the planning, conduct and monitoring of clinical trials and for the manufacture of clinical drug supplies and drug product;
  - potential changes in regulatory requirements, and delays or negative outcomes from the regulatory approval process;
  - our estimates of the size and characteristics of the markets that may be addressed by reloxaliase and ALLN-346;
  - the market acceptance of reloxaliase, ALLN-346 or any future product candidates that are approved for marketing in the United States or other countries;
  - our ability to successfully commercialize reloxaliase with a targeted sales force, if approved;
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- the safety and efficacy of therapeutics marketed by our competitors that are targeted to indications which our product candidates have been developed to treat;
- the impact of natural disasters, global pandemics (including the recent outbreak of a novel strain of the COVID-19 coronavirus), labor disputes, lack of raw material supply, issues with facilities and equipment or other forms of disruption to business operations at our manufacturing facilities;
- our ability to utilize our proprietary technological approach to develop and commercialize ALLN-346 and future product candidates;
- potential collaborators to license and commercialize reloxaliase, if approved, or any products for which we receive regulatory approval in the future outside of the United States;
- our heavy dependence on licensed intellectual property, including our ability to source and maintain licenses from third-party owners;
- our ability to protect our intellectual property and operate our business without infringing upon the intellectual property rights of others;
- our ability to attract, retain and motivate key personnel; and
- our ability to generate revenue and become profitable.

These risks are not exhaustive. Other sections of this Quarterly Report on Form 10-Q may include additional factors that could adversely impact our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements.

We have included important factors in the cautionary statements included in this Quarterly Report on Form 10-Q, particularly in the “Risk Factors” section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make. No forward-looking statement is a guarantee of future performance.

You should read this Quarterly Report on Form 10-Q and the documents that we reference in this Quarterly Report on Form 10-Q and have filed as exhibits to the registration statement of which this Quarterly Report on Form 10-Q is a part completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements in this Quarterly Report on Form 10-Q represent our views as of the date of this Quarterly Report on Form 10-Q. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Quarterly Report on Form 10-Q.

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PART I—FINANCIAL INFORMATION

Item 1. Financial Statements.

**Allena Pharmaceuticals, Inc.**  
**Condensed Consolidated Balance Sheets**  
**(unaudited)**  
**(in thousands, except share and per share data)**

	September 30, 2021	December 31, 2020
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 40,421	\$ 35,042
Prepaid expenses and other current assets	1,533	2,207
Total current assets	41,954	37,249
Property and equipment, net	1,270	881
Operating lease assets	518	678
Other assets	128	123
Total assets	<u>\$ 43,870</u>	<u>\$ 38,931</u>
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 3,027	\$ 2,410
Accrued expenses and other current liabilities	4,346	3,421
Operating lease liabilities, net of discount	300	291
Total current liabilities	7,673	6,122
Loan payable, net of current portion and discount	9,893	9,853
Operating lease liabilities, net of current portion	274	387
Total liabilities	17,840	16,362
Commitments and contingencies (Note 6)		
Stockholders' equity:		
Undesignated preferred stock, \$0.001 par value; 5,000,000 shares authorized; no shares issued or outstanding	—	—
Common stock, \$0.001 par value; 200,000,000 and 125,000,000 shares authorized at September 30, 2021 and December 31, 2020, respectively; 80,140,728 and 50,821,361 shares issued and outstanding at September 30, 2021 and December 31, 2020, respectively	80	51
Additional paid-in capital	262,039	220,307
Accumulated deficit	(236,089)	(197,789)
Total stockholders' equity	26,030	22,569
Total liabilities and stockholders' equity	<u>\$ 43,870</u>	<u>\$ 38,931</u>

*See accompanying notes.*

**Allena Pharmaceuticals, Inc.**  
**Condensed Consolidated Statements of Operations and Comprehensive Loss**  
**(unaudited)**  
**(in thousands, except share and per share data)**

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Operating expenses:				
Research and development	\$ 9,024	\$ 4,952	\$ 26,966	\$ 13,406
General and administrative	3,407	2,966	10,562	8,595
Total operating expenses	<u>12,431</u>	<u>7,918</u>	<u>37,528</u>	<u>22,001</u>
Loss from operations	(12,431)	(7,918)	(37,528)	(22,001)
Other expense:				
Interest expense, net	(250)	(104)	(738)	(261)
Other expense, net	(11)	(4)	(34)	(325)
Other expense, net	<u>(261)</u>	<u>(108)</u>	<u>(772)</u>	<u>(586)</u>
Net loss	<u>\$ (12,692)</u>	<u>\$ (8,026)</u>	<u>\$ (38,300)</u>	<u>\$ (22,587)</u>
Net loss per share attributable to common stockholders— basic and diluted	<u>\$ (0.17)</u>	<u>\$ (0.22)</u>	<u>\$ (0.61)</u>	<u>\$ (0.77)</u>
Weighted-average common shares outstanding— basic and diluted	<u>76,658,487</u>	<u>36,260,973</u>	<u>63,283,268</u>	<u>29,317,787</u>
Net loss	<u>\$ (12,692)</u>	<u>\$ (8,026)</u>	<u>\$ (38,300)</u>	<u>\$ (22,587)</u>
Comprehensive loss	<u>\$ (12,692)</u>	<u>\$ (8,026)</u>	<u>\$ (38,300)</u>	<u>\$ (22,587)</u>

*See accompanying notes.*

**Allena Pharmaceuticals, Inc.**  
**Condensed Consolidated Statements of Stockholders' Equity**  
**(unaudited)**  
**(in thousands, except share amounts)**

*Three Months Ended September 30,*

	Common stock		Additional paid-in capital	Accumulated deficit	Total stockholders' equity
	Shares	Amount			
<b>Balance at June 30, 2020</b>	32,224,734	\$ 32	\$ 197,846	\$ (179,505)	\$ 18,373
Issuance of common stock, net of issuance costs	5,894,191	6	6,723	—	6,729
Stock-based compensation	—	—	1,103	—	1,103
Net loss	—	—	—	(8,026)	(8,026)
<b>Balance at September 30, 2020</b>	<u>38,118,925</u>	<u>\$ 38</u>	<u>\$ 205,672</u>	<u>\$ (187,531)</u>	<u>\$ 18,179</u>
<b>Balance at June 30, 2021</b>	58,782,984	\$ 59	\$ 235,605	\$ (223,397)	\$ 12,267
Issuance of common stock and accompanying warrants, net of issuance costs	21,357,744	21	25,399	—	25,420
Stock-based compensation	—	—	1,035	—	1,035
Net loss	—	—	—	(12,692)	(12,692)
<b>Balance at September 30, 2021</b>	<u>80,140,728</u>	<u>\$ 80</u>	<u>\$ 262,039</u>	<u>\$ (236,089)</u>	<u>\$ 26,030</u>

*See accompanying notes*

**Allena Pharmaceuticals, Inc.**  
**Condensed Consolidated Statements of Stockholders' Equity**  
**(unaudited)**  
**(in thousands, except share amounts)**

*Nine Months Ended September 30,*

	Common stock		Additional paid-in capital	Accumulated deficit	Total stockholders' equity
	Shares	Amount			
<b>Balance at December 31, 2019</b>	24,735,009	\$ 25	\$ 182,117	\$ (164,944)	\$ 17,198
Issuance of common stock, net of issuance costs	13,211,265	13	20,374	—	20,387
Exercise of common stock options	11,928	—	18	—	18
Issuance of common stock through employee stock purchase plan ("ESPP")	20,003	—	27	—	27
Issuance of common stock through release of restricted stock units ("RSUs")	140,720	—	—	—	—
Stock-based compensation	—	—	3,136	—	3,136
Net loss	—	—	—	(22,587)	(22,587)
<b>Balance at September 30, 2020</b>	<b>38,118,925</b>	<b>\$ 38</b>	<b>\$ 205,672</b>	<b>\$ (187,531)</b>	<b>\$ 18,179</b>
<b>Balance at December 31, 2020</b>	50,821,361	\$ 51	\$ 220,307	\$ (197,789)	\$ 22,569
Issuance of common stock and accompanying warrants, net of issuance costs	29,067,050	29	38,865	—	38,894
Issuance of common stock through employee stock purchase plan ("ESPP")	4,206	—	5	—	5
Issuance of common stock through release of restricted stock units ("RSUs")	248,111	—	—	—	—
Stock-based compensation	—	—	2,862	—	2,862
Net loss	—	—	—	(38,300)	(38,300)
<b>Balance at September 30, 2021</b>	<b>80,140,728</b>	<b>\$ 80</b>	<b>\$ 262,039</b>	<b>\$ (236,089)</b>	<b>\$ 26,030</b>

*See accompanying notes.*



**Allena Pharmaceuticals, Inc.**  
**Condensed Consolidated Statements of Cash Flows**  
**(unaudited)**  
**(in thousands)**

	Nine Months Ended September 30,	
	2021	2020
<b>Cash flows from operating activities:</b>		
Net loss	\$ (38,300)	\$ (22,587)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	2,862	3,136
Depreciation expense	241	123
Non-cash interest expense	40	20
Non-cash lease expense	281	401
Loss on sale of equipment	9	—
Changes in assets and liabilities:		
Prepaid expenses and other current assets	674	1,846
Other assets	(5)	(50)
Accounts payable	623	(1,920)
Accrued expenses	925	(937)
Operating lease liabilities	(225)	(361)
Net cash used in operating activities	(32,875)	(20,329)
<b>Cash flows from investing activities:</b>		
Purchases of property and equipment	(642)	—
Net cash used in investing activities	(642)	—
<b>Cash flows from financing activities:</b>		
Proceeds from the issuance of common stock and common stock warrants, net of issuance costs	38,891	20,437
Proceeds from exercise of stock options	—	18
Proceeds from the issuance of stock through ESPP	5	27
Proceeds of loan payable	—	10,000
Repayment of loan payable	—	(10,000)
Other	—	(24)
Net cash provided by financing activities	38,896	20,458
Net increase in cash and cash equivalents	5,379	129
Cash and cash equivalents, beginning of period	35,042	30,007
Cash and cash equivalents, end of period	\$ 40,421	\$ 30,136
<b>Supplemental disclosures:</b>		
Property and equipment purchases included in accounts payable	\$ —	\$ 36
Common stock issuance costs included in accounts payable	\$ —	\$ 50
Debt issuance costs included in accrued expenses	\$ 3	\$ 172

*See accompanying notes.*

**Allena Pharmaceuticals, Inc.**  
**Notes to Condensed Consolidated Financial Statements**  
**(Unaudited)**  
**(in thousands, except share and per share data)**

**1. Nature of Business**

Allena Pharmaceuticals, Inc. (the "Company") is a late-stage clinical biopharmaceutical company dedicated to discovering, developing and commercializing first-in-class, oral biological therapeutics to treat patients with rare and severe metabolic and kidney disorders. The Company's lead product candidate, reloxaliase (formerly known as ALLN-177), is currently being evaluated in a pivotal Phase 3 clinical program for the treatment of enteric hyperoxaluria, a metabolic disorder characterized by markedly elevated urinary oxalate levels and commonly associated with kidney stones, chronic kidney disease ("CKD") and other serious kidney disorders. There are currently no approved therapies for the treatment of enteric hyperoxaluria. The Company is also developing ALLN-346 for the treatment of hyperuricemia and gout in the setting of advanced CKD. The Company completed a Phase 1b multiple-ascending dose study in the second quarter of 2021 and recently initiated dosing in two Phase 2a studies. The Company was incorporated under the laws of the State of Delaware on June 24, 2011 and is located in Newton, Massachusetts.

The Company is subject to risks common to companies in the biotechnology industry, including but not limited to, risks of failure of preclinical studies and clinical trials, the need to obtain marketing approval for any drug product candidate that it may identify and develop, the need to successfully commercialize and gain market acceptance of its product candidates, dependence on key personnel, protection of proprietary technology, compliance with government regulations, development by competitors of technological innovations, reliance on third party manufacturers, ability to transition from pilot-scale manufacturing to large-scale production of products and the need to obtain adequate additional financing to fund the development of its product candidates.

***Liquidity and Going Concern***

The Company had an accumulated deficit of \$236.1 million at September 30, 2021 and will require substantial additional capital to fund operations. The future success of the Company is dependent on its ability to identify and develop its product candidates and ultimately upon its ability to attain profitable operations. At September 30, 2021, the Company had \$40.4 million of cash and cash equivalents.

On July 16, 2021, the Company completed a registered direct offering, in which the Company issued and sold 17,416,096 shares of its common stock, pre-funded warrants ("Pre-funded Warrants") to purchase up to an aggregate of 3,941,648 shares of its common stock in lieu of shares of common stock, and warrants ("Warrants") to purchase up to 10,678,872 shares of the Company's common stock through a securities purchase agreement with several healthcare-focused institutional and accredited investors. The combined price of each share of common stock and accompanying Warrant to purchase one-half of a share of common stock was \$1.311 per share. The purchase price of each Pre-funded Warrant was \$1.301, which was the combined purchase price per share of common stock and accompanying Warrant to purchase one-half of a share of common stock, minus \$0.01. Gross proceeds of the transaction were \$28.0 million. As a result of the registered direct offering, the Company received approximately \$25.4 million after deducting offering costs. Each Warrant is exercisable for one share of the Company's common stock at an exercise price of \$1.25 per share. The Warrants are immediately exercisable and expire on July 16, 2026. Each Pre-funded Warrant is exercisable for one share of our Common Stock at an exercise price of \$0.01 per share. All Pre-funded Warrants were exercised on July 16, 2021.

The Company entered into an At Market Issuance Sales Agreement with B. Riley Securities, Inc. ("B. Riley ATM Agreement") on March 29, 2021. During the second quarter of 2021, the Company issued and sold 1,650,988 shares of its common stock under the B. Riley ATM Agreement at a weighted average price of \$1.25 per share for net proceeds of approximately \$1.8 million. During the fourth quarter of 2021 through the filing date of this Quarterly Report, the Company issued and sold 2,430,350 shares of its common stock under the B. Riley ATM Agreement at a weighted average price of \$1.02 per share for net proceeds of \$2.4 million.

During the first quarter of 2021, the Company issued and sold 6,058,318 shares of its common stock under an At-the Market Equity Offering Sales Agreement with Cowen and Company, LLC ("Cowen ATM Agreement") at a weighted average price of \$1.99 per share for net proceeds of \$11.7 million. The Cowen ATM Agreement was terminated at the time the Company entered into the B. Riley ATM Agreement.

The Company's available cash and cash equivalents as of September 30, 2021 are not sufficient to fund the Company's current operating plan for at least the next twelve months following the filing of this Quarterly Report. The Company requires additional capital to sustain its operations, including its reloxaliase and ALLN-346 development program. Management is exploring opportunities to secure additional funding through equity or debt financings or through collaborations, licensing transactions or other sources. The Company may be unable to obtain equity or debt financings or enter into collaboration or

licensing transactions. Market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact the Company's ability to access capital as and when needed. If the Company is unable to raise capital when needed or on attractive terms, it may decide to delay, reduce or eliminate its research and development programs or future commercialization efforts and its ability to continue operations will be jeopardized. These factors raise substantial doubt about the Company's ability to continue as a going concern as of the filing date of this Quarterly Report. The Company may implement cost reduction strategies, which may include amending, delaying, limiting, reducing, or terminating one or more of its ongoing or planned clinical trials or development programs of its product candidates. The accompanying condensed consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the ordinary course of business. The consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of this uncertainty.

## 2. Summary of Significant Accounting Policies

### *Basis of Presentation*

The Company's unaudited interim condensed consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States ("U.S. GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB"). Certain information and footnote disclosures normally included in financial statements prepared in accordance with U.S. GAAP have been condensed or omitted from this report, as is permitted by such rules and regulations. Accordingly, these financial statements should be read in conjunction with the audited financial statements as of and for the year ended December 31, 2020 and notes thereto, included in the Company's Annual Report on Form 10-K for the year ended December 31, 2020 filed with the SEC on March 11, 2021. The unaudited interim consolidated financial statements have been prepared on the same basis as the audited financial statements. In the opinion of the Company's management, the accompanying unaudited interim condensed consolidated financial statements contain all adjustments which are necessary to present fairly the Company's financial position as of September 30, 2021, the results of its operations for the three and nine months ended September 30, 2021 and September 30, 2020 and cash flows for the nine months ended September 30, 2021 and September 30, 2020. Such adjustments are of a normal and recurring nature. The results for the three and nine months ended September 30, 2021 are not necessarily indicative of the results for the year ending December 31, 2021, or for any future period.

### *Principles of Consolidation*

The consolidated financial statements include the accounts of Allena Pharmaceuticals, Inc. and its wholly owned subsidiaries, Allena Pharmaceuticals Security Corporation ("Security Corporation"), which was incorporated in December 2014, and Allena Pharmaceuticals Ireland Limited, which was incorporated in March 2017. All intercompany transactions and balances have been eliminated.

### *Fair Value of Financial Instruments*

Fair value is defined as the price that would be received upon sale of an asset or paid to transfer a liability between market participants at measurement dates. ASC Topic 820, *Fair Value Measurement* ("ASC 820"), establishes a three-level valuation hierarchy for instruments measured at fair value. The hierarchy is based on the transparency of inputs to the valuation of an asset or liability as of the measurement date. The hierarchy defines three levels of valuation inputs, of which the first two are considered observable and the last is considered unobservable:

- Level 1 inputs: Quoted prices in active markets for identical assets or liabilities.
- Level 2 inputs: Inputs other than quoted prices included within Level 1 that are either directly or indirectly observable, such as quoted market prices, interest rates and yield curves.
- Level 3 inputs: Unobservable inputs developed using estimates or assumptions developed by the Company, which reflect those that a market participant would use in pricing the asset or liability.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

## ***Use of Estimates***

The preparation of the Company's condensed consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, expenses and related disclosure of contingent assets and liabilities at the date of the financial statements and reported amounts of expenses during the reporting period. On an ongoing basis, the Company's management evaluates its estimates, which include, but are not limited to, management's judgment of prepaid and accrued research and development expenses and the valuation of share-based awards. Actual results could differ from those estimates.

The remainder of the Company's significant accounting policies are described in the Annual Report filed on Form 10-K for the year ended December 31, 2020 that was filed with the United States Securities and Exchange Commission on March 11, 2021.

## ***Warrants***

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

## ***Recently Adopted Accounting Pronouncements***

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* ("ASU 2019-12"), which is intended to simplify various aspects related to accounting for income taxes. The new guidance became effective for the Company on January 1, 2021. The adoption of ASU 2019-12 did not have a material impact on the Company's condensed consolidated financial statements.

## ***Recently Issued Accounting Pronouncements***

In 2016, the FASB issued ASU 2016-13, *Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"), which requires entities to record expected credit losses for certain financial instruments, including trade receivables, as an allowance that reflects the entity's current estimate of credit losses expected to be incurred. For available-for-sale debt securities in unrealized loss positions, ASU 2016-13 requires allowances to be recorded instead of reducing the amortized cost of the investment. ASU 2016-13 is effective for smaller reporting companies on January 1, 2023. Early adoption is permitted. The Company does not expect that the adoption of ASU 2016-13 will have a material impact on its condensed consolidated financial statements.

In 2020, the FASB issued ASU 2020-06, *Debt -Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging-Contracts in Entity's Own Equity (Subtopic 815-40)*, simplifies the accounting for convertible debt and convertible preferred stock by removing the requirements to separately present certain conversion features in equity. In addition, the amendments in the ASU also simplify the guidance in ASC 815-40, *Derivatives and Hedging: Contracts in Entity's Own Equity* ("ASU 2020-06"), by removing certain criteria that must be satisfied in order to classify a contract as equity, which is expected to decrease the number of freestanding instruments and embedded derivatives accounted for as assets or liabilities. Finally, the amendments revise the guidance on calculating earnings per share, requiring use of the if-converted method for all convertible instruments and rescinding an entity's ability to rebut the presumption of share settlement for instruments that may be settled in cash or other assets. ASU 2020-06 is effective for smaller reporting companies on January 1, 2022. Early adoption is permitted. The Company does not expect that the adoption of ASU 2020-06 will have a material impact on its condensed consolidated financial statements.

### 3. Net Loss per Share

Basic net loss per share is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of common shares outstanding for the period, without consideration for potentially dilutive securities. The Company has computed diluted net loss per common share after giving consideration to all potentially dilutive common shares, including options to purchase common stock, restricted stock units, common stock issuable upon the conversion of outstanding debt and warrants to purchase common stock, outstanding during the period determined using the treasury-stock and if-converted methods, except where the effect of including such securities would be antidilutive. Because the Company has reported net losses since inception, these potential common shares have been anti-dilutive and basic and diluted loss per share have been the same.

Basic and diluted net loss per share attributable to common stockholders was calculated as follows (in thousands, except share and per share data):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
<b>Numerator:</b>				
Net loss	\$ (12,692)	\$ (8,026)	\$ (38,300)	\$ (22,587)
Net loss attributable to common stockholders	\$ (12,692)	\$ (8,026)	\$ (38,300)	\$ (22,587)
<b>Denominator:</b>				
Weighted-average common shares—basic and diluted	76,658,487	36,260,973	63,283,268	29,317,787
Net loss per share attributable to common stockholders—basic and diluted	\$ (0.17)	\$ (0.22)	\$ (0.61)	\$ (0.77)

The following table sets forth the potentially dilutive securities that have been excluded from the calculation of diluted net loss per share because to include them would be anti-dilutive (in common stock equivalent shares):

	Nine Months Ended September 30,	
	2021	2020
Stock options	7,188,457	3,678,241
Restricted stock units	372,166	547,319
Warrants	10,687,912	9,040
Common stock issuable upon conversion of outstanding debt	2,439,024	2,439,024
Total	20,687,559	6,673,624

### 4. Fair Value Measurements

The following tables present information about the Company's financial assets and liabilities that have been measured at fair value at September 30, 2021 and December 31, 2020, and indicates the fair value hierarchy of the valuation inputs utilized to determine such fair value (in thousands):

Description	September 30, 2021	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
<b>Assets:</b>				
Money market funds, included in cash and cash equivalents	\$ 39,421	\$ 39,421	\$ —	\$ —
Total assets	\$ 39,421	\$ 39,421	\$ —	\$ —

Description	December 31, 2020	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
<b>Assets:</b>				
Money market funds, included in cash and cash equivalents	\$ 34,698	\$ 34,698	\$ —	\$ —
Total assets	<u>\$ 34,698</u>	<u>\$ 34,698</u>	<u>\$ —</u>	<u>\$ —</u>

At September 30, 2021 and December 31, 2020, substantially all of the Company's cash equivalents were comprised of money market funds.

There were no changes to the valuation methods during the three months ended September 30, 2021 and the year ended December 31, 2020. There were no transfers within the fair value hierarchy during the three and nine months ended September 30, 2021 and the year ended December 31, 2020.

The carrying amounts reflected in the consolidated balance sheets for cash and cash equivalents, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their carrying values. The Company believes the terms of the loan payable reflect current market conditions for an instrument with similar terms and maturity and therefore the carrying value of the Company's debt approximates its fair value based on Level 3 of the fair value hierarchy.

## 5. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	September 30, 2021	December 31, 2020
Payroll and employee-related expenses	\$ 2,137	\$ 1,945
Third-party research and development expenses	1,661	984
Professional fees	306	250
Loan interest	239	242
Other	3	—
Total accrued expenses	<u>\$ 4,346</u>	<u>\$ 3,421</u>

## 6. Commitments and Contingencies

The Company is a party to an operating lease for approximately 11,691 square feet of laboratory and office space in Sudbury, MA (Sudbury Lease). The Sudbury Lease expires on February 28, 2026. The Company has a one-time option to cancel the lease effective February 28, 2023 for any reason or no reason at all. Annualized base rent for the Sudbury Lease is approximately \$0.3 million.

Maturities of the Company's operating lease liabilities in accordance with ASC 842 as of September 30, 2021 are as follows (in thousands):

Remainder of 2021	\$ 75
2022	300
2023	227
Total maturities	602
Less: Amount representing interest	(28)
Present value of operating lease liabilities	<u>\$ 574</u>

Lease costs included in the Company's condensed consolidated statements of operations and comprehensive loss was \$0.1 million and \$0.3 million for the three and nine months ended September 30, 2021 and 2020, respectively. The Company's operating leases had a weighted average remaining lease term of 1.5 years and a weighted average discount rate of 5.5% at September 30, 2021.

The Company is also a party to an operating lease for approximately 6,055 square feet of office space in Newton, MA (Newton Lease). The Newton Lease terminates on the last day of the month following the month either party notifies the other that the term of the lease shall end. The annualized base rent for the Newton Lease is approximately \$0.3 million. Due to the

short nature of the minimum lease term of the Newton Lease, the Newton Lease was not considered as an operating lease liability in accordance with ASC 842 as of September 30, 2021 and December 31, 2020.

## 7. Loan and Security Agreement

On June 29, 2018, the Company entered into a loan agreement with Pacific Western Bank (“PWB Loan Agreement”) providing up to \$12.0 million of borrowings, of which \$10.0 million was advanced on June 29, 2018. The remaining \$2.0 million of borrowings were available to the Company through one additional advance request until December 31, 2019. Borrowings were secured by a lien on all Company assets, excluding intellectual property, and amounts borrowed had a floating per annum interest rate of the greater of 5.0% or the prime rate. The PWB Loan Agreement had a term of 48 months and an interest only period of 18 months. Upon the expiration of the interest only period on December 31, 2019, amounts borrowed were to be repaid over 30 equal monthly payments of principal plus accrued but unpaid interest. At its option, the Company could prepay all, but not less than all, of the outstanding borrowings subject to a prepayment premium as defined in the PWB Loan Agreement. Upon the closing of one or more financings in which the Company receives aggregate gross proceeds of at least \$25 million, a success fee of \$300,000 would be due and payable to PWB. As a result of the gross proceeds of \$15.0 million received from the registered direct offering completed on June 5, 2020, combined with \$10.0 million of gross proceeds received from the registered direct offering completed in June 2019, and \$2.7 million of gross proceeds received through the At-the-Market offering completed in December 2019, the conditions required to trigger the success fee were fulfilled and the success fee was paid to PWB at the time of the closing of the registered direct offering in June 2020. The success fee was recorded as other expense on the Company’s condensed consolidated statements of operations and comprehensive loss at the time the registered direct offering was completed.

On September 29, 2020, the Company terminated the PWB Loan Agreement and repaid the \$7.0 million outstanding principal to PWB. At the time the Company terminated the PWB Loan Agreement, the requirement to make a prepayment premium with respect to the Company prepaying the remaining outstanding borrowings under the PWB Loan Agreement had lapsed and no prepayment penalty payment was required upon termination of the PWB Loan Agreement.

## 8. Convertible Debt Agreement

On September 29, 2020, the Company entered into a loan and security agreement with Pontifax Medison Finance (Israel) L.P. and Pontifax Medison Finance (Cayman) L.P. (together “Pontifax”) (“Pontifax Agreement”) providing up to \$25.0 million of borrowings through three facilities of a term loan. An initial loan (“Initial Loan”) of \$10.0 million was advanced on September 29, 2020 (“Closing Date”). An additional \$5.0 million credit line (“Credit Line”) was available to the Company for withdrawal for a period of 12 months from the Closing Date. The Company paid a fee of 1.0% per annum to Pontifax for the daily average amount not withdrawn under the Credit Line. A third installment loan (“Third Installment Loan”) of \$10.0 million was conditioned upon achievement of one of the following milestones by no later than 15 months from the Closing Date: (i) the Company receives non-contingent, non-refundable gross proceeds from one or more equity financings and/or strategic partnerships, in each case consummated following the Closing Date, in the aggregate amount of at least \$15.0 million for all such equity financings and strategic partnerships or (ii) the 65<sup>th</sup> patient has been enrolled in the URIROX-2 trial. During the three months ended December 31, 2020, the additional \$10 million under the Third Installment Loan became available to the Company when the milestone of at least \$15 million of gross proceeds from equity financings was achieved. Upon withdrawal of the Third Installment Loan, the Company shall pay Pontifax a one-time fee of 1.0% of the Third Installment Loan. As of September 30, 2021, the Company had not withdrawn any amounts available under the Credit Line or the Third Installment Loan. The availability to withdraw amounts available under the Credit Line expired unused on September 29, 2021.

Amounts outstanding under the Pontifax Agreement have a fixed interest rate of 9.0% per annum. The Pontifax Agreement has a term of 48 months and an interest only period of 24 months. Upon the expiration of the interest only period on September 29, 2022, amounts borrowed will be repaid over eight equal quarterly payments of principal and interest. At its option, the Company may prepay all or part of the outstanding borrowings at any time without any prepayment premium or penalty.

The Pontifax Agreement contains negative covenants restricting the Company’s activities, including limitations on dispositions, mergers or acquisitions, incurring indebtedness or liens, paying dividends or making investments and certain other business transactions. There are no financial covenants associated with the Pontifax Agreement. The obligations under the Pontifax Agreement are subject to acceleration upon the occurrence of specified events of default, including a material adverse change in the Company’s business, operations or financial or other condition. The Company has determined that the risk of subjective acceleration under the material adverse events clause is remote and therefore has classified the outstanding principal based on scheduled principal payments.

Pontifax, at its option, has the right to convert at any time any portion of the then outstanding borrowings and all accrued but unpaid interest into shares of the Company’s common stock, at the applicable conversion price. The conversion

price for borrowings outstanding under the Pontifax Agreement is fixed at \$4.10 per share. If the Company consummates a stock split, stock combination, reclassification payment of stock dividend, recapitalization or other similar transaction (each a “Stock Event”), then the applicable conversion price will be proportionately increased or decreased as necessary to reflect the proportionate change in shares of the Company’s common stock issued and outstanding as a result of such Stock Event.

The Company has the right to convert at any time any portion of the then outstanding borrowings and all accrued but unpaid interest into shares of the Company’s common stock, at the applicable conversion price, subject to the fulfillment of both of the following conditions: (i) during a period of 30 consecutive trading days prior to the date on which the Company provides notice of the exercise of its conversion right, the closing price of the Company’s common stock was higher than 1.4 times the applicable conversion price of the term loans on at least 20 trading days, including on the trading day preceding the date on which the Company provides notice of the exercise of its conversion right, (ii) the number of shares of common stock issuable upon conversion by the Company shall not exceed the average weekly number of shares of the Company’s common stock traded on the stock market for the four weeks immediately preceding the date on which the Company provides notice of the exercise of its conversion right.

The shares of the Company’s common stock issued upon conversion will be free of any restrictions and the Company is required to hold at all times a sufficient number of authorized, unreserved and unissued shares of its common stock required to settle any such conversion. As of September 30, 2021, the Company has reserved 2,439,024 shares of its common stock for conversion of the outstanding debt balance.

The Company evaluated the Pontifax Agreement for embedded features that require bifurcation, noting certain features were required to be bifurcated, but were concluded to be de minimis in value at September 30, 2021 and December 31, 2020. The Company determined the conversion feature was not required to be accounted for separately. The Company concluded that the embedded conversion option is not subject to separate accounting pursuant to either the cash conversion guidance or the beneficial conversion feature guidance.

The minimum aggregate future loan and interest payments at September 30, 2021 are as follows (in thousands):

<b>Years Ending December 31,</b>	
2021	\$ 239
2022	1,927
2023	5,015
2024	4,880
Total minimum payments	\$ 12,061
Less: Amount representing interest	(2,061)
Less: Discount	(107)
Less: Current portion	—
Loan payable, net of current portion	<u>\$ 9,893</u>

## 9. Stockholders’ Equity

### *Common Stock*

During the first quarter of 2021, the Company issued and sold 6,058,318 shares of its common stock under the Cowen ATM Agreement at a weighted average price of \$1.99 per share for net proceeds of \$11.7 million.

During the second quarter of 2021, the Company issued and sold 1,650,988 shares of its common stock under the B. Riley ATM Agreement at a weighted average price of \$1.25 per share for net proceeds of \$1.8 million. During the fourth quarter of 2021 through the filing date of this Quarterly Report, the Company issued and sold 2,430,350 shares of its common stock under the B. Riley ATM Agreement at a weighted average price of \$1.02 per share for net proceeds of \$2.4 million.

On July 16, 2021, the Company completed a registered direct offering, in which the Company issued and sold 17,416,096 shares of its common stock, pre-funded warrants to purchase up to an aggregate of 3,941,648 shares of its common stock in lieu of shares of common stock and warrants to purchase up to 10,678,872 shares of the Company’s common stock through a securities purchase agreement. The combined price of each share of common stock and accompanying Warrant to purchase one-half of a share of common stock was \$1.311. The purchase price of each Pre-funded Warrant was \$1.301, which was the combined purchase price per share of common stock and accompanying Warrant, minus \$0.01. Gross proceeds of the transaction were \$28.0 million. As a result of the registered direct offering, the Company received approximately \$25.4 million after deducting estimated offering costs. Each Warrant is exercisable for one share of the Company’s common stock at an exercise price of \$1.25 per share. The Warrants are immediately exercisable and expire on July 16, 2026. Each Pre-funded Warrant is exercisable for one share of our common stock at an exercise price of \$0.01 per share. All Pre-Funded Warrants were exercised on July 16, 2021.



The holders of common stock are entitled to one vote for each share held. Common stockholders are not entitled to receive dividends, unless declared by the Board of Directors.

The Company has reserved for future issuances the following shares of common stock as of September 30, 2021 and December 31, 2020:

	September 30, 2021	December 31, 2020
Stock options and restricted stock units	8,744,479	5,359,736
Common stock issuable upon conversion of outstanding debt	2,439,024	2,439,024
Employee stock purchase plan	332,704	336,910
Warrants	10,687,912	9,040
<b>Total</b>	<b>22,204,119</b>	<b>8,144,710</b>

## 10. Stock Incentive Plan

On October 31, 2017, the Company adopted the 2017 Stock Option and Incentive Plan (“2017 Plan”). Upon the adoption of the 2017 Plan, no further grants would be made under the 2011 Stock Incentive Plan (“2011 Plan”). The 2017 Plan initially provided for the grant of awards for 2,038,021 shares of common stock. In addition to the shares available for grant under the 2017 Plan, shares underlying any awards outstanding under the 2011 Plan as of the October 31, 2017 that are cancelled, forfeited or otherwise terminated without being exercised will be available for future grant under the 2017 Plan. The 2017 Plan also provides that an additional number of shares will automatically be added to the shares authorized for issuance under the 2017 Plan on January 1 of each year. The number of shares added each year will be equal to the lesser of: (i) 4% of the outstanding shares on the immediately preceding December 31 or (ii) such amount as determined by the Compensation Committee of the Board of Directors. On January 1, 2019, 2020 and 2021, the shares available for grant under the 2017 Plan were automatically increased by 832,361, 989,400 and 2,032,854 shares, respectively.

All of the Company’s employees, officers, directors, consultants and advisors are eligible to be granted options, restricted stock units (“RSUs”), and other share-based awards under the terms of the 2017 Plan. As of September 30, 2021, 430,856 shares of common stock were available for future grant under the 2017 Plan.

On January 22, 2021, the Company adopted the 2021 Inducement Equity Plan (“2021 Plan”). The 2021 Plan provides for the grant of awards for 1,600,000 shares of common stock. The purpose of the 2021 plan is to enable the Company to grant equity awards to induce highly qualified prospective officers and employees who are not currently employed by the Company to accept employment and provide them with an equity interest in the Company. The Company is utilizing the 2021 Plan for awards the Company may make without stockholder approval as an inducement pursuant to Rule 5635(c)(4) of the Marketplace Rules of the Nasdaq Stock Market, Inc. As of September 30, 2021, 753,000 shares of common stock were available for future grant under the 2021 Plan.

All stock option grants are nonstatutory stock options except option grants to employees (including officers and directors) intended to qualify as incentive stock options under the Internal Revenue Code of 1986, as amended. Incentive stock options may not be granted at less than the fair market value of the Company’s common stock on the date of grant, as determined in good faith by the Board of Directors at its sole discretion. Nonqualified stock options may be granted at an exercise price established by the Board of Directors at its sole discretion (which has not been less than fair market value on the date of grant) and the vesting periods may vary. Vesting periods are generally four years and are determined by the Board of Directors or a delegated subcommittee. Stock options become exercisable as they vest. Options granted under both the 2011 Plan and 2017 Plan expire no more than 10 years from the date of grant.

Stock-based compensation expense included in the Company’s statements of operations and comprehensive loss is as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Research and development	\$ 329	\$ 337	\$ 879	\$ 1,046
General and administrative	706	766	1,983	2,090
<b>Total</b>	<b>\$ 1,035</b>	<b>\$ 1,103</b>	<b>\$ 2,862</b>	<b>\$ 3,136</b>

The fair value of each stock option granted to employees and directors during the three and nine months ended September 30, 2021 was estimated on the date of grant using the Black-Scholes option-pricing model, with the following range of assumptions:

	Three Months Ended September 30, 2021	Nine Months Ended September 30, 2021
Risk-free interest rate	0.7%-1.1%	0.4%-1.4%
Expected dividend yield	—%	—%
Expected term (in years)	5.5-7.0	5.0-7.0
Expected volatility	92%-95%	92%-95%

The Company did not grant any stock options during the three and nine months ended September 30, 2020. A summary of the stock option activity under the 2011, 2017 and 2021 Plans is as follows:

	Shares	Weighted- Average Exercise Price	Weighted- Average Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2020	4,110,691	\$ 3.89	7.3	\$ 124
Granted	3,341,350	1.87		
Exercised	—	—		
Cancelled	(263,584)	6.92		
Outstanding at September 30, 2021	<u>7,188,457</u>	\$ 2.84	7.9	\$ 24
Exercisable at September 30, 2021	<u>3,024,808</u>	\$ 3.68	6.2	\$ 24

As of September 30, 2021, total unrecognized stock-based compensation expense relating to unvested stock options was \$6.4 million. This amount is expected to be recognized over a weighted-average period of 2.6 years.

#### **Restricted Stock Units (RSUs)**

In December 2020, the Company awarded 620,277 RSUs to employees of the Company. 248,111 shares of common stock were issued on May 10, 2021 upon vesting of a portion of the RSUs. The remaining RSUs vest on November 10, 2021. The RSUs are generally forfeited if the employment relationship terminates with the Company prior to vesting. For the three and nine months ended September 30, 2021, the Company recognized \$0.2 million and \$0.6 million of stock-based compensation expense, respectively, related to these awards. As of September 30, 2021, the total remaining unrecognized compensation cost related to all unvested RSUs amounted to \$0.1 million, which is expected to be recognized during the remainder of 2021.

A summary of the status of nonvested RSUs as of September 30, 2021 and the changes during the nine months then ended are presented below:

	Shares	Weighted-Average Grant Date Fair Value
Nonvested at December 31, 2020	620,277	\$ 1.29
Granted	—	—
Vested	(248,111)	1.29
Forfeited	—	—
Nonvested at September 30, 2021	<u>372,166</u>	\$ 1.29

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

*The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our unaudited financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q and our Annual Report on Form 10-K for the year ended December 31, 2020 that was filed with the United States Securities and Exchange Commission, or the SEC, on March 11, 2021.*

*Our actual results and timing of certain events may differ materially from the results discussed, projected, anticipated, or indicated in any forward-looking statements. We caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this Quarterly Report. In addition, even if our results of operations, financial condition and liquidity, and the development of the industry in which we operate are consistent with the forward-looking statements contained in this Quarterly Report, they may not be predictive of results or developments in future periods.*

*The following information and any forward-looking statements should be considered in light of factors discussed elsewhere in this Quarterly Report on Form 10-Q, including those risks identified under Part II, Item 1A. Risk Factors.*

*We caution readers not to place undue reliance on any forward-looking statements made by us, which speak only as of the date they are made. We disclaim any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.*

### Overview

We are a late-stage, clinical biopharmaceutical company dedicated to discovering, developing and commercializing first-in-class, oral biological therapeutics to treat patients with rare and severe metabolic and kidney disorders. Our lead product candidate, reloxaliase (formerly known as ALLN-177), is currently being evaluated in a pivotal Phase 3 clinical program for the treatment of enteric hyperoxaluria, a metabolic disorder characterized by markedly elevated urinary oxalate ("UOx") levels and commonly associated with kidney stones, chronic kidney disease ("CKD") and other serious kidney disorders. There are currently no approved therapies for the treatment of enteric hyperoxaluria. We are also developing ALLN-346 for the treatment of hyperuricemia and gout in the setting of advanced CKD. We completed a Phase 1b multiple-ascending dose study in the second quarter of 2021 and recently initiated dosing in two Phase 2a studies. Initial data from the Phase 2a program are expected during the fourth quarter of 2021.

We have conducted a robust clinical development program of reloxaliase, including three Phase 2 clinical trials and the first of two Phase 3 clinical trials, which have demonstrated significant reductions in UOx excretion in patients with enteric hyperoxaluria. Reloxaliase has also been well tolerated in all studies conducted to date. We initiated URIROX-1<sup>TM</sup> (URIROX-1, formerly Study 301), the first of our two Phase 3 clinical trials in support of our planned Biologic License Application, or BLA, for reloxaliase in patients with enteric hyperoxaluria in March 2018. In November 2019, we reported that the primary endpoint in the URIROX-1 study had been met, with a mean reduction of 22.6% in average 24-hour UOx excretion measured during Weeks 1-4 among patients treated with reloxaliase, compared to a mean reduction of 9.7% in the placebo group (least square, or LS, mean treatment difference of -14.3%, p=0.004). In the fourth quarter of 2018, we initiated URIROX-2<sup>TM</sup> (URIROX-2, formerly Study 302), our second pivotal Phase 3 trial of reloxaliase in patients with enteric hyperoxaluria.

In February 2020, following engagement with the U.S. Food and Drug Administration, or FDA, we announced that we reached agreement with the FDA on a streamlined design for URIROX-2, based on the high rate of on-study kidney stone events and the UOx results observed in the completed URIROX-1 trial, which enrolled essentially the same patient population as URIROX-2. The FDA has also advised us that it agrees that, if positive, biomarker data on 24-hour UOx excretion in URIROX-1 and URIROX-2 would be used for a BLA submission for reloxaliase using the accelerated approval regulatory pathway. For the long-term follow-up phase of the trial, subjects would continue in URIROX-2 for a minimum treatment period of two years to confirm clinical benefit post-approval, including the ability of reloxaliase to reduce the incidence and severity of kidney stone disease and renal impairment.

The execution and enrollment of the URIROX-2 trial have been adversely affected by the COVID-19 pandemic. We had previously planned to conduct the first interim analysis of the URIROX-2 study after 130 subjects had been treated for at least six months and had estimated the timing of this analysis to be in the second or third quarter of 2022. In July 2021, given the adverse impact of the COVID-19 global pandemic on the rate of patient enrollment in this global study, and considering as well that enrollment in this study began in 2019, we modified our plans and now expect to conduct the first interim analysis,

which will include all subjects who were enrolled in the trial as of the end of November 2021, during the first quarter of 2022. We estimate that this revised interim analysis would include UOx data during weeks 1-4 for approximately 80 patients but would not include sufficient data to evaluate UOx levels during weeks 16-24 or the blinded rate of kidney stone events, as previously planned. We have submitted our revised plan for the first interim analysis to the FDA as part of our planned update to the URIROX-2 statistical analysis plan and adaptive design charter. The revised interim analysis, which will be conducted by an independent data monitoring committee, will assess whether the study continues to be adequately powered to evaluate efficacy against the primary endpoint, the change in UOx levels during weeks 1-4 versus baseline, with the planned enrollment of 200 subjects, or whether the study size should be increased. As previously planned, the interim analysis will also include an assessment of futility with respect to the primary endpoint. We do not anticipate any changes to the planned second interim analysis, which will also include an assessment of the secondary endpoint of change in UOx levels during weeks 16-24 and of unblinded kidney stone events. The second interim analysis is expected to be conducted once 200 subjects have reached six months of treatment and is designed to enable a potential filing for accelerated approval for reloxaliase.

In addition to our Phase 3 program of reloxaliase for enteric hyperoxaluria, we also evaluated reloxaliase in Study 206, a Phase 2 basket trial in adults and adolescents with primary hyperoxaluria or enteric hyperoxaluria with advanced CKD and elevated plasma oxalate levels (hyperoxalemia), which we initiated in March 2018. The data from this study has been published in *Nephrology Dialysis Transplantation* (Pfau 2021). Based on the substantial reductions from baseline to Weeks 4- 12 in both UOx and plasma oxalate, or POx, observed in subjects with enteric hyperoxaluria and advanced CKD, we obtained feedback from the FDA on potential expedited approval pathways for reloxaliase in this patient population. The FDA recognized that the high oxalate burden in these patients represents a serious, life-threatening condition, which is a requirement for considering an expedited approval pathway. However, the FDA advised us that reloxaliase would not currently qualify for breakthrough designation in this patient population based on the lack of placebo-controlled data from open-label Study 206. In this setting, and given our current financial resources, we remain focused on executing URIROX-2 and plan to evaluate potential clinical development of reloxaliase in patients with enteric hyperoxaluria and advanced CKD in the future.

In addition, we have designed our second product candidate, ALLN-346, an orally administered, novel, urate degrading enzyme, for patients with hyperuricemia and gout in the setting of advanced CKD. Hyperuricemia, or elevated levels of uric acid in the blood, results from overproduction or insufficient excretion of urate, or often a combination of the two. We have conducted two preclinical proof-of-concept studies that support the potential of ALLN-346 as an oral therapy for the treatment of hyperuricemia in patients with gout and associated CKD. We filed an IND for ALLN-346 with the FDA in December 2019. We have conducted both single ascending dose and multiple ascending dose studies of ALLN-346 in healthy volunteers. In both studies, ALLN-346 was well tolerated, and there were no safety signals observed. During the second half of 2021 we initiated our Phase 2a program for ALLN-346, consisting of a 7-day inpatient study in patients with hyperuricemia and a 14-day outpatient study in patients with hyperuricemia and gout. We recently received notice from the FDA that ALLN-346 has received fast track designation, which is granted to drug candidates that address a serious or life-threatening condition and demonstrate the potential to address an unmet medical need. The fast track process is designed to facilitate the development and expedite the review of drug candidates that meet these criteria.

On July 16, 2021, we completed a registered direct offering, in which we issued and sold 17,416,096 shares of our common stock, pre-funded warrants to purchase up to an aggregate of 3,941,648 shares of our common stock in lieu of shares of common stock and warrants to purchase up to 10,678,872 shares of our common stock through a securities purchase agreement. The combined price of each share of common stock and accompanying Warrant to purchase one-half of a share was \$1.311. The purchase price of each Pre-funded Warrant was \$1.301, which was the combined purchase price per share of common stock and accompanying Warrant, minus \$0.01. Gross proceeds of the transaction were \$28.0 million. As a result of the registered direct offering, we received approximately \$25.4 million after deducting estimated offering costs. Each Warrant is exercisable for one share of our common stock at an exercise price of \$1.25 per share. The Warrants are immediately exercisable and expire on July 16, 2026. Each Pre-funded Warrant is exercisable for one share of common stock at an exercise price of \$0.01 per share. The Pre-funded Warrants are immediately exercisable and may be exercised at any time until all Pre-funded Warrants are exercised in full. All Pre-funded Warrants were exercised on July 16, 2021.

During the first quarter of 2021, we issued and sold 6,058,318 shares of our common stock under the Cowen ATM Agreement at a weighted average price of \$1.99 per share for net proceeds of \$11.7 million. On March 29, 2021, we terminated the Cowen ATM Agreement and entered into the B. Riley ATM Agreement. During the second quarter of 2021, we issued and sold 1,650,988 shares of our common stock under the B. Riley ATM Agreement, at a weighted average price of \$1.25 per share for net proceeds of \$1.8 million. During the fourth quarter of 2021, through the filing date of this Quarterly Report, we issued and sold 2,430,350 shares of our common stock under the B. Riley ATM Agreement at a weighted average price of \$1.02 per share for net proceeds of \$2.4 million.

On December 4, 2020, we completed a public underwritten offering of 11,960,000 shares of our common stock, including the exercise in full of the underwriter's option to purchase an additional 1,560,000 shares of common stock, at a price to the public of \$1.25 per share for net proceeds of \$13.5 million.

On July 30, 2020, we completed a public underwritten offering of 5,894,191 shares of our common stock, including the exercise in full of the underwriter's option to purchase an additional 768,807 shares of common stock, at a price to the public of \$1.30 per share for net proceeds of \$6.7 million.

On June 5, 2020, we completed a registered direct offering, in which we issued and sold 7,317,074 shares of our common stock, at a purchase price of \$2.05 per share, for net proceeds of \$13.7 million through a securities purchase agreement with certain institutional and accredited investors. The shares of common stock sold in this offering were offered by us pursuant to our shelf registration statement on Form S-3 filed with the SEC, which was declared effective on December 26, 2018 and a prospectus supplement thereunder filed on June 5, 2020.

Our operations to date have been primarily focused on organizing and staffing our company, business planning, raising capital, developing our technology, identifying potential product candidates, manufacturing our product candidates and conducting preclinical studies and clinical trials of reloxaliase and ALLN-346. We do not have any products approved for sale and have not generated any revenue to date. As of September 30, 2021, we had cash and cash equivalents totaling \$40.4 million.

We have incurred significant net operating losses in every year since our inception and expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. Our net losses may fluctuate significantly from quarter to quarter and year to year. Our net losses were \$12.7 million and \$8.0 million for the three months ended September 30, 2021 and 2020, respectively, and \$38.3 million and \$22.6 million for the nine months ended September 30, 2021 and 2020, respectively. As of September 30, 2021, we had an accumulated deficit of \$236.1 million. We anticipate that our expenses will increase significantly as we:

- conduct clinical trials of our lead product candidate, reloxaliase;
- manufacture additional material for our pivotal Phase 3 clinical program and potential future clinical studies we might conduct for our product candidates;
- scale up our manufacturing process for reloxaliase to prepare for the filing of a potential Biologics License Application, or BLA, and commercialization if our clinical development program is successful;
- advance the development and conduct future clinical trials of ALLN-346;
- conduct research on the discovery and development of additional product candidates;
- seek regulatory and marketing approvals for product candidates that successfully complete clinical trials, if any;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain regulatory approval in geographies in which we plan to commercialize our products ourselves;
- maintain, expand and protect our intellectual property portfolio;
- hire additional staff, including clinical, scientific, technical, operational, and financial personnel, to execute our business plan; and
- add clinical, scientific, operational, financial and management information systems to support our product development and potential future commercialization efforts, and to enable us to operate as a public company.

We do not expect to generate revenue from product sales unless and until we successfully complete development and obtain regulatory approval for a product candidate. Additionally, we currently use contract research organizations, or CROs, and contract manufacturing organizations, or CMOs, to carry out our preclinical and clinical development activities. We do not yet have a sales organization. If we obtain regulatory approval for our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Furthermore, we expect to incur additional costs associated with operating as a public company. Accordingly, we may seek to fund our operations through public or private equity or debt financings or other sources, including strategic collaborations. We may, however, be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop our current product candidates, or any additional product candidates, if developed.

## ***NASDAQ Delisting Notification***

On August 25, 2021, we received a letter from the Listing Qualifications Department (the “Staff”) of the Nasdaq Stock Market (“Nasdaq”) notifying us that, for the 30 consecutive business day period between July 14, 2021 through August 24, 2021, our common stock had not maintained a minimum closing bid price of \$1.00 per share (the “Minimum Bid Price Requirement”) required for continued listing on The Nasdaq Global Select Market pursuant to Nasdaq Listing Rule 5550(a)(2). The Nasdaq letter does not result in the immediate delisting of the Company’s common stock from The Nasdaq Global Select Market.

In accordance with Nasdaq Listing Rule 5810(c)(3)(A) (the “Compliance Period Rule”), we have been provided an initial period of 180 calendar days, or until February 21, 2022 (the “Compliance Date”), to regain compliance with the Minimum Bid Price Requirement. If, at any time during this 180-day period, the closing bid price for our common stock closes at \$1.00 or more per share for a minimum of 10 consecutive business days, as required under the Compliance Period Rule, the Staff will provide written notification to us that we comply with the Minimum Bid Price Requirement and the common stock will continue to be eligible for listing on The Nasdaq Global Select Market.

If we do not regain compliance with the Minimum Bid Price Requirement by the Compliance Date, we may be eligible for an additional 180 calendar day compliance period. To qualify, we would be required to transfer to The Nasdaq Capital Market and meet the continued listing requirement for the market value of publicly held shares and all other initial listing standards for The Nasdaq Capital Market, with the exception of the Minimum Bid Price Requirement, and would need to provide written notice to Nasdaq of our intention to cure the deficiency during the additional compliance period.

If it appears to the Staff that we will not be able to cure the deficiency, the Staff will provide written notice to us that our common stock will be subject to delisting. At that time, we may appeal the Staff’s delisting determination to a Nasdaq Hearing Panel (the “Panel”). We expect that our stock would remain listed pending the Panel’s decision. There can be no assurance that, if we do appeal the Staff’s delisting determination to the Panel, such appeal would be successful.

We intend to monitor the closing bid price of our common stock and may, if appropriate, consider available options to regain compliance with the Minimum Bid Price Requirement, which could include seeking to effect a reverse stock split. However, there can be no assurance that we will be able to regain compliance with the Minimum Bid Price Requirement, secure a second period of 180 days to regain compliance, or maintain compliance with any of the other Nasdaq continued listing requirements.

## **Financial Operations Overview**

### ***Revenue***

To date, we have not generated any revenue from product sales or any other source and do not expect to generate any revenue from the sale of products for the foreseeable future. If our development efforts for reloxaliase or other product candidates that we may develop in the future are successful and result in marketing approval or collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from such collaboration or license agreements.

### ***Research and Development Expenses***

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery efforts and the development of our product candidates, which include:

- employee-related expenses, including salaries, benefits and stock-based compensation expense;
- costs incurred under agreements with third parties, including CROs, that conduct research and development, preclinical studies and clinical trials on our behalf;
- costs related to production of preclinical and clinical materials, including fees paid to CMOs;
- consulting, licensing and professional fees related to research and development activities;
- costs of purchasing laboratory supplies and non-capital equipment used in our research and development activities;
- costs related to compliance with clinical regulatory requirements; and
- facility costs and other allocated expenses, which include expenses for rent and maintenance of facilities, insurance, depreciation and other supplies.

We expense research and development costs as incurred. We recognize costs for certain development activities, such as clinical trials, based on an evaluation of the progress to completion of specific tasks using data such as clinical site activations,

patient enrollment, or information provided to us by our vendors and our clinical investigative sites. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and may be reflected in our consolidated financial statements as prepaid or accrued research and development expenses. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized, even when there is no alternative future use for the research and development. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

The following summarizes our most advanced current research and development programs:

- reloxaliase is our lead product candidate which we are developing for the treatment of enteric hyperoxaluria. A substantial majority of our research and development costs to date have been used to fund this program.
- ALLN-346 is our second product candidate which we are developing for the treatment of hyperuricemia and gout in the setting of CKD.

We typically use our employee and infrastructure resources across our development programs. We track outsourced development costs by product candidate or development program, but we do not allocate personnel costs and other internal costs to specific product candidates or development programs.

The following table summarizes our research and development expenses by program (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Reloxaliase external costs	\$ 2,988	\$ 2,021	\$ 11,851	\$ 4,717
ALLN-346 external costs	2,600	737	5,501	1,435
Employee compensation and benefits	2,650	1,765	7,361	6,122
Other	786	429	2,253	1,132
<b>Total research and development expenses</b>	<b>\$ 9,024</b>	<b>\$ 4,952</b>	<b>\$ 26,966</b>	<b>\$ 13,406</b>

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages, primarily due to the increased size and duration of later-stage clinical trials. Since inception, we have incurred \$103.7 million of external research and development costs for reloxaliase and \$16.0 million of external research and development costs for ALLN-346. We expect that our research and development costs will continue to increase for the foreseeable future as we advance the URIROX-2 trial for reloxaliase, conduct the Phase 2a program and initiate additional clinical trials for ALLN-346 and scale our manufacturing processes of reloxaliase and ALLN-346.

The successful development of reloxaliase, ALLN-346 and other potential future product candidates is highly uncertain. Accordingly, at this time, we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the development of these product candidates. We are also unable to predict when, if ever, we will generate revenue and material net cash inflows from the commercialization and sale of any of our product candidates for which we may obtain marketing approval. We may never succeed in achieving regulatory approval for any of our product candidates. The duration, costs and timing of preclinical studies, clinical trials and development of our product candidates will depend on a variety of factors, including:

- successful enrollment in, and completion of, clinical trials for reloxaliase;
- successful data from our clinical program of reloxaliase that supports an acceptable benefit-risk profile of reloxaliase in the intended populations;
- successful enrollment in, and completion of, clinical trials for ALLN-346;
- establishing an appropriate safety profile for any potential future product candidates with studies to enable the filing of investigational new drug application, or INDs;
- approval of INDs for any potential future product candidate to commence planned or future clinical trials;
- significant and changing government regulation and regulatory guidance;
- timing and receipt of marketing approvals from applicable regulatory authorities;
- making arrangements with CMOs for third-party commercial manufacturing of our product candidates;

- obtaining and maintaining patent and other intellectual property protection and regulatory exclusivity for our product candidates;
- commercializing the product candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of the product, if and when approved, by patients, the medical community and third-party payors; and
- maintenance of a continued acceptable safety profile of the drugs following approval.

A change in the outcome of any of these variables with respect to the development, manufacture or commercialization enabling activities of any of our product candidates could mean a significant change in the costs, timing and viability associated with the development of that product candidate.

#### ***General and Administrative Expenses***

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance, accounting, business development and human resources functions. Other significant costs include directors' and officers' insurance, facility costs not otherwise included in research and development expenses, legal fees relating to patent and corporate matters and professional fees for accounting, auditing, tax and consulting services.

We expect that our general and administrative expenses will increase in the future to support continued research and development activities and potential commercialization of our product candidates. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, attorneys and accountants, among other expenses.

#### ***Interest Expense, Net***

Interest expense, net primarily consists of interest income earned on our cash and cash equivalents, interest expense incurred on our credit facility and amortized debt discount related to debt issuance costs.

#### ***Other Expense, Net***

Other expense, net, consists of a success fee paid to PWB at the time the conditions required to trigger the success fee as defined in the PWB Loan Agreement were met in June 2020 and gain (loss) on foreign currency transactions.

#### **Critical Accounting Policies and Use of Estimates**

Our management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with U.S. GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements during the reporting periods. These items are monitored and analyzed by us for changes in facts and circumstances, and material changes in these estimates could occur in the future. We base our estimates on historical experience, known trends and events, and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ materially from these estimates under different assumptions or conditions.

Our significant accounting policies are described in detail in the notes to our consolidated financial statements appearing in the Annual Report filed on Form 10-K for the year ended December 31, 2020. There have been no changes to our significant accounting policies other than as follows.

#### ***Warrants***

We account for issued warrants either as a liability or equity in accordance with ASC 480-10, *Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity* ("ASC 480-10") or ASC 815-40, *Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock* ("ASC 815-40"). Under ASC 480-10, warrants are considered a liability if they are mandatorily redeemable and they require settlement in cash, other assets, or a variable number of shares. If warrants do not meet liability classification under ASC 480-10, we consider the requirements of ASC 815-40 to determine whether the warrants should be classified as a liability or as equity. Under ASC 815-40, contracts that may require settlement for cash are liabilities, regardless of the probability of the occurrence of the triggering event. Liability-classified warrants are measured at fair value on the issuance date and at the end of each reporting period. Any change in the fair value of the warrants after the issuance date is recorded in the consolidated statement of



operations as a gain or loss. If warrants do not require liability classification under ASC 815-40, in order to conclude warrants should be classified as equity, we assess whether the warrants are indexed to our common stock and whether the warrants are classified as equity under ASC 815-40 or other applicable GAAP standard. Equity-classified warrants are accounted for at fair value on the issuance date with no changes in fair value recognized after the issuance date. The Warrants and Pre-funded Warrants do not meet the requirements for liability classification under ASC-480-10 or ASC-815-40. Therefore, the Warrants and Pre-funded Warrants were treated as equity at the time of issuance.

## Results of Operations

### Comparison of the three months ended September 30, 2021 and 2020

The following table summarizes our results of operations for the three months ended September 30, 2021 and 2020 (in thousands):

	Three Months Ended September 30,		Dollar Change
	2021	2020	
Operating expenses:			
Research and development	\$ 9,024	\$ 4,952	\$ 4,072
General and administrative	3,407	2,966	441
Total operating expenses	12,431	7,918	4,513
Loss from operations	(12,431)	(7,918)	(4,513)
Other expense:			
Interest expense, net	(250)	(104)	(146)
Other expense, net	(11)	(4)	(7)
Other expense, net	(261)	(108)	(153)
Net loss	<u>\$ (12,692)</u>	<u>\$ (8,026)</u>	<u>\$ (4,666)</u>

### Research and Development Expense

Research and development expense increased by \$4.1 million from \$5.0 million for the three months ended September 30, 2020 to \$9.0 million for the three months ended September 30, 2021. The following table summarizes our research and development expenses for the three months ended September 30, 2021 and 2020 (in thousands):

	Three Months Ended September 30,		Dollar Change
	2021	2020	
Clinical development external costs	\$ 4,007	\$ 2,104	\$ 1,903
Manufacturing external costs	1,453	399	1,054
Employee compensation and benefits	2,650	1,766	884
Other	914	683	231
Total research and development expenses	<u>\$ 9,024</u>	<u>\$ 4,952</u>	<u>\$ 4,072</u>

The \$4.1 million increase in research and development expense was primarily attributable to the following:

- Our clinical development external costs increased by \$1.9 million from \$2.1 million for the three months ended September 30, 2020 to \$4.0 million for the three months ended September 30, 2021:
  - o Our URIROX-2 costs increased \$0.4 million from \$1.7 million for the three months ended September 30, 2020 to \$2.1 million for the three months ended September 30, 2021. During the first half of 2020, we limited the opening of new trial sites for the ongoing URIROX-2 trial while we assessed revisions to the study design and sought additional funds to support the development of reloxaliase. During the three months ended September 30, 2020, we began expanding URIROX-2 to additional geographies and clinical trial sites; and
  - o Our ALLN-346 costs increased \$1.4 million from \$0.3 million for the three months ended September 30, 2020 to \$1.7 million for the three months ended September 30, 2021. During the three months ended September 30, 2021, we initiated dosing in two Phase 2a studies. We incurred \$1.4 million of costs for the Phase 2a program during the three months ended September 30, 2021, for which there were no comparable costs during the three months ended September 30, 2020. In April 2021, we initiated a Phase 1b multiple ascending dose trial in healthy volunteers and announced initial data from this study in July 2021.
- Our manufacturing external costs increased by \$1.1 million from \$0.4 million for the three months ended September 30, 2020 to \$1.5 million for the three months ended September 30, 2021:
  - o Our reloxaliase costs increased \$0.3 million from \$0.2 million for the three months ended September 30, 2020 to \$0.5 million for the three months ended September 30, 2021, primarily due to increased costs for consumables and raw materials; and
  - o Our ALLN-346 costs increased \$0.5 million from \$0.1 million for the three months ended September 30, 2020 to \$0.6 million for the three months ended September 30, 2021, primarily due to increased formulation and development costs.
- Our employee compensation and benefits costs increased \$0.9 million from \$1.8 million for the three months ended September 30, 2020 to \$2.7 million for the three months ended September 30, 2021, primarily due to an increase in research and development headcount from 22 employees at September 30, 2020 to 35 employees at September 30, 2021.

#### General and Administrative Expenses

General and administrative expense increased \$0.4 million from \$3.0 million for the three months ended September 30, 2020 to \$3.4 million for the three months ended September 30, 2021. The following table summarizes our general and administrative expenses for the three months ended September 30, 2021 and 2020 (in thousands):

	Three Months Ended September 30,		Dollar Change
	2021	2020	
Employee compensation and benefits	\$ 1,814	\$ 1,698	\$ 116
Consulting and professional services	869	695	174
Market research and commercialization planning	—	35	(35)
Other	724	538	186
<b>Total general and administrative expenses</b>	<b>\$ 3,407</b>	<b>\$ 2,966</b>	<b>\$ 441</b>

General and administrative expense included the following:

- Our employee compensation and benefits costs were \$1.8 million and \$1.7 million for the three months ended September 30, 2021 and 2020, respectively;
- Our consulting and professional services costs increased \$0.2 million for the three months ended September 30, 2021. The increase is primarily due to a \$0.1 million increase in consulting costs and \$0.1 million of website design costs for the three months ended September 30, 2021; and
- Our other costs increased \$0.2 million for the three months ended September 30, 2021, primarily due to an increase in insurance costs.

### *Interest Expense, net*

Interest income (expense), net consists of interest income earned on our cash and cash equivalents and interest expense incurred on our outstanding debt. Net interest expense increased \$0.1 million for the three months ended September 30, 2021 due to increased interest expense associated with amounts outstanding under the Pontifax Agreement. In September 2020, we terminated the PWB Agreement, under which we were paying an annualized interest rate of 5.0% and entered into the Pontifax Agreement, under which we are paying an annualized interest rate of 9.0% on outstanding borrowings. In addition, we were paying Pontifax an annualized fee of 1.0% for the \$5.0 million that was available under the Credit Line of the Pontifax Agreement. The availability to withdraw amounts available under the Credit Line expired unused on September 29, 2021.

### *Other Expense, net*

Other (expense), net consists of gain (loss) on foreign currency transactions.

### **Comparison of the Nine Months Ended September 30, 2021 and 2020**

The following table summarizes our results of operations for the nine months ended September 30, 2021 and 2020 (in thousands):

	Nine Months Ended September 30,		Dollar Change
	2021	2020	
Operating expenses:			
Research and development	\$ 26,966	\$ 13,406	\$ 13,560
General and administrative	10,562	8,595	1,967
Total operating expenses	37,528	22,001	15,527
Loss from operations	(37,528)	(22,001)	(15,527)
Other expense:			
Interest expense, net	(738)	(261)	(477)
Other expense, net	(34)	(325)	291
Other income (expense), net	(772)	(586)	(186)
Net loss	<u>\$ (38,300)</u>	<u>\$ (22,587)</u>	<u>\$ (15,713)</u>

### *Research and Development Expenses*

Research and development expense increased by \$13.6 million from \$13.4 million for the nine months ended September 30, 2020 to \$27.0 million for the nine months ended September 30, 2021. The following table summarizes our research and development expenses for the nine months ended September 30, 2021 and 2020 (in thousands):

	Nine Months Ended September 30,		Dollar Change
	2021	2020	
Clinical development external costs	\$ 12,614	\$ 4,288	\$ 8,326
Manufacturing external costs	4,443	1,528	2,915
Employee compensation and benefits	7,361	6,122	1,239
Other	2,548	1,468	1,080
Total research and development expenses	<u>\$ 26,966</u>	<u>\$ 13,406</u>	<u>\$ 13,560</u>

The \$13.6 million increase in research and development expense was primarily attributable to the following:

- Our clinical development external costs increased by \$8.3 million from \$4.3 million for the nine months ended September 30, 2020 to \$12.6 million for the nine months ended September 30, 2021:
  - o Our URIROX-2 costs increased \$5.6 million from \$3.0 million for the nine months ended September 30, 2020 to \$8.6 million for the nine months ended September 30, 2021. During the nine months ended September 30, 2020, we limited the opening of new trial sites for the ongoing URIROX-2 trial while we assessed revisions to the study design and sought additional funds to support the development of relaxaliase. We began expanding URIROX-2 to additional geographies and clinical trial sites using a portion of the \$13.7 million of net proceeds received from a registered direct offering completed in June 2020 and the \$6.7 million of net proceeds received from a public offering completed in July 2020. We continued to expand URIROX-2 to additional geographies and clinical trial sites and enrolling subjects during the nine months ended September 30, 2021; and
  - o Our ALLN-346 costs increased \$2.9 million from \$0.3 million for the nine months ended September 30, 2020 to \$3.2 million for the nine months ended September 30, 2021.
    - During the nine months ended September 30, 2021, we initiated dosing in two Phase 2a studies. We incurred \$2.1 million of costs for the Phase 2a program during the nine months ended September 30, 2021, for which there were no comparable costs during the nine months ended September 30, 2020.
    - We incurred costs for our Phase 1 program of \$1.1 million and \$0.3 million for the nine months ended September 30, 2021 and 2020, respectively, as follows:
      - In April 2021, we initiated a Phase 1b multiple ascending dose trial in healthy volunteers and announced initial data from this study in July 2021. We incurred \$0.9 million of clinical costs for this trial during the nine months ended September 30, 2021, for which there were no comparable costs during the nine months ended September 30, 2020; and
      - We incurred \$0.2 million and \$0.3 million of costs during the nine months ended September 30, 2021 and 2020, respectively, for our Phase 1a single ascending dose trial in healthy volunteers, which we completed in the fourth quarter of 2020.
- Our manufacturing external costs increased by \$2.9 million from \$1.5 million for the nine months ended September 30, 2020 to \$4.4 million for the nine months ended September 30, 2021.
  - o Formulation and development related costs for relaxaliase increased \$1.7 million from \$0.7 million for the nine months ended September 30, 2020 to \$2.4 million for the nine months ended September 30, 2021; and
  - o Formulation and development related costs for ALLN-346 increased \$0.7 million from \$0.6 million for the nine months ended September 30, 2020 to \$1.3 million for the nine months ended September 30, 2021.
- Our employee compensation and benefits costs increased by \$1.2 million from \$6.1 million for the nine months ended September 30, 2020 to \$7.4 million for the nine months ended September 30, 2021. The increase is primarily due to an increase in headcount from 22 employees at September 30, 2020 to 35 employees at September 30, 2021, partially offset by a decrease in stock-based compensation costs.

We expect that our research and development expenses will increase in future periods as we continue our clinical development of relaxaliase, scale our manufacturing processes for relaxaliase and advance development of ALLN-346.

#### *General and Administrative Expenses*

General and administrative expense increased by \$2.0 million from \$8.6 million for the nine months ended September 30, 2020 to \$10.6 million for the nine months ended September 30, 2021. The following table summarizes our general and administrative expenses for the nine months ended September 30, 2021 and 2020 (in thousands):

	Nine Months Ended September 30,		Dollar Change
	2021	2020	
Employee compensation and benefits	\$ 5,396	\$ 5,012	\$ 384
Consulting and professional services	2,738	1,930	808
Market research and commercialization planning	133	35	98
Other	2,295	1,618	677
<b>Total general and administrative expenses</b>	<b>\$ 10,562</b>	<b>\$ 8,595</b>	<b>\$ 1,967</b>

The increase in general and administrative expense was primarily attributable to the following:

- Our employee compensation and benefits costs increased by \$0.4 million from \$5.0 million for the nine months ended September 30, 2020 to \$5.4 million for the nine months ended September 30, 2021, primarily due to an increase in the number of employees;
- Our consulting and professional services costs increased by \$0.8 million from \$1.9 million for the nine months ended September 30, 2020 to \$2.7 million for the nine months ended September 30, 2021. The increase was primarily due to a \$0.4 million increase in consulting costs and \$0.3 million of recruiting costs for the nine months ended September 30, 2021, for which there were no comparable costs for the nine months ended September 30, 2020; and
- Our other costs increased by \$0.7 million from \$1.6 million for the nine months ended September 30, 2020 to \$2.3 million for the nine months ended September 30, 2021, primarily due to an increase in insurance costs.

#### *Interest Expense, net*

Interest expense, net consists of interest income earned on our cash and cash equivalents and interest expense charged on our outstanding debt. Net interest expense increased \$0.5 million for the nine months ended September 30, 2021 due to increased interest expense associated with amounts outstanding under the Pontifax Agreement.

#### *Other Expense, net*

Other expense, net consists gain (loss) on foreign currency transactions. Included in other expense, net for nine months ended September 30, 2020 was a success fee of \$0.3 million paid to PWB.

### **Liquidity and Capital Resources**

#### *Sources of Liquidity*

We have funded our operations from inception through September 30, 2021 through gross proceeds of \$96.0 million from sales of our convertible preferred stock, net proceeds of \$67.0 million from our IPO which was completed in November 2017, net proceeds totaling \$33.8 million from follow-on offerings of common stock during 2020, borrowings of \$10.0 million under our credit facilities, net proceeds of \$14.6 million and \$1.8 million from the sale of our common stock under the Cowen ATM Agreement and the B. Riley ATM Agreement, respectively, and net proceeds of \$25.4 million from the registered direct offering completed in July 2021. Our total cash and cash equivalents were \$40.4 million as of September 30, 2021.

On May 6, 2021, we filed a shelf registration statement on Form S-3, which was declared effective on May 12, 2021 (File No. 333-255837), for the offering of up to \$200 million in the aggregate of common stock, preferred stock, debt securities, warrants and/or units (“securities”) from time to time in one or more offerings. As of the filing of this Quarterly Report on Form 10-Q, we have not offered any securities pursuant to this shelf registration.

On September 29, 2020, we entered into a loan and security agreement with Pontifax Medison Finance (Israel) L.P. and Pontifax Medison Finance (Cayman) L.P. (together “Pontifax”) (“Pontifax Agreement”) providing up to \$25.0 million of borrowings through three facilities of a term loan. An initial loan (“Initial Loan”) of \$10.0 million was advanced on September 29, 2020. A portion of these proceeds were used to pay the remaining balance of our credit facility with PWB and terminate the PWB Loan Agreement. We also had an additional \$5.0 million credit line (“Credit Line”) that was available to us for withdrawal until September 29, 2021. We did not withdraw any amounts available through the Credit Line prior to the expiration of the availability period. We paid a fee of 1.0% per annum to Pontifax for the daily average amount not withdrawn under the Credit Line during the period amounts were available for withdrawal. A third installment loan (“Third Installment Loan”) of an additional \$10.0 million was conditioned upon achievement of one of the following milestones by no later than December 29, 2021: (i) we receive non-contingent, non-refundable gross proceeds from one or more equity financings and/or strategic partnerships, in each case consummated following the Closing Date, in the aggregate amount of at least \$15.0 million for all such equity financings and strategic partnerships or (ii) the 65<sup>th</sup> patient has been enrolled in the URIROX-2 trial. During the three months ended December 31, 2020, the additional \$10 million under the Third Installment Loan became available to us for withdrawal until December 29, 2021 when we satisfied the milestone of at least \$15 million of gross proceeds from equity financings. Upon withdrawal of the Third Installment Loan, if withdrawn, we shall pay Pontifax a one-time fee of 1.0% of the Third Installment Loan.

The Pontifax Agreement has a term of 48 months and an interest only period of 24 months. Amounts outstanding under the Pontifax Agreement have a fixed interest rate of 9.0% per annum. Upon the expiration of the interest only period on

September 29, 2022, amounts borrowed will be repaid over eight equal quarterly payments of principal and interest. At our option, we may prepay all or part of the outstanding borrowings at any time without any prepayment premium or penalty.

At the option of Pontifax, amounts outstanding under the Pontifax Agreement may be converted at any time into shares of our common stock at a conversion price of \$4.10 per share. In addition, we have the right to convert at any time any portion of the then outstanding borrowings and all accrued but unpaid interest into shares of our common stock, at the applicable conversion price, subject to the fulfillment of both of the following conditions: (i) during a period of 30 consecutive trading days prior to the date on which we provide notice of the exercise of our conversion right, the closing price of our common stock was higher than 1.4 times the applicable conversion price of the term loans on at least 20 trading days, including on the trading day preceding the date we provide notice of the exercise of our conversion right and (ii) the number of shares of common stock issuable upon conversion by us shall not exceed the average weekly number of shares of our common stock traded on the stock market for the four weeks immediately preceding the date on which we provide notice of the exercise of our conversion right.

The borrowings under the Pontifax Agreement are secured by a lien on all of our assets except intellectual property. The Pontifax Agreement contains customary representations, warranties and covenants by us, including negative covenants restricting our activities, such as disposing of our business or certain assets, incurring additional debt or liens or making payments on other debt, making certain investments and declaring dividends, acquiring or merging with another entity, engaging in transactions with affiliates or encumbering intellectual property, among others. The obligations under the Pontifax Agreement are subject to acceleration upon occurrence of specified events of default, including a material adverse change in our business, operations or financial or other condition.

### **Cash Flows**

The following table provides information regarding our cash flows for the nine months ended September 30, 2021 and 2020 (in thousands):

	<b>Nine Months Ended September 30,</b>	
	<b>2021</b>	<b>2020</b>
Net cash used in operations	\$ (32,875)	\$ (20,329)
Net cash used in investing activities	(642)	—
Net cash provided by financing activities	38,896	20,458
Net increase in cash and cash equivalents	<u>\$ 5,379</u>	<u>\$ 129</u>

#### *Net Cash Used in Operating Activities*

The net cash used in operating activities resulted primarily from our net losses adjusted for non-cash charges and changes in components of working capital.

Net cash used in operating activities was \$32.9 million for the nine months ended September 30, 2021 compared to \$20.3 million for the nine months ended September 30, 2020. The increase in cash used in operating activities of \$12.5 million was attributable to:

- an increase in net loss of \$15.7 million;
- a decrease in non-cash items of \$0.2 million; partially offset by
- an increase of \$3.4 million due to changes in the components of net working capital.

#### *Net Cash Used in Investing Activities*

Net cash used in investing activities of \$0.6 million for the nine months ended September 30, 2021 consisted of purchases of property and equipment. We did not have any cash flow activity relating to investment activities during the nine months ended September 30, 2020.

#### *Net Cash Provided by Financing Activities*

Net cash provided by financing activities was \$38.9 million for the nine months ended September 30, 2021 compared to \$20.5 million for the nine months ended September 30, 2020. The net cash provided by financing activities for the nine months ended September 30, 2021 consisted of net proceeds of \$11.7 million and \$1.8 from the sale of common stock under the Cowen ATM Agreement and the B. Riley ATM Agreement, and \$25.4 million of net proceeds from the issuance and sale

of 17,416,096 shares of our common stock, pre-funded warrants to purchase up to an aggregate of 3,941,648 shares of our common stock in lieu of shares of common stock and warrants to purchase up to 10,678,872 shares of our common stock completed on July 16, 2021 through a registered direct offering, respectively. The net cash provided by financing activities for the nine months ended September 30, 2020 consisted primarily of \$13.7 million of net proceeds from the issuance and sale of 7,317,074 shares of our common stock completed on June 5, 2020 through a registered direct offering and \$6.7 million of net proceeds from the issuance of 5,894,191 shares of our common stock completed on July 30, 2020 through a public underwritten offering.

### ***Funding Requirements***

If we are able to fund our operations, we expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development, initiate later stage clinical trials and seek marketing approval for our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations.

### ***Going Concern***

As of September 30, 2021, we had cash and cash equivalents totaling \$40.4 million. Based on our current operating plans, we do not have sufficient cash and cash equivalents to fund our operating expenses and capital expenditures for at least the next 12 months from the filing date of this Quarterly Report. We do believe that our cash and cash equivalents at September 30, 2021 will enable us to fund our operating expenses and capital requirements into the second quarter of 2022. We will require additional capital to sustain our operations, including our reloxaliase and ALLN-346 development programs, beyond that time. We are exploring opportunities to secure additional funding through equity or debt financings or through collaborations, licensing transactions or other sources. However, there can be no assurance that we will be able to complete any such transaction on acceptable terms or otherwise. Market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed. If we are unable to raise capital when needed or on attractive terms, we may decide to delay, reduce or eliminate our research and development programs or future commercialization efforts and our ability to continue operations will be jeopardized. These factors raise substantial doubt about our ability to continue as a going concern. We may implement cost reduction strategies, which may include amending, delaying, limiting, reducing, or terminating one or more of our ongoing or planned clinical trials or development programs of our product candidates. The accompanying condensed consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the ordinary course of business for the foreseeable future. The condensed consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of this uncertainty.

Our future capital requirements will depend on many factors, including;

- the costs of conducting clinical trials of reloxaliase, including any unforeseen costs we may incur as a result of clinical trial delays due to the COVID-19 pandemic or other causes;
- the costs of manufacturing additional material for our pivotal Phase 3 clinical program and potential future clinical studies we might conduct for reloxaliase;
- the costs of scaling up our manufacturing process for reloxaliase to prepare for the potential filing of a BLA and commercialization if our clinical development program is successful;
- the costs of conducting future clinical trials and other development activities to advance ALLN-346;
- the scope, progress, results and costs of discovery, preclinical development, laboratory testing and clinical trials for other potential product candidates we may develop, if any;
- the costs, timing and outcome of regulatory review of our product candidates;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any collaboration agreements we might have at such time;
- the costs and timing of future commercialization activities, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;

- the amount of revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, obtaining, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the expansion of our workforce and associated costs as we expand our business operations and our research and development activities; and
- the costs of operating as a public company.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. Except for the Third Installment Loan under the Pontifax Agreement, we do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interests may be diluted, and the terms of these securities may include liquidation or other preferences that could adversely affect your rights as a common stockholder. Additional debt financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business. If we raise funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

#### **Off-Balance Sheet Arrangements**

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules.



**Item 3. Quantitative and Qualitative Disclosures About Market Risk.**

We are exposed to market risk related to changes in interest rates. As of September 30, 2021, our cash equivalents consisted primarily of short-term money market funds. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term nature of the cash equivalents in our portfolio and the low risk profile of our cash equivalents, an immediate 10% change in interest rates would not have a material effect on the fair market value of our financial position or results of operations.

We are not currently exposed to significant market risk related to changes in foreign currency exchange rates; however, we have contracted with and may continue to contract with foreign vendors that are located in Europe. Our operations may be subject to fluctuations in foreign currency exchange rates in the future.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the three and nine months ended September 30, 2021 and 2020.

**Item 4. Controls and Procedures.***Management's Evaluation of our Disclosure Controls and Procedures*

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms and (2) accumulated and communicated to our management, including our principal executive and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our disclosure controls and procedures are designed to provide reasonable assurance of achieving their control objectives.

Our management, with the participation of our principal executive officer and principal financial and accounting officer, evaluated the effectiveness of our disclosure controls and procedures the end of the period covered by this Quarterly Report on Form 10-Q. Based upon such evaluation, our principal executive officer and principal financial and accounting officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of such date.

*Changes in Internal Control over Financial Reporting*

There was no change in our internal control over financial reporting that occurred during the period covered by this Quarterly Report on Form 10-Q that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

**Item 1. Legal Proceedings**

From time to time, we may become involved in litigation relating to claims arising from the ordinary course of business. Our management believes that there are currently no claims or actions pending against us, the ultimate disposition of which could have a material adverse effect on our results of operations or financial condition.

**ITEM 1A. RISK FACTORS**

*Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Quarterly Report on Form 10-Q and in our other public filings before making an investment decision. Our business, prospects, financial condition, or operating results could be harmed by any of these risks, as well as other risks not currently known to us or that we currently consider immaterial. If any such risks or uncertainties actually occur, our business, financial condition or operating results could differ materially from the plans, projections and other forward-looking statements included in the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and elsewhere in this report and in our other public filings. The trading price of our common stock could decline due to any of these risks, and as a result, you may lose all or part of your investment.*

*Those risk factors below denoted with a “\*” are newly added or have been materially updated from our Annual Report on Form 10-K filed with the Securities and Exchange Commission, or the SEC, on March 11, 2021.*

**Summary of the Material Risks Associated with Our Business**

- **We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.**
- **We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development, other operations or commercialization efforts.**
- **We have incurred significant losses since inception, expect to incur significant and increasing losses for at least the next several years, have not generated any revenue, may never generate any revenue, and may never achieve or maintain profitability.**
- **We are heavily dependent on the regulatory approval of reloxaliase (formerly referred to as ALLN-177) in the United States and Europe, and subsequent commercial success of reloxaliase, both of which may never occur.**
- **Although we have reached alignment with the FDA on the design of URIROX-2, our second pivotal Phase 3 trial of reloxaliase in patients with enteric hyperoxaluria, and our strategy to pursue a BLA submission for reloxaliase using the accelerated approval regulatory pathway, the clinical data we generate from our Phase 3 clinical program and/or the data we derive from third party datasets may not be sufficient to meet the FDA requirements for filing and obtaining marketing authorization via the accelerated approval regulatory pathway. If we are unable to obtain accelerated approval, we may be required to conduct additional preclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, reduce the likelihood of obtaining and/or delay the timing of obtaining, necessary marketing approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw accelerated approval.**
- **Our proprietary technological approach is a new approach to the design and development of stable, non-absorbable oral biological therapies and may not result in any additional product candidates or ultimately any products of commercial value.**
- **Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.**

- **Foreign regulators may not agree with our proposed Phase 3 clinical program for reloxaliase, in which case we may be required to modify our planned clinical trials, or run additional clinical trials, before we can submit foreign applications for marketing approval for reloxaliase.**
- **Because we are developing product candidates for the treatment of diseases in which there is little clinical trial experience and, in some cases, using new endpoints or methodologies, there is increased risk that the FDA or other regulatory authorities may not consider the endpoints of our clinical program to provide clinically meaningful results and that these results may be hard to analyze.**
- **If we experience delays or difficulties in the enrollment or continuation of patients in our clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.**
- **Even if we receive regulatory approval for any of our product candidates, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our drugs.**
- **The manufacture and packaging of pharmaceutical products such as reloxaliase is subject to FDA requirements and those of similar foreign regulatory bodies. If we or our third-party manufacturers fail to satisfy these requirements, our product development and commercialization efforts may be harmed.**
- **We must reach agreement with FDA and foreign regulatory agencies on an appropriate method for evaluating bioavailability and/or bioequivalence in connection with our planned BLA submission for reloxaliase and in support of any scale up of commercial supply of reloxaliase in anticipation of a commercial launch. Failure to reach agreement or failure to demonstrate bioavailability and/or bioequivalence may require that we run additional preclinical or clinical studies, which could delay the timing of a potential BLA submission or approval.**
- **Manufacture and supply of drug substance, drug product and finished drug product is a complex and technically challenging undertaking, particularly for oral biologics, and there is potential for failure at many points in the manufacturing, testing, quality assurance and distribution supply chain, as well as the potential for latent defects after a product has been manufactured and distributed.**
- **The incidence and prevalence for target patient populations of our product candidates have not been established with precision. If the market opportunities for our product candidates are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer. Our ability to successfully identify patients and acquire a significant market share will be necessary for us to achieve profitability and growth.**
- **We face substantial competition, which may result in others discovering, developing or commercializing drugs before or more successfully than we do, and reducing or eliminating our commercial opportunity.**
- **We currently have no sales and marketing organization and, as a company, have not commercialized any products. If we are unable to establish effective sales and marketing capabilities in the United States and access them in Europe and other international markets, we may not succeed in commercializing our product candidates.**
- **We expect to expand our development, regulatory, and future sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.**
- **The COVID-19 pandemic has had and could continue to have an adverse impact on our developmental programs and our financial condition.**
- **We only have a limited number of employees to manage and operate our business.**

- **We depend on the knowledge and skill of our senior management and other key employees, and if we are unable to retain or if we fail to recruit additional highly skilled personnel, our business will be harmed.**
- **The third parties upon whom we rely for the supply of the drug product and drug substance used in our product candidates are our sole source of supply, and the loss of any of these suppliers could significantly harm our business.**
- **If we are unable to obtain and maintain sufficient patent protection for our product candidates, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to commercialize our product candidates successfully may be adversely affected.**
- **If we fail to maintain the listing of our common stock with a United States national securities exchange, the liquidity of our common stock could be adversely affected.**
- **The price of our common stock may be volatile and fluctuate substantially.**

#### **Risks Related to Our Financial Position and Need for Additional Capital**

##### Risks Related to Future Financial Condition

#### **\* We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.**

We may be forced to amend, delay, limit, reduce or terminate the scope of our development programs and/or limit or cease our operations if we are unable to obtain additional funding. As of September 30, 2021, we had cash and cash equivalents totaling \$40.4 million. Based on our current operating plans, we do not have sufficient cash and cash equivalents to fund our operating expenses and capital expenditures for at least the next 12 months from the filing date of this Quarterly Report on Form 10-Q. We do believe that our cash and cash equivalents at September 30, 2021 will enable us to fund our operating expenses and capital requirements into the second quarter of 2022. We will require additional capital to sustain our operations, including our reloxaliase and ALLN-346 development programs, beyond that time. We are exploring opportunities to secure additional funds through equity or debt financings or through collaborations, licensing transactions or other sources. However, there can be no assurance that we will be able to complete any such transaction on acceptable terms or otherwise. The failure to obtain sufficient funds on commercially acceptable terms when needed would have a material adverse effect on our business, results of operations and financial condition and jeopardize our ability to continue operations. We may need to implement additional cost reduction strategies, which may include amending, delaying, limiting, reducing, or terminating one or more of our ongoing or planned clinical trials or development programs of our product candidates. These factors raise substantial doubt about our ability to continue as a going concern.

#### **\* We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development, other operations or commercialization efforts.**

Since our inception, most of our resources have been dedicated to the nonclinical and clinical development of our lead product candidate, reloxaliase. As of September 30, 2021, we had working capital of \$34.3 million and capital resources consisting of cash and cash equivalents of \$40.4 million. Based on our current operating plans, we will continue to expend substantial resources for the foreseeable future as we continue clinical development of reloxaliase, seek regulatory approval and prepare for the potential commercialization of reloxaliase, conduct post-marketing studies of reloxaliase that could be required by regulatory authorities, and develop ALLN-346 and any other product candidates we may choose to pursue. These expenditures will include costs associated with research and development, conducting nonclinical studies and clinical trials, obtaining regulatory approvals, sales and marketing, and manufacturing and supply. In addition, other unanticipated costs may arise. Because the outcome of any clinical trial and/or regulatory approval process is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development, regulatory approval process and commercialization of reloxaliase and any future product candidates. In addition, as noted above, we have identified conditions and events that raise substantial doubt as to our ability to continue as a going concern if we are unable to obtain funding on a timely basis.

Based on our current operating plans, we do not have sufficient cash and cash equivalents to fund our operating expenses and capital expenditures for at least the next 12 months from the filing date of this Quarterly Report. We do believe that our cash and cash equivalents at September 30, 2021 will enable us to fund our operating expenses and capital requirements into the second quarter of 2022. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity, debt financings or other sources, such as strategic collaborations. Such financing may result in dilution to stockholders, imposition of debt covenants and repayment obligations, or other restrictions that may affect our business. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Our future funding requirements will depend on many factors, including, but not limited to:

- the time and cost necessary to complete our URIROX-2 pivotal Phase 3 clinical program and obtain regulatory approvals for reloxaliase and the costs of post-marketing studies that could be required by regulatory authorities, including any unforeseen costs we may incur as a result of clinical trial delays due to the COVID-19 pandemic or other causes;
- the costs of manufacturing clinical trial supplies of reloxaliase;
- our ability to successfully commercialize reloxaliase, if approved;
- the selling and marketing costs associated with reloxaliase, including the cost and timing of building our sales and marketing capabilities, if approved;
- the amount of sales and other revenues from reloxaliase, including the sales price and the availability of adequate third-party reimbursement;
- the cash requirements of any future acquisitions or discovery of product candidates;
- the progress, timing, scope and costs of our nonclinical studies and clinical trials, including the ability to enroll patients in a timely manner for potential future clinical trials;
- our ability to comply with the covenants under our current and future credit facilities;
- the time and cost necessary to respond to technological and market developments; and
- the costs of filing, prosecuting, maintaining, defending and enforcing any patent claims and other intellectual property rights.

Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate:

- clinical trials or other development activities for reloxaliase, ALLN-346 or any other product candidate;
- our preclinical research and development activities; or
- our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize reloxaliase or any future product candidate.

**Our existing and any future indebtedness could adversely affect our ability to operate our business.**

As of September 30, 2021, we had \$10.0 million of outstanding borrowings under the Pontifax Agreement. We are currently making quarterly interest payments. Beginning October 1, 2022, we will be required to repay any outstanding borrowings under the convertible debt facility with eight equal quarterly payments of principal and interest, or until such time as the then outstanding borrowings convert into shares of our common stock. Subject to the restrictions in this existing credit facility, we could in the future incur additional indebtedness beyond our borrowings from Pontifax.

Our outstanding indebtedness, including any additional indebtedness beyond our borrowings from Pontifax, combined with our other financial obligations and contractual commitments could have significant adverse consequences, including:

- requiring us to dedicate a portion of our cash resources to the payment of interest and principal, reducing money available to fund working capital, capital expenditures, product development and other general corporate purposes;
- increasing our vulnerability to adverse changes in general economic, industry and market conditions;
- subjecting us to restrictive covenants that may reduce our ability to take certain corporate actions or obtain further debt or equity financing;
- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete; and
- placing us at a competitive disadvantage compared to our competitors that have less debt or better debt servicing options.

We intend to satisfy our current and future debt service obligations with our existing cash and cash equivalents and future financings. However, we may not have sufficient funds, and may be unable to arrange for additional financing, to pay the amounts due under our existing credit facility or any other debt instruments. Failure to make payments or comply with other covenants under our existing credit facility or such other debt instruments could result in an event of default and acceleration of amounts due. Under our loan and security agreement with Pontifax, the occurrence of an event that would reasonably be expected to have a material adverse effect on our business, operations, assets or condition is an event of default. If an event of default occurs and Pontifax accelerates the amounts due, we may not be able to make accelerated payments, and the lenders could seek to enforce security interests in the collateral securing such indebtedness, which includes substantially all of our assets other than our intellectual property. In addition, the covenants under our existing credit facility, the pledge of our assets as collateral and the negative pledge with respect to our intellectual property could limit our ability to obtain additional debt financing.

#### Risks Related to Past Financial Condition

**\* We have incurred significant losses since inception, expect to incur significant and increasing losses for at least the next several years, have not generated any revenue, may never generate any revenue, and may never achieve or maintain profitability.**

We have incurred significant annual net operating losses in every year since our inception. We expect to continue to incur significant and increasing net operating losses for at least the next several years. Our net losses were \$12.7 million and \$8.0 million for the three months ended September 30, 2021 and 2020, respectively, and \$38.3 million and \$22.6 million for the nine months ended September 30, 2021 and 2020, respectively. As of September 30, 2021, we had an accumulated deficit of \$236.1 million. We have not generated any revenue, have not completed the development of any product candidate and may never have a product candidate approved for commercialization. We have funded our operations from inception through September 30, 2021 through gross proceeds of \$96.0 million from sales of our convertible preferred stock, net proceeds of \$67.0 million from our IPO which was completed in November 2017, net proceeds totaling \$33.8 million from follow-on offerings of common stock during 2020, borrowings of \$10.0 million under our credit facilities, net proceeds of \$14.6 million and \$1.8 million from the sale of our common stock under the Cowen ATM Agreement and the B. Riley ATM Agreement, respectively, and net proceeds of \$25.4 million from the registered direct offering completed in July 2021. We have devoted substantially all of our financial resources and efforts to the research and development of reloxaliase and, to a lesser extent, ALLN-346 and general and administrative expense to support such research and development. Our net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital.

We anticipate that our expenses will increase substantially if and as we:

- conduct future clinical trials of our lead product candidate, reloxaliase, including URIROX-2, our pivotal Phase 3 clinical program in adult patients with enteric hyperoxaluria;
- manufacture additional material for these potential future clinical trials;
- scale up our manufacturing process for reloxaliase to prepare for the submission of a potential biologics license application, or BLA, and commercialization if our clinical development program is successful;
- advance the development of ALLN-346;
- seek to identify and develop additional product candidates;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical trials, if any;
- establish sales, marketing, distribution and other commercial infrastructure in the future to commercialize various products for which we may obtain marketing approval, if any;
- obtain, maintain, expand and protect our intellectual property portfolio;
- hire and retain additional personnel, such as clinical, manufacturing, quality control and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and help us comply with our obligations as a public company; and
- add equipment and physical infrastructure to support our research and development programs.

Our ability to become and remain profitable depends on our ability to generate revenue. We do not expect to generate significant revenue unless and until we are, or any future collaborator is, able to obtain marketing approval for, and successfully commercialize, one or more of our product candidates. Successful commercialization will require achievement of key milestones, including initiating and successfully completing clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products for which we, or any of our future collaborators, may obtain marketing approval, satisfying any post-marketing requirements and obtaining reimbursement for our products from private insurance or government payors. Because of the uncertainties and risks associated with these activities, we are unable to accurately predict the timing and amount of revenues, if any, and if or when we might achieve profitability. We and any future collaborators may never succeed in these activities and, even if we do, or any future collaborators do, we may never generate revenues that are large enough for us to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates or continue our operations and cause a decline in our stock price. Market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed.

**We have a limited operating history, no products approved for sale and no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability.**

We commenced operations in 2011. Our operations to date have been limited to financing and staffing our company and developing our product candidates. We have not yet demonstrated an ability to obtain marketing approvals, manufacture a commercial-scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Accordingly, you should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by companies in the early stages of development, especially clinical stage biopharmaceutical companies such as ours. Any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will eventually need to transition from a company with a development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

## Risks Related to Drug Development, Regulatory Approval and Commercialization

### Risks Related to Clinical Development

**We are heavily dependent on the regulatory approval of reloxaliase (formerly referred to as ALLN-177) in the United States and Europe, and subsequent commercial success of reloxaliase, both of which may never occur.**

We are a late-stage biopharmaceutical company with no products approved by regulatory authorities or available for commercial sale. We have generated no revenue to date and do not expect to do so for the foreseeable future. As a result, our future success is currently dependent upon the clinical trial results, regulatory approval and commercial success of reloxaliase in one or more of the indications for which we seek approval. Our ability to generate revenues in the near term will depend on our ability to obtain regulatory approval and successfully commercialize reloxaliase on our own in the United States, if approved. We may experience delays in obtaining regulatory approval in the United States for reloxaliase, if it is approved at all, and our stock price may be negatively impacted. Even if we receive regulatory approval, the timing of the commercial launch of reloxaliase in the United States is dependent upon a number of factors, including, but not limited to, hiring sales and marketing personnel, pricing and reimbursement timelines, the production of sufficient quantities of commercial drug product and implementation of marketing and distribution infrastructure.

In addition, we have incurred and expect to continue to incur significant expenses as we continue to pursue the approval of reloxaliase in the United States, Europe and elsewhere. We plan to devote a substantial portion of our effort and financial resources in order to continue to grow our operational capabilities. This represents a significant investment in the clinical and regulatory success of reloxaliase, which is uncertain. The success of reloxaliase, if approved, and revenue from commercial sales, will depend on several factors, including:

- execution of an effective sales and marketing strategy for the commercialization of reloxaliase;
- acceptance by patients, the medical community and third-party payors;
- our success in educating physicians and patients about the benefits, administration and use of reloxaliase;
- the incidence and prevalence of patient populations with enteric hyperoxaluria in those markets in which reloxaliase is approved;
- the prevalence and severity of side effects, if any, experienced by patients treated with reloxaliase;
- the availability, perceived advantages, cost, safety and efficacy of alternative treatments, including potential alternate treatments that may currently be available or in development or may later be available or in development or regulatory approval or marketing of a generic, biosimilar, or any other version of oxalate decarboxylase, the active enzyme in reloxaliase;
- successful implementation of our manufacturing processes that are included in our BLA and production of sufficient quantities of commercial drug product;
- maintaining compliance with regulatory requirements, including current good manufacturing practices, or cGMPs, good laboratory practices, or GLP, and good clinical practices, or GCPs; and
- obtaining and maintaining patent, trademark and trade secret protection and regulatory exclusivity and otherwise protecting our rights in our intellectual property portfolio.

We may also fail in our efforts to develop and commercialize future product candidates, including ALLN-346 for patients with hyperuricemia and chronic kidney disease, or CKD. If this were to occur, we would continue to be heavily dependent on the regulatory approval and successful commercialization of reloxaliase, our development costs may increase and our ability to generate revenue or profits, or to raise additional capital, could be impaired.

**Results of earlier studies, or interim data from ongoing trials, may not be predictive of future clinical trial results, and planned or ongoing studies may not establish an adequate safety or efficacy profile for reloxaliase and other product candidates that we may pursue to justify proceeding to an application for regulatory approval or be worthy of regulatory approval if such an application is made.**

The results of preclinical studies and clinical trials of reloxaliase conducted to date and future studies and trials of reloxaliase, including our pivotal Phase 3 clinical trials, and other product candidates that we may pursue, may not be predictive of the results of subsequent clinical trials. For example, in November 2019, we announced topline data from our URIROX-1 clinical trial, our first Phase 3 pivotal trial of reloxaliase; these data may not be replicated in subsequent studies and trials of reloxaliase, including URIROX-2. Additionally, interim results of a clinical trial do not necessarily predict final



results. In June and November 2019, respectively, we announced interim data from our ongoing Study 206 of reloxaliase; these data may not be replicated in subsequent studies and trials of reloxaliase, in particular well-controlled clinical trials. Data, our interpretation of data and results from our Phase 2 clinical trials of reloxaliase in adults with enteric hyperoxaluria, or results from Study 206, do not ensure that we will achieve similar results in our URIROX-2 pivotal Phase 3 clinical trial in enteric hyperoxaluria or in clinical trials of reloxaliase in other patient populations. In addition, preclinical and clinical data are often susceptible to various interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and early-stage clinical trials have nonetheless failed to replicate results in later-stage clinical trials and subsequently failed to obtain marketing approval. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy despite having progressed through nonclinical studies and earlier clinical trials.

In particular, as is common with Phase 2 clinical trials, particularly clinical trials first conducted in a patient population with disease, we explored numerous endpoints and analyzed the data from our Phase 2 clinical trials of reloxaliase in a number of ways. In order to obtain approval for reloxaliase, we expect that the results of our URIROX-1 and URIROX-2 trials will have to demonstrate statistically significant improvement in the percent change from baseline in 24-hour urinary oxalate, or UOx, during Weeks 1-4, comparing reduction in the average UOx excretion across Weeks 1-4 with reloxaliase to placebo, the primary efficacy endpoint of both of our Phase 3 clinical trials. Although we achieved the primary efficacy endpoint in URIROX-1, and our analysis of the URIROX-1 clinical results confirmed a significant kidney stone and chronic kidney disease burden among patients with enteric hyperoxaluria and a correlation between kidney stone risk and UOx levels, there can be no guarantee that we will observe similar data in our URIROX-2 trial or our planned post-marketing studies of reloxaliase. Of note, two of our randomized Phase 2 clinical trials of reloxaliase (Study 713 and Study 649) did not demonstrate statistically significant results in the pre-specified primary endpoints. The design of our later-stage clinical trials differs in significant ways from our Phase 2 clinical trials of reloxaliase, which we believe may cause the outcome of these later-stage trials to differ from what we observed in our Phase 2 clinical trials. These differences include changes to inclusion and exclusion criteria, efficacy endpoints and statistical design.

Product candidates in Phase 3 clinical trials, such as reloxaliase in our URIROX pivotal Phase 3 clinical program, may fail to demonstrate sufficient efficacy despite having progressed through initial clinical trials, even if certain analyses of primary or secondary endpoints in those early trials showed potential treatment effects. Some of the data we present on the use of reloxaliase for the treatment of enteric hyperoxaluria is drawn from pre-specified analyses and other data is from post-hoc analyses. While we believe all the data from the Phase 2 program were useful in informing the design of our pivotal Phase 3 program, and will remain useful for clinical trials evaluating reloxaliase, the post-hoc analyses involve the inherent bias of post-hoc rendering of data and choice of analytical methods.

The primary efficacy endpoint in our pivotal Phase 3 program is percent change from baseline in 24-hour urinary oxalate, which is a biochemical measurement of the daily amount of oxalate handling by the kidney and therefore its reduction would indicate lessening of potential kidney damage by oxalate. However, based on published scientific literature and data generated in our own clinical trials, daily urinary oxalate excretion is a biomarker that demonstrates significant variability between patients and day-to-day for the same patient. This variability in 24 hour urinary oxalate excretion, especially in enteric hyperoxaluria patients, can be attributed to changes in diet, metabolic activity, hydration status or other factors. It can also be attributed to the manner in which these measurements are taken. In our completed Phase 2 clinical trials, we relied heavily on the efforts and contributions of investigative clinical sites and study patients to comply with accurate timing of 24 hour urine collection, with the complete collection of all of the patient's urine during a given 24 hour period and with the proper handling of collected urine specimens, including storage, documentation, sample handling and shipping to the testing laboratory. Following our completed Phase 2 clinical trials, we conducted a post-hoc review of these collection procedures. Although we are not aware of any case where the data reported in our prior clinical trials were inaccurate, due to the variability inherent in these data collection techniques, we cannot provide assurance that in all cases the data reported in our clinical trials accurately reflect the actual biochemical responses experienced by patients in these trials. We believe that capturing multiple measurements of 24 hour urinary oxalate excretion over the course of a clinical trial mitigates the risks of inherent variability, dietary change and sample handling associated with the testing of each individual 24 hour urine specimen, but no assurance can be given that any such variability will be fully addressed by this approach.

In addition, due to this variability in 24 hour urinary oxalate excretion, we may observe reductions in 24 hour urinary oxalate excretion in the placebo arms of our placebo-controlled trials. For example, although our URIROX-1 clinical trial met its primary endpoint with a -14.3% least square mean treatment difference relative to placebo, we did observe a higher reduction in urinary oxalate in the placebo group than we observed in our Phase 2 study, Study 713. As noted above, factors like diet and metabolic activity can play a role in urinary oxalate excretion, and these factors and others could partially explain the level of reduction observed in the URIROX-1 trial, which involved eight 24-hour urine collections over the course of the 28 days of the trial. Based on our review of the scientific literature, we expect that dietary restrictions and lifestyle changes would be difficult to maintain over real-world periods of time longer than a four-week study such as URIROX-1, and that it is unlikely that the level of urinary oxalate reduction observed in the placebo arm of the URIROX-1 trial would ultimately have a

clinically meaningful benefit to patients. However, if such observations are observed in URIROX-2 or future clinical trials that we conduct, it may have an adverse impact on the clinical benefit our trials demonstrate relative to placebo, which in turn could have an adverse impact on our ability to obtain regulatory approval for reloxaliase, on an accelerated approval basis or otherwise.

Additionally, several of our past clinical trials utilize an “open-label” trial design, including some of our Phase 2 clinical trials of reloxaliase. An “open-label” clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a “patient bias” where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an “investigator bias” where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results with any of our product candidates.

A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies, and we cannot be certain that we will not face similar setbacks. Even if early stage clinical trials are successful, we may need to conduct additional clinical trials for product candidates in additional patient populations or under different treatment conditions before we are able to seek approvals from the U.S. Food and Drug Administration, or FDA, and comparable foreign regulators to market and sell these product candidates. Our failure to demonstrate the required characteristics to support marketing approval for reloxaliase or any other product candidate we may choose to develop in any ongoing or future clinical trials would substantially harm our business, prospects, financial condition and results of operations.

**\* Although we have reached alignment with the FDA on the design of URIROX-2, our second pivotal Phase 3 trial of reloxaliase in patients with enteric hyperoxaluria, and our strategy to pursue a BLA submission for reloxaliase using the accelerated approval regulatory pathway, the clinical data we generate from our Phase 3 clinical program and/or the data we derive from third party datasets may not be sufficient to meet the FDA requirements for filing and obtaining marketing authorization via the accelerated approval regulatory pathway. If we are unable to obtain accelerated approval, we may be required to conduct additional preclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, reduce the likelihood of obtaining and/or delay the timing of obtaining, necessary marketing approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw accelerated approval.**

We intend to seek an accelerated approval development pathway for reloxaliase, and we may do so for our other product candidates. Under the accelerated approval provisions of the Federal Food, Drug, and Cosmetic Act and the FDA’s implementing regulations, the FDA may grant accelerated approval to a product designed to treat a serious or life-threatening condition that provides meaningful therapeutic advantage over available therapies and demonstrates an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval development pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is contingent on the sponsor’s agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug’s clinical profile or risks and benefits for accelerated approval. The FDA may require that any such confirmatory study be initiated or substantially underway prior to the submission of an application for accelerated approval. If such post-approval studies fail to confirm the drug’s clinical profile or risks and benefits, the FDA may withdraw its approval of the drug.

We have reached agreement with the FDA on the design of URIROX-2, our second pivotal Phase 3 clinical trial of reloxaliase in patients with enteric hyperoxaluria, and the FDA has advised us that they agree with our overall strategy to obtain accelerated approval for this product candidate. The data generated from the URIROX-1 and URIROX-2 trials could thus potentially form the basis of an accelerated approval of reloxaliase using reduction in UOx as a surrogate endpoint, with the final results from the URIROX-2 trial used to confirm clinical benefit post-approval. We believe 24 hour urinary oxalate excretion is an appropriate metric of the therapeutic effect of reloxaliase because 24 hour urinary oxalate excretion is a

biochemical measurement of the daily amount of oxalate handling by the kidney and therefore its reduction would indicate lessening of potential kidney damage by oxalate. However, the data generated in our clinical trials may not be sufficient to support an accelerated approval of reloxaliase, or any approval.

In February 2020, we announced that we reached an agreement in principle with the FDA on a streamlined design for URIROX-2. The FDA advised us then that, while it agreed in principle with the planned revisions to URIROX-2, certain details, to be specified in the protocol amendment and associated study documents for the revised trial design, remained subject to further clarification and confirmation. In March 2020, we submitted the protocol amendment for the streamlined design for URIROX-2 along with the Adaptive Design Charter. The revised trial design became effective following the FDA's 30-day review period and has been implemented in URIROX-2. Subsequently, in reaction to COVID, we submitted another protocol amendment in May 2020 to address COVID-related issues and further facilitate the conduct of the study. We have submitted another protocol amendment in order to accelerate the timing of the first of two planned interim analyses for the URIROX-2 trial. It is possible that additional modifications to URIROX-2 may be required, which could be material. Any unexpected requests from the FDA could delay the completion of the trial, result in additional costs and potentially jeopardize our ability to develop reloxaliase.

The FDA has advised us that part of its assessment of the adequacy of the URIROX-2 trial to support accelerated approval will be both the size of the effect seen on UOx in this trial and the predictive model from this UOx reduction effect that further supports a relationship between UOx levels and kidney stone formation rates, which model can be informed by data generated in the URIROX-2 trial or other data sources. This approach is consistent with the FDA's published guidance on the accelerated approval pathway, which provides that clinical data from a single clinical trial can be used to both support accelerated approval and verify the clinical benefit. This guidance also stipulates that the protocol and statistical analysis plan should clearly account for an analysis of the surrogate endpoint data to provide support for accelerated approval, with continuation of the randomized trial(s) to obtain data on the clinical endpoint that will be the basis for verifying the clinical benefit. In light of this guidance, URIROX-2 incorporates adaptive design elements that, through sample size re-estimations, will, if necessary, allow for increases in sample size and duration of treatment, based on accrued kidney stone disease progression rates and the conditional probability of achieving ultimate statistical success in the long-term follow-up phase of the trial as reviewed by the FDA.

As part of the URIROX-2 adaptive design, we had previously planned to conduct the first interim analysis after 130 subjects had been treated for at least six months. Given the adverse impact of the COVID-19 global pandemic on the rate of patient enrollment in this global study, and considering as well that enrollment in the study began in early 2019, we now plan to conduct the first interim analysis, which will include all subjects who were enrolled in the trial as of the end of November 2021, during the first quarter of 2022. Based upon the number of subjects enrolled to date, the number of subjects currently in screening, and management's estimate of expected enrollment through November, we currently estimate that this revised interim analysis would include UOx data during weeks 1-4 for approximately 80 patients but would not include sufficient data to evaluate UOx levels during weeks 16-24 or the blinded rate of kidney stone events, as previously planned. We have submitted a revised plan for the first interim analysis to the FDA as part of a planned update to the URIROX-2 statistical analysis plan and adaptive design charter, but the FDA may not agree with this proposal. The revised interim analysis, which will be conducted by an independent data monitoring committee, will assess whether the study continues to be adequately powered to evaluate efficacy against the primary endpoint, the change in UOx levels during weeks 1-4 versus baseline, with the planned enrollment of 200 subjects, or whether the study size should be increased. As a result of conducting an earlier interim analysis with a smaller sample size than previously planned, we anticipate that the ultimate size of the study may be larger than would have otherwise been required. Any adjustment in study size would be designed to ensure that the statistical power of the study remains sufficiently robust. As previously planned, the interim analysis will also include an assessment of futility with respect to the primary endpoint. We do not anticipate any changes to the planned second interim analysis, which will also include an assessment of the secondary endpoint of change in UOx levels during weeks 16-24 and of unblinded kidney stone events. The second interim analysis is expected to be conducted once 200 subjects have reached six months of treatment and is designed to enable a potential filing for accelerated approval for reloxaliase.

The data generated in our clinical trials may not be sufficient to provide additional support for the relationship between UOx levels and stone formation rates or to demonstrate the conditional probability of achieving ultimate statistical success. Based on the interim data we generate in the URIROX-2 trial, we may be required to increase the number of patients treated and/or extend the follow-up period before we are able to submit a BLA for reloxaliase seeking accelerated approval, if ever. If we are required to increase the number of patients treated and/or extend the follow-up period in our clinical trials, it could have a material adverse effect on our expected clinical and regulatory timelines, business, prospects, financial condition and results of operations.

We expect that our data package for accelerated approval would include a conditional power estimate based on the effect of reloxaliase on reducing kidney stone disease progression as assessed with interim data from the URIROX-2 trial, the effects of reloxaliase on reduction of UOx in the URIROX-1 and URIROX-2 trials, and further support for the model relating UOx

levels to kidney stone disease progression, including but not limited to available data obtained in the URIROX-2 trial. We expect we will continue to work with scientific experts to identify additional third-party datasets to further substantiate the relationship between urinary oxalate levels and the risk of kidney stones and kidney dysfunction. The FDA has advised us that we have not yet provided sufficient data regarding UOx excretion necessary to support its use as a surrogate endpoint for these clinical trials and questioned whether changes in UOx of the magnitude expected would be reasonably likely to predict clinical benefit. We have provided the FDA with the details of analyses we conducted using available data collected from a third-party clinical database and data from our URIROX-1 trial, in order to demonstrate an increased probability of kidney stone events in patients with enteric hyperoxaluria and increasing UOx levels. The FDA has advised us that it remains concerned about the strength of this relationship, based in part on the limited clinical data currently available and whether other factors may play a role in the production of kidney stones. The data we generate from the URIROX-1 and URIROX-2 trials, together with additional data we identify from third-party datasets, may not be sufficient to satisfy the FDA that we have generated a model that supports a relationship between UOx levels and stone formation rates as necessary to use the accelerated approval regulatory pathway for reloxaliase. If we are unable to reach consensus with the FDA on the magnitude of UOx reduction significant enough to predict clinical benefit, we may be required to demonstrate effectiveness by showing an effect on stone formation directly, or conduct one or more additional clinical trials to demonstrate this effect, prior to the submission of a BLA for reloxaliase.

Furthermore, even if we generate clinical data sufficient to support a BLA submission seeking accelerated approval, there can be no assurance that such application will be accepted or that approval will be granted on a timely basis, or at all. For example, the FDA may require demonstration that we have initiated or made substantial progress in our clinical follow-up of trial subjects, or any such clinical outcomes trial, prior to the submission of our BLA for accelerated approval of reloxaliase. The FDA notes in its guidance that when the same trial is used to support accelerated approval and verify clinical benefit, the data to verify the clinical benefit may be, in some cases, nearly complete by the time of accelerated approval. In addition, if another company receives full approval from the FDA to market a product for treatment of enteric hyperoxaluria, our ability to seek and obtain accelerated approval for reloxaliase in the same or similar indication may be materially adversely affected. The FDA or foreign regulatory authorities also could require us to conduct further studies or trials prior to considering our application or granting approval of any type. We might not be able to fulfill the FDA's requirements in a timely manner, which would cause delays, or approval might not be granted because our submission is deemed incomplete by the FDA. A failure to obtain accelerated approval or any other form of expedited development, review or approval for a product candidate would result in a longer time period to obtain approval for and commercialize such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

Even if we receive accelerated approval from the FDA for reloxaliase or any of our other product candidates, we will be subject to rigorous post-marketing requirements, including the completion of confirmatory post-market clinical trial(s) to verify the clinical benefit of the product, and submission to the FDA of all promotional materials prior to their dissemination. The FDA could seek to withdraw accelerated approval for multiple reasons, including if we fail to conduct any required post-market study with due diligence, a post-marketing study does not confirm the predicted clinical benefit, other evidence shows that the product is not safe or effective under the conditions of use, or we disseminate promotional materials that are found by the FDA to be false and misleading. We anticipate that whether the reduction in kidney stone formation we observe in our Phase 3 clinical program for reloxaliase is sufficient to demonstrate a clinical benefit will ultimately be a review issue with FDA.

A failure to obtain accelerated approval or any other form of expedited development, review or approval for a product candidate that we may choose to develop would result in a longer time period prior to commercializing such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

**Our proprietary technological approach is a new approach to the design and development of stable, non-absorbable oral biological therapies and may not result in any additional product candidates or ultimately any products of commercial value.**

We have developed our proprietary know-how in enzyme technology which allows us to design, formulate and deliver non-absorbed and stable enzymes orally and in sufficient doses for activity in the GI tract. While the general therapeutic approach of deploying a non-absorbed drug into the GI tract to reduce metabolic disease burden in patients with kidney disease has been proven successful in several therapeutic categories, we cannot assure you that our technological approach will ultimately work for reloxaliase, ALLN-346, or any other product candidates we may develop. In addition, while we believe our enzyme therapeutic candidates will not be absorbed, future clinical trials may find this not to be true. We also cannot guarantee that any other aspects of our proprietary technological approach will yield product candidates that could enter clinical development, receive regulatory approval and, ultimately, be commercially valuable.

**Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.**

Our Phase 3 clinical program for reloxaliase consists of two Phase 3 clinical trials of reloxaliase in adult patients with enteric hyperoxaluria. We have also conducted scientific advisory meetings with regulatory authorities in three countries within the European Union, or the EU. Even though we have received and incorporated guidance from these regulatory authorities, foreign regulators could disagree that we have satisfied their requirements to commence our clinical trials in those jurisdictions. Further, the FDA or other regulatory authorities could change their position on the acceptability of our trial designs, or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials or impose stricter approval conditions than we currently expect. We may need to conduct additional clinical trials or other testing for, among other parameters, drug-drug interactions, the generation of formate (i.e. a metabolic byproduct resulting from the degradation of oxalate by reloxaliase) and increased dosages of our product candidates. Successful completion of our clinical trials is a prerequisite to submitting a BLA to the FDA and a Marketing Authorization Application, or MAA, in Europe for each product candidate and, consequently, the ultimate approval and commercial marketing of reloxaliase, ALLN-346 and any product candidates we may develop in the future. We do not know whether any of our clinical trials will be completed on schedule, if at all.

We may experience delays in initiating or completing our planned clinical trials or additional preclinical studies or clinical trials in the future, and we may experience numerous unforeseen events during, or as a result of, any future clinical trials that we conduct that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulators or institutional review boards, or IRBs, or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations, or CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- we may experience delays in recruiting, or be unable to recruit, a sufficient number of suitable patients to participate in our clinical trials;
- the patients and sites who participate in our trials may not comply with protocols, such as compliance with the capsule and timing regimen and urine collection requirements, rendering the results insufficient or uninterpretable;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials or we may decide to abandon drug development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our third party contractors may fail to comply with regulatory or legal requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators or IRBs or ethics committees may require that we or our investigators, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- the occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- any changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs or ethics committees to suspend or terminate the trials, or reports may arise from preclinical or clinical testing of other therapies that raise safety or efficacy concerns about our product candidates; and
- the FDA or other comparable foreign regulators may require us to submit additional data or impose other requirements before permitting us to initiate a clinical trial.

We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board for such trial or by the FDA or other comparable foreign regulators. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements, GCP or our clinical protocols, inspection of the clinical trial operations or trial sites by the FDA or other comparable foreign regulators resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Further, the FDA may disagree with our clinical trial design and our interpretation of data from clinical trials or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials.

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

**The regulatory approval processes of the FDA and comparable foreign regulators are lengthy, time-consuming and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for reloxaliase or our other product candidates, our business will be substantially harmed.**

We are not permitted to market reloxaliase or any of our other product candidates in the United States or the EU until we receive approval of a BLA from the FDA or an MAA from the EMA, respectively. Prior to submitting a BLA to the FDA or an MAA to the EMA for approval of any of our product candidates for a specific indication, we are required to complete preclinical studies and clinical trials.

Successfully initiating and completing our clinical program and obtaining approval of a BLA or an MAA is a complex, lengthy, expensive and uncertain process, and the FDA, the EMA or other comparable foreign regulators may delay, limit or deny approval of any of our candidates for many reasons, including, among others:

- we may not be able to demonstrate that our product candidates are safe and effective to the satisfaction of the FDA or the EMA;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or the EMA for marketing approval;
- the FDA or the EMA may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the FDA or the EMA may require that we conduct additional clinical trials;
- the FDA or the EMA or other applicable foreign regulators may not approve the formulation, labeling or specifications of reloxaliase or our other product candidates;
- the CROs that we retain to conduct our clinical trials may take actions outside of our control that materially adversely impact our clinical trials;
- the FDA or the EMA may find the data from preclinical studies and clinical trials insufficient to demonstrate that the clinical and other benefits of reloxaliase and our other product candidates outweigh their safety risks;
- the FDA or the EMA may disagree with our interpretation of data from our preclinical studies and clinical trials, including our characterization of observed toxicities;
- the FDA or the EMA may not accept data generated at our clinical trial sites;
- if our BLAs or MAAs, if and when submitted, are reviewed by the FDA or the EMA, as applicable, the regulatory agency may have difficulties scheduling the necessary review meetings in a timely manner, advisory committees or reviewers may recommend against approval of our application or may recommend that the FDA or the EMA, as applicable, require, as a condition of approval, additional preclinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;
- the FDA may require development of a Risk Evaluation and Mitigation Strategy as a condition of approval or post-approval, and the EMA may grant only conditional approval or impose specific obligations as a condition for marketing authorization, or may require us to conduct post-authorization safety studies;
- the FDA, the EMA or other applicable foreign regulators may find deficiencies with or not approve the manufacturing processes or facilities of third-party manufacturers with which we contract; or
- the FDA or the EMA may change their approval policies or adopt new regulations.

Any of these factors, many of which are beyond our control, could jeopardize our ability to obtain regulatory approval for and successfully market reloxaliase or any of our other product candidates. Any such setback in our pursuit of regulatory approval would have a material adverse effect on our business and prospects.

In addition to the United States and Europe, we or potential collaborators intend to market our product candidates, if approved, in other international markets. Such marketing will require separate regulatory approvals in each market and

compliance with numerous and varying regulatory requirements. The approval procedures vary from country-to-country and may require additional testing. Moreover, the time required to obtain approval may differ from that required to obtain FDA or EMA approval. In addition, in many countries, a product candidate must be approved for reimbursement before it can be approved for sale in that country, even if regulatory approval has been obtained. Approval by the FDA or the EMA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA or the EMA. The regulatory approval process in other international markets may include all of the risks associated with obtaining FDA or EMA approval.

Health regulatory agencies globally may experience disruptions in their operations as a result of COVID-19. The FDA and comparable foreign regulatory agencies may have slower response times or be under-resourced to continue to monitor our clinical trials and, as a result, review, inspection, and other timelines may be materially delayed. It is unknown how long these disruptions could continue, were they to occur. Any elongation or de-prioritization of our clinical trials or delay in regulatory review resulting from such disruptions could materially affect the development and study of our product candidates. For example, regulatory authorities may require that we not distribute a product candidate lot until the relevant agency authorizes its release. Such release authorization may be delayed as a result of the COVID-19 pandemic and could result in delays to our ongoing clinical trials.

#### Risks Related to Clinical Trials

##### **Foreign regulators may not agree with our proposed Phase 3 clinical program for reloxaliase, in which case we may be required to modify our planned clinical trials, or run additional clinical trials, before we can submit foreign applications for marketing approval for reloxaliase.**

In January 2019, we announced that we had reached agreement with the FDA on both the design of URIROX-2, our second pivotal Phase 3 trial of reloxaliase in patients with enteric hyperoxaluria, and our strategy to pursue a BLA submission for reloxaliase using the accelerated approval regulatory pathway. In February 2020, we announced that we reached an agreement in principle with the FDA on a streamlined design for URIROX-2. However, our Phase 3 program may not be sufficient to support the submission of applications for marketing approval in foreign jurisdictions, including the European Union. Although our preliminary discussions with regulatory authorities in select countries within the European Union lead us to believe our Phase 3 program, if successful, may be sufficient to support the submission of an MAA in Europe via the conditional approval pathway, which is similar to the FDA's accelerated approval pathway, these discussions are not binding on such authorities or the EMA. Accordingly, no assurance can be given that our Phase 3 program will be sufficient to support the submission of an MAA in Europe, and we may be required to modify the design of these planned trials, or run additional clinical trials, before seeking marketing approval. Any of these decisions could have a material adverse effect on our expected clinical and regulatory timelines, business, prospects, financial condition and results of operations.

##### **Because we are developing product candidates for the treatment of diseases in which there is little clinical trial experience and, in some cases, using new endpoints or methodologies, there is increased risk that the FDA or other regulatory authorities may not consider the endpoints of our clinical program to provide clinically meaningful results and that these results may be hard to analyze.**

Only one drug has previously been approved by the FDA on the basis of a biochemical measurement of 24 hour UOx excretion or plasma oxalate, or POx, reductions, endpoints used in our Phase 2 clinical program and for our pivotal Phase 3 clinical program. The FDA retains discretion to reserve judgment on whether our clinical endpoints and the results we obtain in our pivotal Phase 3 clinical program sufficiently demonstrate clinical meaningfulness until the FDA reviews the data included in our planned BLA submission, which will not occur for several years from now, if at all. As a result, the design and conduct of clinical trials for the treatment of hyperoxaluria, and the underlying conditions and disorders that drive the metabolic disease, are subject to increased risk.

Moreover, even if the FDA does find our success criteria to be sufficiently validated and clinically meaningful, we may not achieve the pre-specified endpoint to a degree of statistical significance, in either or both of the Phase 3 clinical trials that we believe will be necessary for approval. Further, even if we do achieve the pre-specified criteria, we may produce results that are unpredictable or inconsistent with the results of the secondary efficacy endpoints in the trials. The FDA also could give overriding weight to other efficacy endpoints, even if we achieve statistically significant results on the primary endpoint, if we do not achieve statistically significant or clinically meaningful results on any of our secondary efficacy endpoints. The FDA also weighs the benefits of a product against its risks and the FDA may view the efficacy results in the context of safety as not being supportive of regulatory approval. Other regulatory authorities in the EU and other countries may take similar positions.

In addition, we conducted a Phase 2 clinical trial of reloxaliase utilizing an open-label, basket trial design that enrolled subsets of patients suffering from complications of severe hyperoxaluria, including adolescents and adults with primary



hyperoxaluria or severe forms of secondary hyperoxaluria, both of which can lead to systemic oxalosis. We announced interim data from Study 206 in June 2019 and topline data in November 2019. Based on results from this trial, we are currently exploring a possible registrational path for reloxaliase for patients with enteric hyperoxaluria and advanced CKD. Basket trial designs permit the exploration of a study drug in patient populations with common biochemical markers, such as patients afflicted with different forms of cancer, but the same genetic mutation. We cannot predict whether the design of our pivotal Phase 3 clinical program, or any other future trials that we may conduct may successfully demonstrate reloxaliase or any future product candidate's safety and efficacy.

**If clinical trials of our product candidates fail to satisfactorily demonstrate safety and efficacy to the FDA and other comparable foreign regulators, we, or any future collaborators, may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of these product candidates.**

We, and any future collaborators, are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Comparable foreign regulators, such as the European Medicines Agency, or EMA, impose similar restrictions. We, and any future collaborators, may never receive such approvals. We, and any future collaborators, must complete extensive preclinical development and clinical trials to demonstrate the safety and efficacy of our product candidates in humans before we, or they, will be able to obtain these approvals.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We have not previously submitted a BLA to the FDA or similar drug approval applications to comparable foreign regulators for any of our product candidates. Any inability to complete preclinical and clinical development successfully could result in additional costs to us, or any future collaborators, and impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. Moreover, if (1) we, or any future collaborators, are required to conduct additional clinical trials or other testing of our product candidates beyond the trials and testing that we, or they contemplate, (2) we, or any future collaborators, are unable to successfully complete clinical trials of our product candidates or other testing, (3) the results of these trials or tests are unfavorable, uncertain or are only modestly favorable, or (4) there are unacceptable safety concerns associated with our product candidates, we, or any future collaborators, may:

- incur additional unplanned costs, including as a result of any delays in our research programs resulting from factors related to the COVID-19 pandemic;
- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post-marketing testing or other requirements; or
- be required to remove the product from the market after obtaining marketing approval.

Our failure to successfully complete clinical trials of our product candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of our product candidates would significantly harm our business, prospects, financial condition and results of operations.

**\* We depend heavily on the success of our most advanced program, reloxaliase, and, to a lesser extent, that of ALLN-346, which is in Phase 2a clinical development. Preclinical testing and clinical trials of product candidates may not be successful. If we are unable to commercialize any product candidates we may develop or experience significant delays in doing so, our business will be materially harmed.**

We have invested substantially all of our efforts and financial resources in the identification and development of our most advanced product program, reloxaliase for the treatment of hyperoxaluria, and, to a lesser extent, ALLN-346 for the treatment of gout. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of reloxaliase, ALLN-346 and our future product

candidates. The success of reloxaliase, ALLN-346 and future product candidates we may identify and develop will depend on many factors, including the following:

- sufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials for our most advanced program;
- successful completion of preclinical studies;
- successful enrollment in, and completion of, clinical trials;
- addressing any delays in our preclinical studies and clinical trials resulting from factors related to the COVID-19 pandemic;
- receipt of marketing approvals from applicable regulatory authorities in our target indications and potential additional indications;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and non-patent exclusivity for our medicines;
- launching commercial sales of the medicines, if and when approved, whether alone or in collaboration with others;
- acceptance of the medicines, if and when approved, by patients, the medical community, and third-party payors;
- effectively competing with other therapies and treatment options;
- a continued acceptable safety profile of the medicines following approval;
- enforcing and defending intellectual property and proprietary rights and claims; and
- achieving desirable medicinal properties for the intended indications.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize reloxaliase, ALLN-346, or any other product candidates we may develop, which would materially harm our business.

Of the large number of biologics and drugs in development in the pharmaceutical industry, only a small percentage result in the submission of a BLA or NDA to the FDA or an MAA to the EMA. Not all BLAs, NDAs or MAAs that are submitted to a regulatory agency are approved for commercialization. Reloxaliase is an oral biologic product candidate, which is a less common formulation in the biotech industry. Accordingly, there are few oral biologic therapeutics that have achieved regulatory approval. Furthermore, even if we do receive regulatory approval to market our most advanced program or any other product candidates that we may identify and develop, any such approval may be subject to limitations on the indicated uses for which we may market the product. Accordingly, even if we are able to obtain the requisite financing to continue to fund our research programs, we cannot assure you that we will successfully develop or commercialize reloxaliase, ALLN-346, or any of our other research programs. If we or any of our future development partners are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize reloxaliase, ALLN-346, or any product candidates we may identify and develop, we may not be able to generate sufficient revenue to continue our business.

**\* Changes in regulatory requirements and guidance may also occur and we may need to amend clinical trial protocols submitted to applicable regulatory authorities to reflect these changes. Amendments may require us to resubmit clinical trial protocols to IRBs or ethics committees for re-examination, which may impact the costs, timing or successful completion of a clinical trial.**

The FDA's and other comparable foreign regulators' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of reloxaliase and any future product candidates we may develop. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States, the EU or other countries or jurisdictions. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability, which would harm our business, prospects, financial condition and results of operations.

If we are required to conduct additional clinical trials or other studies with respect to reloxaliase or any future product candidates we may develop beyond those that we currently contemplate, or if we are unable to successfully complete our clinical trials or other studies, we may be delayed in obtaining regulatory approval of reloxaliase, ALLN-346, or any future product candidates we may develop, we may obtain approval of indications that are not as broad as intended or we may not be able to obtain regulatory approval at all. Our product development costs will also increase if we experience delays in testing or

approvals, and we may not have sufficient funding to complete the testing and approval process for reloxaliase, ALLN-346, or any future product candidates we may develop. Significant clinical trial delays could allow our competitors to bring products to market before we do and impair our ability to commercialize our products if and when approved. If any of this occurs, our business would be harmed.

**\* If we experience delays or difficulties in the enrollment or continuation of patients in our clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.**

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or comparable foreign regulators, or if a significant number of patients withdraw from our clinical trials. In particular, because we are focused on patients with enteric hyperoxaluria with respect to our Phase 3 development of reloxaliase, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. For example, in part because of the impact of the pandemic, during the first quarter of 2021 we determined that site initiation and patient enrollment in the URIROX-2 study was proceeding at a slower rate than we had originally projected. Accordingly, we revised our estimate for the expected timing of the first interim analysis from the first quarter of 2022 to the second or third quarter of 2022, and our estimate for the expected timing of the topline data from the third quarter of 2022 to the fourth quarter of 2022 or the first quarter of 2023. During the third quarter of 2021, we further revised our plans and timing for the first interim analysis. Although our initial plan for the first interim analysis had been to assess six-month data on 130 patients, our revised plan is now to assess one-month data on patients enrolled as of the end of November 2021, which we estimate will be approximately 80 patients. We expect that we will conduct the first interim analysis during the first quarter of 2022. Given uncertainty regarding the timeline for completion of enrollment, we are not currently providing an estimate for the timing of the second interim analysis and topline data from the URIROX-2 study.

Patient enrollment may be affected by other factors including, but not limited to:

- the severity of the disease under investigation;
- the design of the clinical trial;
- the size and nature of the patient population;
- the eligibility criteria for the clinical trial in question;
- the availability of appropriate screening tests for study subjects;
- the perceived risks and benefits of the product candidate under study;
- availability of competing therapies and clinical trials;
- clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies or treatment approaches;
- the efforts to facilitate timely enrollment in clinical trials;
- the ability to obtain and maintain patient consents and the risk that patients enrolled in clinical trials will not complete a clinical trial;
- the patient referral practices of physicians;
- the ability of patients to comply with the protocol, including capsule and timing regimen and urine collection requirements;
- the ability to monitor patients adequately during and after treatment;
- the proximity and availability of clinical trial sites for prospective patients and any limitations on travel or access to trial sites (including due to the COVID-19 pandemic); and
- the extent to which our competitors have ongoing clinical trials for product candidates that treat the same indications as our product candidates.

In addition, patients may withdraw from our clinical trials prematurely, which could also have a negative effect on our ability to complete our clinical trials or obtain and retain regulatory approvals. For example, both of our Phase 3 clinical trials for reloxaliase are randomized, double-blind and placebo controlled, and our URIROX-2 trial is intended to potentially enable a BLA submission using the accelerated approval pathway, following which patients would continue in the study for a minimum treatment period of two years to confirm clinical benefit post-approval. Patients enrolled in our ongoing Phase 3 clinical trial may elect to withdraw from the trial prematurely, particularly in the event we are able to obtain an accelerated

approval. If a significant number of patients withdraw from the trial prematurely it could potentially jeopardize the interpretability of the results from our clinical trials, which could have a material adverse effect on our ability to obtain, or retain, regulatory approval for reloxaliase.

Further, timely enrollment in clinical trials is reliant on clinical trial sites which may be adversely affected by global health matters, including, among other things pandemics. For example, our clinical trial sites may be located in regions currently being afflicted by the COVID-19 pandemic. Some factors from the COVID-19 pandemic that we believe may adversely affect enrollment in our trials include:

- the diversion of healthcare resources away from the conduct of clinical trial matters to focus on pandemic concerns, including the attention of physicians serving as our clinical trial investigators, hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- limitations on travel that interrupt key trial activities, such as clinical trial site initiations and monitoring;
- interruption in global shipping affecting the transport of clinical trial materials, such as investigational drug candidates and comparator drugs used in our trials; and
- employee furlough days that delay necessary interactions with local regulators, ethics committees and other important agencies and contractors.

These and other factors arising from the COVID-19 coronavirus could worsen in countries that are already afflicted with the virus or could continue to spread to additional countries, each of which may further adversely impact our clinical trials. The global outbreak of the COVID-19 coronavirus continues to evolve (with some areas reporting increasing cases of COVID-19) and the conduct of our trials may continue to be adversely affected, despite efforts to mitigate this impact.

**\* Our product candidates may cause undesirable side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.**

Undesirable side effects caused by our product candidates could cause us to interrupt, delay or halt preclinical studies or could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulators. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects. Although the incidences of adverse events that were considered related to study drug in our Phase 2 trials and URIROX-1 were low and no drug-related serious or severe adverse events were observed, it is possible that our URIROX-2 trial or future clinical trials we conduct may not demonstrate a favorable safety profile. In addition, while we have not observed reloxaliase to be absorbed into the bloodstream in our clinical trials to date, it is possible absorption could occur in our URIROX trials, particularly with a target population of patients with enteric hyperoxaluria, who are predisposed to chronic hyperabsorption. We may also need to conduct additional clinical trials or other testing for, among other things, drug-drug interactions, the generation of formate and increased dosages of our product candidates. In the event of adverse safety issues, our trials could be suspended or terminated, and the FDA or comparable foreign regulator could order us to cease further development of or deny approval of reloxaliase, ALLN-346 or any future product candidate we may develop for any or all targeted indications. Any drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Further, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients and limited duration of exposure, rare and severe side effects of our product candidates may only be uncovered with a significantly larger number of patients exposed to the product candidate. If reloxaliase or our other product candidates receive

marketing approval and we or others identify undesirable side effects caused by such product candidates (or any other similar drugs) after such approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of such product candidates;
- regulatory authorities may require the addition of labeling statements, such as a "boxed" warning or a contraindication;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way such product candidates are distributed or administered, conduct additional clinical trials or change the labeling of the product candidates;
- regulatory authorities may require a Risk Evaluation and Mitigation Strategy plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools;
- we may be subject to regulatory investigations and government enforcement actions;
- we may decide to remove such product candidates from the marketplace;
- we could be sued and held liable for injury caused to individuals exposed to or taking our product candidates; and
- our reputation may suffer.

We believe that any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidates and could substantially increase the costs of commercializing our product candidates, if approved, and significantly impact our ability to successfully commercialize our product candidates and generate revenues.

#### Risks Related to Regulatory Approval

**Even if we receive regulatory approval for any of our product candidates, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our drugs.**

If the FDA, the EMA or a comparable foreign regulator approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the drug will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and GCPs for any clinical trials that we conduct post-approval. Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the drug. Later discovery of previously unknown problems with a drug, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the drug, withdrawal of the drug from the market, or voluntary or mandatory drug recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of drug approvals;
- drug seizure or detention, or refusal to permit the import or export of the drug; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

Accordingly, assuming we, or any collaborators we may have, receive marketing approval for one or more product candidates we develop, we, and such collaborators, and our and their contract manufacturers will continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance, and quality control. If we and such collaborators are not able to comply with post-approval regulatory requirements, we and such collaborators could have the marketing approvals for our products withdrawn by regulatory authorities and our, or such collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our business, operating results, financial condition, and prospects.

**The manufacture and packaging of pharmaceutical products such as reloxaliase is subject to FDA requirements and those of similar foreign regulatory bodies. If we or our third-party manufacturers fail to satisfy these requirements, our product development and commercialization efforts may be harmed.**

The manufacture and packaging of pharmaceutical products, such as reloxaliase, if approved, is regulated by the FDA and similar foreign regulatory bodies and must be conducted in accordance with the FDA's cGMP and comparable requirements of foreign regulatory bodies. There are a limited number of manufacturers that operate under these cGMP regulations who are both capable of manufacturing reloxaliase and willing to do so. We may not be able to identify or secure contracts with manufacturers with suitable capability to manufacture reloxaliase according to FDA requirements on favorable terms or at all. Failure by us or our third-party manufacturers to comply with applicable regulations or requirements could result in sanctions being imposed on us, including fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approval of our products, delays, suspension or withdrawal of approvals, seizures or voluntary or mandatory recalls of product, operating restrictions and criminal prosecutions, any of which could harm our business. The same requirements and risks are applicable to the suppliers of the key raw material used to manufacture reloxaliase, including the specific bacterial strains that are used to manufacture the oxalate decarboxylase enzyme, which is an active ingredient in reloxaliase.

Changes in the manufacturing process or procedure, including a change in the location where the product is manufactured or a change of a third-party manufacturer, may require prior FDA review and approval of the manufacturing process and procedures in accordance with the FDA's cGMPs. Any new facility is subject to a pre-approval inspection by the FDA and would again require us to demonstrate product comparability to the FDA. There are comparable foreign requirements. This review may be costly and time consuming and could delay, constrain or prevent the launch or supply of a product.

Furthermore, in order to obtain approval of our product candidates, including reloxaliase, by the FDA and foreign regulatory agencies, we will be required to consistently produce the drug substance and the finished product in commercial quantities and of specified quality on a repeated basis and document our ability to do so. This requirement is referred to as process validation. We have not yet met with the FDA or foreign regulatory agencies to understand the complete manufacturing requirements which must be met for reloxaliase to receive regulatory approval. Each of our potential suppliers will likely use a different method to manufacture drug substance, which has the potential to increase the risk to us that our manufacturers will fail to meet applicable regulatory requirements. We also need to complete process validation on the finished product in the packaging we propose for commercial sales. This includes testing of stability, measurement of impurities and testing of other product specifications by validated test methods. If the FDA or foreign regulatory agencies do not consider the result of the process validation or required testing to be satisfactory, we may not obtain approval to launch the product or approval, launch or availability of commercial supply after launch may be delayed.

The FDA and similar foreign regulatory bodies may also implement new requirements, or change their interpretation and enforcement of existing requirements, for manufacture, packaging or testing of products at any time. If we are unable to comply, we may be subject to regulatory, civil actions or penalties which could harm our business.

**We must reach agreement with FDA and foreign regulatory agencies on an appropriate method for evaluating bioavailability and/or bioequivalence in connection with our planned BLA submission for reloxaliase and in support of any scale up of commercial supply of reloxaliase in anticipation of a commercial launch. Failure to reach agreement or failure to demonstrate bioavailability and/or bioequivalence may require that we run additional preclinical or clinical studies, which could delay the timing of a potential BLA submission or approval.**

To meet the increased clinical demand for reloxaliase following Phase 1 and Phase 2 clinical trials, we moved the site of production and increased the production scale of both drug substance and drug product. Changes in the manufacturing process or procedure, including a change in the location where the product is manufactured or a change of a third-party manufacturer, may require prior FDA review and approval of the manufacturing process and procedures in accordance with the FDA's cGMPs. Any new facility is subject to a pre-approval inspection by the FDA and requires us to demonstrate product comparability to the FDA. There are comparable foreign requirements. In the past, we have utilized established scientific

methodology to demonstrate the chemical comparability of relaxaliase after each of these successive changes and used these comparability data to support the production of clinical trial materials for Phase 1, Phase 2, and global Phase 3 trials.

The unique crystalline nature of relaxaliase and its expected mechanism of action, on food in the gastrointestinal tract, without absorption of the enzyme across the gut lining, precludes the use of traditional absorption-dependent methods for determining bioavailability and bioequivalence. As a result, we have developed an *in vitro* method to describe an area under the curve (AUC) of catalytic potency over time in simulated gastric fluid. We believe that the method is sufficiently discriminating to detect potential variation in the product and provide evidence of bioequivalence in the event of future changes to the manufacturing process or sites of production. In preparation for our planned future BLA submission, we expect to meet with the FDA in 2021 to discuss the suitability of this method as a tailored, product-specific alternative to traditional bioavailability and/or bioequivalence studies.

It is possible that the FDA or comparable foreign authorities may not agree with the methods we propose to use to demonstrate bioequivalence across our clinical trials for purposes of obtaining regulatory approvals and/or in connection with manufacturing commercial supply, or they may not accept the results of those methods as sufficient to demonstrate bioequivalence. In this case, we may be required to perform additional *in vivo* animal studies or confirmatory human studies. If the FDA requires us to pursue these actions, this could significantly increase the cost of our clinical and manufacturing development and/or delay the timing of a potential BLA submission or approval.

**\* Manufacture and supply of drug substance, drug product and finished drug product is a complex and technically challenging undertaking, particularly for oral biologics, and there is potential for failure at many points in the manufacturing, testing, quality assurance and distribution supply chain, as well as the potential for latent defects after a product has been manufactured and distributed.**

Manufacture and supply of drug substance, drug product and finished drug product is technically challenging, particularly for oral biologics. Changes that may be made outside the purview of our direct control can have an impact on the success of our processes, on quality, and on successful delivery of finished drug product. Mistakes and mishandling could affect successful production and supply. Some of these risks include:

- failure to follow cGMP requirements or mishandling of our product while in production or in preparation for transit;
- delays in analytical results or failure of analytical techniques that we depend on for quality control and release of drug product;
- natural disasters, global pandemics (including the COVID-19 pandemic), labor disputes, lack of raw material supply, issues with facilities and equipment or other forms of disruption to business operations at our manufacturing facilities; and
- latent defects that may become apparent after drug product has been released and which may result in recall or required destruction of drug product.

If any of these risks materialize, it would have a material and adverse impact on our ability to develop, obtain regulatory approval for and market relaxaliase or ALLN-346, if approved.

## Risks Related to Sales, Marketing and Competition

**The incidence and prevalence for target patient populations of our product candidates have not been established with precision. If the market opportunities for our product candidates are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer. Our ability to successfully identify patients and acquire a significant market share will be necessary for us to achieve profitability and growth.**

We focus our research and product development on treatments for enteric hyperoxaluria and hyperuricemia. The precise incidence and prevalence for these diseases are unknown. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. For example, we estimate there are approximately 200,000 to 250,000 patients in the United States with enteric hyperoxaluria and kidney stones. In addition, an estimated 375,000 patients in the United States have refractory gout and CKD, the target population for our ALLN-346 product candidate. These estimates have been derived from a variety of sources, including the scientific literature and market research projects with third-party consultants, and may prove to be incorrect. Further, new studies and future developments in patient care or treatment paradigms may change the estimated incidence or prevalence of this disorder. The number of patients may turn out to be lower than expected. The potentially addressable patient population for each of our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for one or more of our product candidates, because certain of our potential target populations are small, including our target populations for which reloxaliase has received orphan drug designation, we may never achieve profitability despite obtaining such significant market share.

**Even if one of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success and the market opportunity for such product candidate may be smaller than we estimate.**

We have never obtained marketing approval for a product candidate or commercialized a product. Even if one of our product candidates is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of reimbursement for existing therapies.



Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If any one of our product candidates is approved but does not achieve an adequate level of market acceptance, we may not generate significant revenues and we may not become profitable. The degree of market acceptance of any of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the potential advantages of the product compared to alternative treatments;
- the prevalence and severity of any side effects;
- the clinical indications for which the product is approved;
- the potential absence of the results of a late-stage clinical trial with a clinically meaningful primary endpoint;
- whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy;
- limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling;
- our ability, or the ability of any future collaborators, to offer the product for sale at competitive prices;
- the product's convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try, and of physicians to prescribe, the product;
- the strength of our sales, marketing and distribution support;
- the approval of other new products for the same indications;
- changes in the standard of care for the targeted indications for the product;
- the timing of market introduction of our approved products as well as competitive products;
- availability and amount of reimbursement from government payors, managed care plans and other third-party payors;
- adverse publicity about the product or favorable publicity about competitive products; and
- potential product liability claims.

The potential market opportunities for our product candidates are difficult to estimate precisely. Our estimates of the potential market opportunities are predicated on many assumptions, including industry knowledge and publications, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, these assumptions involve the exercise of significant judgment on the part of our management, are inherently uncertain and the reasonableness of these assumptions has not been assessed by an independent source. If any of the assumptions proves to be inaccurate, the actual markets for our product candidates could be smaller than our estimates of the potential market opportunities, which would adversely affect our results of operations and our business.

**\* We face substantial competition, which may result in others discovering, developing or commercializing drugs before or more successfully than we do, and reducing or eliminating our commercial opportunity.**

Our industry is highly competitive and subject to rapid and significant technological change as researchers learn more about diseases and develop new technologies and treatments. Our potential competitors include primarily large pharmaceutical companies, biotechnology companies and specialty pharmaceutical companies. Key competitive factors affecting the commercial success of reloxaliase, ALLN-346 and any other product candidates we may develop are likely to be efficacy, safety and tolerability profile, reliability, convenience of administration, price and reimbursement.

There is no approved pharmacologic therapy for the reduction of urinary oxalate excretion in patients with enteric hyperoxaluria. Existing treatment options for hyperoxaluria generally are non-specific and include high fluid intake to increase urine output to more than two to three liters per day, a diet low in salt and oxalate, oral citrate and/or calcium and/or magnesium supplementation and orthophosphate and Vitamin B6, exclusively for the specific subset of responsive patients with the most severe form of primary hyperoxaluria (PH1).

We are aware of other companies pursuing oxalate reduction in both primary and secondary hyperoxaluria. For example, Oxlumio, developed by Alnylam, was approved in the fourth quarter of 2020 by the FDA and EMA as the first therapy for the treatment of primary hyperoxaluria Type 1. Dicerna is conducting ongoing clinical development for the treatment of primary hyperoxaluria Types 1-3. Chinook is in preclinical development for a small molecule to treat primary hyperoxaluria. Oxthera AB (Sweden) and Oxidien Pharmaceuticals (U.S.) are developing orally delivered products to degrade oxalate in the stomach

and GI tract. Oxthera is conducting Phase 3 clinical trials for Oxabact, *Oxalobacter formigenes*, indicated for the treatment of primary hyperoxaluria. Several microbiome companies including Synlogic, Novome and Oxalo are at various stages of discovery and development with potential assets for the treatment of primary and secondary hyperoxaluria. These microbiome approaches largely target oxalate in the distal GI tract (colon), which is downstream of the primary site of oxalate absorption in the upper GI tract.

There are already three classes of drugs approved to treat hyperuricemia and gout including established classes of xanthine oxidase inhibitors and uricosuric agents and more-recently available injectable recombinant uricases. Patients with CKD who have hyperuricemia and gout are often not optimally managed due to limitations of available therapies, including decreased tolerability, dose restrictions, drug-drug interactions, contraindications and increased risk for long-term morbidity and mortality. Despite the significant limitations of these drugs, newer entrants such as KRYSTEXXA, a recombinant uricase sold by Horizon Therapeutics, have been competitive. In addition to Horizon, a number of other competitors have drug candidates in clinical trials, including Selecta Biosciences Inc., which has initiated a Phase 3 trial of a candidate for the treatment of chronic refractory gout. In July 2020, Selecta and Swedish Orphan Biovitrum AB, or Sobi, entered into a strategic licensing agreement under which Sobi will assume responsibility for certain development, regulatory, and commercial activities for this product candidate. In addition, there are several additional candidates in various stages of development for gout patients.

Several of our existing or potential competitors have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a small number of our competitors. Accordingly, our competitors may be more successful than we may be in obtaining FDA approval of drugs and achieving widespread market acceptance. Our competitors' drugs, or drugs they may develop in the future, may be more effective, or more effectively marketed and sold, than any drug we may commercialize and may render reloxaliase, ALLN-346, or any future product candidates we may develop obsolete or non-competitive before we can recover the expenses of developing and commercializing them. Our competitors may also obtain FDA or other regulatory approval of their products more rapidly than we may obtain approval of ours. Our competitors could develop and the FDA could approve a generic or biosimilar version of oxalate decarboxylase or uricase, the active enzyme in reloxaliase and ALLN-346, respectively. We anticipate that we will face intense and increasing competition as new drugs enter the market and more advanced technologies become available. If we are unable to compete effectively, our opportunity to generate revenue from the sale of reloxaliase, ALLN-346, or any future product candidates we may develop, if approved, will be adversely affected.

**\* We currently have no sales and marketing organization and, as a company, have not commercialized any products. If we are unable to establish effective sales and marketing capabilities in the United States and access them in Europe and other international markets, we may not succeed in commercializing our product candidates.**

At present, we have no sales or marketing employees and we rely on part-time consultants. We cannot guarantee that we will be successful in marketing reloxaliase for enteric hyperoxaluria or ALLN-346 for hyperuricemia in the United States, if approved. We may not be able to establish a direct sales force in a cost-effective manner or realize a positive return on this investment. In addition, we will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain sales and marketing personnel. Factors that may inhibit our efforts to commercialize reloxaliase or ALLN-346 in the United States without strategic partners or licensees include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of our planned relatively small sales force to obtain access to or inform adequate numbers of nephrologists, urologists or other practitioners at kidney stone clinics;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- the inability of market-access personnel to obtain sufficient levels of pricing and reimbursement in each jurisdiction; and
- unforeseen costs, expenses and delays associated with creating a commercial organization.

If we are not successful in timely recruiting of sales and marketing personnel or in building a sales and marketing infrastructure or if we do not successfully enter into appropriate collaboration arrangements, we will have difficulty commercializing reloxaliase or ALLN-346, which could harm our business, operating results and financial condition. Expansion of our business into the EU and other international markets will require significant management attention and additional financial resources. We currently intend to explore commercializing reloxaliase or ALLN-346, if approved, in Europe and other international markets by entering into collaboration agreements with other biopharmaceutical companies, and we may not be successful in entering into these collaboration agreements. In the event that we do enter into such agreements, we may have limited or no control over the sales, marketing and distribution activities of these third parties. Additional factors and risks that may inhibit our efforts to commercialize reloxaliase or ALLN-346 in foreign markets include:

- our inability to directly control commercial activities because we are relying on third parties, should we enter into third-party collaborations;
- varying pricing in different foreign markets, which could adversely affect pricing in the United States or other countries;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer collection times for accounts receivable;
- longer lead times for shipping;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries, and related prevalence of generic alternatives to therapeutics;
- the imposition of governmental price controls, political and economic instability, trade restrictions and changes in tariffs;
- foreign currency exchange rate fluctuations;
- our customers' ability to obtain adequate reimbursement for reloxaliase in foreign markets at all, either at all or at prices that exceed our costs; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Our future revenues may depend heavily on the success of the efforts of these third parties. We may not be able to establish a commercial operation in a cost-effective manner or realize a positive return on this investment, even with the assistance of one or more third-party collaborators, should we choose to enter into such an arrangement. In addition, we will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain sales and marketing personnel.

If we or third-party collaborators are not successful in recruiting sales and marketing personnel or in building a sales and marketing infrastructure or if we do not successfully enter into additional collaboration arrangements with third parties, we may not be able to successfully commercialize reloxaliase or ALLN-346 and any future product candidates we may develop in foreign markets, which could impair our business, operating results and financial condition.

Even with the potential assistance of third-party collaborators, we may not be successful in establishing a commercial operation in foreign markets for numerous reasons, including, but not limited to, failing to attract, retain and motivate the necessary skilled personnel and failing to develop a successful marketing strategy. Failure to establish a commercial operation in foreign markets will have a negative outcome on our ability to commercialize reloxaliase or ALLN-346 and generate revenue.

Additionally, if approved for marketing in one or more countries, we and/or our potential third-party collaborators may encounter unexpected or unforeseen delays in establishing our commercial operations that delay the commercial launch in these countries. These delays may increase the cost of, and the resources required for successful commercialization of reloxaliase or ALLN-346 internationally. We do not have any experience in a commercial launch in Europe or elsewhere.

## Risks Related to Business Development

**We expect to expand our development, regulatory, and future sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.**

If we are able to secure adequate financing, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of clinical development, manufacturing, regulatory affairs, and sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational, and financial systems, expand our facilities, and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expected expansion of our operations or recruit and train additional qualified personnel. Moreover, the expected physical expansion of our operations may lead to significant costs and may divert our management and business development resources and attention. Any inability to manage growth could delay the execution of our business plans or disrupt our operations, which could affect our ability to generate revenue.

**\* The longer term growth of our business depends on our ability to expand our portfolio of product candidates, which may require substantial financial resources and may ultimately be unsuccessful.**

The longer term growth of our business depends upon our ability to develop and commercialize multiple product candidates. In addition to the development and commercialization of reloxaliase for hyperoxaluria, we intend to pursue development of ALLN-346 for hyperuricemia and CKD as well as other product candidates. We may never be able to identify other developmental prospects that we can successfully develop into product candidates, let alone receive regulatory approval of or successfully commercialize such product candidates.

A significant portion of the research that we are conducting involves new technologies. Research programs to identify new disease targets and product candidates require substantial technical, financial and human resources whether or not we ultimately identify any product candidates. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including, but not limited to:

- the research methodology used may not be successful in identifying potential product candidates; or
- potential product candidates may on further study be shown to have harmful side effects or other characteristics that indicate they are unlikely to be effective drugs.

There are a number of FDA requirements that we must satisfy before we can commence a clinical trial in the United States. If we are able to identify additional potential product candidates, satisfaction of these regulatory requirements will entail substantial time, effort and financial resources. We may never satisfy these requirements. Any time, effort and financial resources we expend on development of other product candidates may impair our ability to continue efforts to develop and commercialize reloxaliase for the treatment of enteric hyperoxaluria and other indications or ALLN-346 for hyperuricemia and CKD, and we may never commence clinical trials of such development programs despite expending significant resources in pursuit of their development. If we do commence clinical trials of other product candidates, those product candidates may never demonstrate sufficient safety and efficacy to be approved by the FDA or other comparable foreign regulators. If any of these events occur, we may be forced to abandon our development efforts for such program or programs, which would harm our business. If we do not successfully develop and commercialize product candidates based upon our approach, we will not be able to obtain drug revenues in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price.

**We may fail to obtain and maintain orphan drug designations from the FDA for our current and future product candidates, as applicable. Even for reloxaliase for which we have received such designation for treatment of primary hyperoxaluria and pediatric hyperoxaluria, we may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.**

Our strategy includes seeking orphan drug designation where available for our product candidates. Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug or biologic intended to treat a rare disease or condition, which is defined as one occurring in a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug or biologic will be recovered from sales in the United States. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including a NDA, or BLA, to market the same drug or biologic for the same indication for seven years, except in

limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the original manufacturer is unable to assure sufficient product quantity.

The FDA has granted separate orphan drug designations for reloxaliase for treatment of primary hyperoxaluria and for the treatment of pediatric hyperoxaluria. In addition, the European Commission has granted orphan designation for reloxaliase for the treatment of primary hyperoxaluria. Even where we have obtained such designations, we may not be the first to obtain regulatory approval of a product candidate for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. We may also fail to meet requirements to maintain orphan drug designation during our continued development of reloxaliase, which is primarily focused on enteric hyperoxaluria. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the product to meet the needs of patients with the orphan-designated disease or condition. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties may receive and be approved for the same condition, and only the first applicant to receive approval will receive the benefits of marketing exclusivity. Even after an orphan-designated product is approved, the FDA can subsequently approve a later drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior if it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process. In addition, while we may seek orphan drug designation for our product candidates, we may never receive such designations.

## **Risks Related to Our Business and Industry**

### Risks Related to COVID-19 and the Global Economy.

#### **\* The COVID-19 pandemic has had and could continue to have an adverse impact on our developmental programs and our financial condition.**

In December 2019, a novel strain of coronavirus was first identified in Wuhan, Hubei Province, China. This virus continues to spread globally and has spread to a number of countries, including the United States where new cases continue to rise in some states. The outbreak and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. In response to the spread of COVID-19, we have closed our executive offices with our administrative employees continuing their work outside of our offices and limited the number of staff in any given research and development laboratory. Our employees and contractors conducting research and development activities may not be able to access our laboratory for an extended period of time as a result of the closure of our offices and the possibility that governmental authorities further modify current restrictions.

In addition, the COVID-19 pandemic has adversely affected the execution and enrollment progress of the URIROX-2 clinical trial. In part because of the impact of the pandemic, during the first quarter of 2021 we determined that site initiation and patient enrollment in this study was proceeding at a slower rate than we had originally projected. Accordingly, we revised our estimate for the expected timing of the first interim analysis from the first quarter of 2022 to the second or third quarter of 2022, and our estimate for the expected timing of the topline data from the third quarter of 2022 to the fourth quarter of 2022 or the first quarter of 2023. During the third quarter of 2021, we further revised our plans and timing for the first interim analysis. Although our initial plan for the first interim analysis had been to assess six-month data on 130 patients, our revised plan is now to assess one-month data on patients enrolled as of the end of November 2021, which we estimate will be approximately 80 patients. We expect that we will conduct the first interim analysis during the first quarter of 2022. Given uncertainty regarding the timeline for completion of enrollment, we are not currently providing an estimate for the timing of the second interim analysis and topline data from the URIROX-2 study.

As a result of the COVID-19 pandemic we may experience further disruptions that could severely impact our business, preclinical studies and clinical trials, including:

- additional delays or difficulties enrolling patients in our clinical trials;
- additional delays or difficulties in clinical site initiation, including difficulties in receiving approval from local regulatory authorities, recruiting clinical site investigators and clinical site staff;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials, including interruption in global shipping that may affect the transport of clinical trial materials;
- changes in local regulations as part of a response to the COVID-19 coronavirus outbreak or new shelter in place rules from state governments which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue the clinical trials altogether;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others, or interruption of clinical trial subject visits and study procedures, the occurrence of which could affect the integrity of clinical trial data;
- risk that participants enrolled in our clinical trials will acquire COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- interruptions in preclinical studies due to restricted or limited operations at our research and development laboratory facility;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees;
- limitations in employee resources that would otherwise be focused on the conduct of our clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;
- refusal of the FDA to accept data from clinical trials in these affected geographies; and
- interruption or delays to our sourced discovery and clinical activities.

We and the third-party manufacturers, CROs and academic collaborators that we engage have faced in the past and may face in the future disruptions that could affect our ability to initiate and complete preclinical studies or clinical trials, including disruptions in procuring items that are essential for our research and development activities, such as, for example, raw materials used in the manufacture of our product candidates, laboratory supplies for our preclinical studies and clinical trials, or animals that are used for preclinical testing, in each case, for which there may be shortages because of ongoing efforts to address the COVID-19 pandemic. Three vaccines for COVID-19 have been granted Emergency Use Authorization by the FDA since late 2020, and more are likely to be authorized in the coming months. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in these trials. The response to the COVID-19 pandemic may redirect resources with respect to regulatory and intellectual property matters in a way that would adversely impact our ability to pursue marketing approvals and protect our intellectual property. In addition, we may face impediments to regulatory meetings and potential approvals due to measures intended to limit in-person interactions.

The COVID-19 pandemic continues to rapidly evolve and the future progression of the COVID-19 pandemic and its effects on our business and operations are uncertain. The extent to which the outbreak impacts our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the pandemic, travel restrictions and social distancing 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 disease.

#### Risks Related to Employee Matters and Managing Growth

**During the fourth quarter of 2019, we reduced the size of our organization, and we may encounter difficulties in managing this development and restructuring, which could disrupt our operations. In addition, we may not achieve anticipated benefits and savings from the reduction.**

In December 2019, we announced a restructuring to re-align our workforce to match strategic and financial objectives and optimize resources for long term growth, including a reduction in force program impacting a number of employees. The workforce reduction resulted in the loss of longer-term employees, the loss of institutional knowledge and expertise and the reallocation and combination of certain roles and responsibilities across the organization, all of which could adversely affect our operations. Given the complexity of our business, we must continue to implement and improve our managerial, operational and financial systems, manage our facilities and continue to recruit and retain qualified personnel. This will be made more challenging given the workforce reduction described above. As a result, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these activities. Further, the restructuring and possible additional cost containment measures may yield unintended consequences, such as attrition beyond our intended workforce reduction and reduced employee morale. In addition, we may not achieve anticipated benefits from the workforce reduction. Due to our limited resources, we may not be able to effectively manage our operations or recruit and retain qualified personnel, which may result in weaknesses in our infrastructure and operations, risks that we may not be able to comply with legal and regulatory requirements, and loss of employees and reduced productivity among remaining employees. For example, the workforce reduction may negatively impact our clinical and regulatory functions, which would have a negative impact on our ability to successfully develop, and ultimately, commercialize our product candidates. If our management is unable to effectively manage this transition and workforce reduction and additional cost containment measures, our expenses may be more than expected and we may not be able to implement our business strategy. As a result, our future financial performance and our ability to commercialize our product candidates successfully would be negatively affected.

**Restructuring activities could disrupt our business and affect our results of operations.**

In December 2019, we announced a restructuring to re-align our workforce to match strategic and financial objectives and optimize resources for long term growth, including a reduction in force program impacting a number of employees. We may take similar steps in the future as we seek to realize operating synergies, to achieve our target operating model and financial objectives, or to reflect more closely changes in the strategic direction of our business. These changes could be disruptive to our business, including our research and development efforts, and could result in significant expense, including accounting charges for inventory and technology related write-offs, workforce reduction costs and charges relating to consolidation of excess facilities. Substantial expense or charges resulting from restructuring activities could adversely affect our results of operations and use of cash in those periods in which we undertake such actions.

**We only have a limited number of employees to manage and operate our business.**

As of November 5, 2021, we had 47 full-time, part-time, or short-term employees. Our focus on the development of reloxaliase and ALLN-346 requires us to optimize cash utilization and to manage and operate our business in a highly efficient manner. We will need to hire and retain a significant number of new employees to execute our clinical development, manufacturing and commercialization plans. We cannot provide assurance that we will be able to hire and/or retain adequate staffing levels to develop and commercialized reloxaliase, or ALLN-346 or run our operations and/or to accomplish all of the objectives that we otherwise would seek to accomplish.

**We depend on the knowledge and skill of our senior management and other key employees, and if we are unable to retain or if we fail to recruit additional highly skilled personnel, our business will be harmed.**

Our ability to compete in the highly competitive pharmaceuticals industry depends in large part upon our ability to attract and retain highly qualified managerial, commercial, scientific and medical personnel. We are highly dependent on our management, commercial, scientific and medical personnel. In order to induce valuable employees to remain with us, we have provided employees with stock options that vest over time. The value to employees of stock options that vest over time is significantly affected by movements in our stock price that we cannot control and, together with our other compensation programs and benefits, may at any time be insufficient to counteract more lucrative offers from other companies.

We are highly dependent upon the principal members of our management team, including Louis Brenner, M.D., our President and Chief Executive Officer, and Richard Katz, M.D., our Chief Financial Officer, as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time. The loss of any executive or other principal member of our management team would impair our ability to identify, develop and market new products and conduct successful operations.

In addition, our growth will require us to hire a significant number of qualified technical, commercial and administrative personnel. There is intense competition from other companies and research and academic institutions for qualified personnel in the areas of our activities. Other biopharmaceutical companies with which we compete for qualified personnel may have greater financial and other resources, different risk profiles, and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success at which we can develop and commercialize relxaliase, ALLN-346 and any other product candidates we may develop would be impaired and could adversely affect our growth and financial performance.

**Our employees, principal investigators, CROs and consultants 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, principal investigators, CROs and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violate the regulations of the FDA and other comparable foreign regulators, including those laws requiring the reporting of true, complete and accurate information to such authorities; healthcare fraud and abuse laws and regulations in the United States and abroad; or laws that require the reporting of financial information or data accurately. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. Prior to completing our IPO, we adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, 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 Business Disruptions**

**If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.**

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our



use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

### **Our business and operations would suffer in the event of computer system failures, cyber-attacks on our systems or deficiency in our cyber security.**

Despite the implementation of security measures, our internal computer systems, and those of third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, malware, natural disasters, fire, terrorism, war and telecommunication, electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. For example, companies have experienced an increase in phishing and social engineering attacks from third parties in connection with the COVID-19 pandemic. In addition, our systems safeguard important confidential personal data regarding patients enrolled in our clinical trials. If a disruption event were to occur and cause interruptions in our operations, it could result in a disruption of our drug development programs. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of reloxaliase and any other product candidates we may develop could be delayed.

### **The increasing use of social media platforms presents new risks and challenges.**

Social media is increasingly being used to communicate about our clinical development programs and the diseases our therapeutics are being developed to treat, and we intend to utilize appropriate social media in connection with our commercialization efforts following approval of our product candidates, if any. Social media practices in the biopharmaceutical industry continue to evolve and regulations and regulatory guidance relating to such use are evolving and not always clear. This evolution creates uncertainty and risk of noncompliance with regulations applicable to our business, resulting in potential regulatory actions against us, along with the potential for litigation related to off-label marketing or other prohibited activities. For example, patients may use social media channels to comment on their experience in an ongoing blinded clinical trial or to report an alleged adverse event. When such disclosures occur, there is a risk that trial enrollment may be adversely impacted, we fail to monitor and comply with applicable adverse event reporting obligations or that we may not be able to defend our business or the public's legitimate interests in the face of the political and market pressures generated by social media due to restrictions on what we may say about our product candidates. There is also a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on any social networking website. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face regulatory actions or incur other harm to our business.

## **Risks Related to Government Regulation**

### Risks Related to Healthcare Laws

**Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to penalties, including criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm and diminished profits and future earnings.**

Although we do not currently have any drugs on the market, if we obtain FDA approval for any of our investigational product candidates and once we begin commercializing our product candidates, we will be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states, foreign governments and other jurisdictions in which we conduct our business. Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our product candidates for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, 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, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under federal and state healthcare programs such as Medicare and Medicaid. The term remuneration has been interpreted broadly to include anything of value. Further, courts have found that if “one purpose” of remuneration is to induce referrals, the federal Anti-Kickback statute is violated. Violations are subject to significant civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, a claim submitted for payment to any federal healthcare program that includes items or services that were made as a result of a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act, or FCA. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Although there are several statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution, they are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. On November 20, 2020, the Department of Health and Human Services, or HHS, Office of Inspector General, or OIG, finalized further modifications to the federal Anti-Kickback Statute. Under the final rules, OIG added safe harbor protections under the Anti-Kickback Statute for certain coordinated care and value-based arrangements among clinicians, providers, and others. This rule (with exceptions) became effective January 19, 2021. We continue to evaluate what effect, if any, these rules will have on our business;
- the federal False Claims Act imposes criminal and civil penalties and authorizes civil whistleblower or qui tam actions against individuals or entities for: knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent; or making a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the anti-inducement law prohibits, among other things, the offering or giving of remuneration, which includes, without limitation, any transfer of items or services for free or for less than fair market value (with limited exceptions), to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary’s selection of a particular supplier of items or services reimbursable by a federal or state governmental program;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability knowingly and willfully for executing, or attempting to execute a scheme to defraud any healthcare benefit program, (including private third party payors) or obtaining, 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 payor (e.g., public or private), and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. On November 20, 2020, the Department of Health and Human Services, or HHS, Office of Inspector General, or OIG, finalized further modifications to the federal Anti-Kickback Statute. Under the final rules, OIG added safe harbor protections under the Anti-Kickback Statute for certain coordinated care and value-based arrangements among clinicians, providers, and others. This rule (with exceptions) became effective January 19, 2021. We continue to evaluate what effect, if any, these rules will have on our business;
- the federal physician payment transparency requirements, sometimes referred to as the "Sunshine Act" under 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, or ACA, require manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children’s Health Insurance Program to report to HHS, information related to physician payments and other transfers of value and the ownership and investment interests of such physicians and their immediate family members. Effective January 1, 2022, these

reporting obligations will be extended to include transfers of value made in FY 2021 to certain non-physician providers such as physician assistants and nurse practitioners;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and its implementing regulations, which also imposes obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions; and
- analogous state, local and foreign laws and regulations, such as state anti-kickback and false claims laws that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Ensuring that our future business arrangements with third parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including anticipated activities to be conducted by our sales team, were to be found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Any of these occurrences may significantly harm our business, financial condition, prospects and results of operations and adversely affect our stock price.

The risk of us being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. For example, the definition of the "remuneration" under the federal Anti-Kickback Statute has been interpreted to include anything of value. Further, courts have found that if "one purpose" of remuneration is to induce referrals, the federal Anti-Kickback Statute is violated.

Additionally, recent healthcare reform legislation has strengthened federal and state healthcare fraud and abuse laws. For example, the ACA amends the intent requirement of the federal Anti-Kickback Statute and criminal healthcare fraud statutes to clarify that liability under these statutes does not require a person or entity to have actual knowledge of the statutes or a specific intent to violate them. Moreover, the ACA provides that the government may assert that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act.

**We are subject to U.S. and foreign anti-corruption and anti-money laundering laws with respect to our operations and non-compliance with such laws can subject us to criminal and/or civil liability and harm our business.**

We are subject to the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and possibly other state and national anti-bribery and anti-money laundering laws in countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, third-party intermediaries, joint venture partners and collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. We may have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. In addition, we may engage third-party intermediaries to promote our clinical research activities abroad and/or to obtain necessary permits, licenses, and other regulatory approvals. We can be held liable for the corrupt or other illegal activities of these third-party intermediaries, our employees, representatives, contractors, partners, and agents, even if we do not explicitly authorize or have actual knowledge of such activities.

We have a Code of Business Conduct and Ethics, and have prepared and implemented policies and procedures to ensure compliance with such code. The Code of Business Conduct and Ethics mandates compliance with the FCPA and other anti-corruption laws applicable to our business throughout the world. However, we cannot assure you that our employees and third-party intermediaries will comply with this code or such anti-corruption laws. Noncompliance with anti-corruption and anti-money laundering laws could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension and/or debarment from contracting with certain persons, the loss of export privileges, reputational harm, adverse media coverage, and other collateral consequences. If any subpoenas, investigations, or other enforcement actions are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense and compliance costs and other professional fees. In certain cases, enforcement authorities may even cause us to appoint an independent compliance monitor which can result in added costs and administrative burdens.

**Legislative or regulatory reform of the health care system in the United States and foreign jurisdictions may adversely impact our business, operations or financial results.**

Our industry is highly regulated and changes in U.S. and foreign regulations, statutes or the interpretation of existing regulations may adversely impact our business, operations or financial results by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

In the U.S. and in some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative initiatives and regulatory changes regarding the healthcare system directed at broadening the availability of healthcare, improving the quality of healthcare, and containing or lowering the cost of healthcare. For example, in March 2010, the Affordable Care Act and a related reconciliation bill were signed into law. This legislation changes the current system of healthcare insurance and benefits intended to broaden coverage and control costs. The law also contains provisions that will affect companies in the pharmaceutical industry and other healthcare related industries by imposing additional costs and changes to business practices. Provisions affecting pharmaceutical companies include the following:

- mandatory rebates for drugs sold into the Medicaid program have been increased, and the rebate requirement has been extended to drugs used in risk-based Medicaid managed care plans;
- the definition of "average manufacturer price" was revised for reporting purposes, which could increase the amount of Medicaid drug rebates by state;
- the 340B Drug Pricing Program under the Public Health Service Act has been extended to require mandatory discounts for drug products sold to certain critical access hospitals, cancer hospitals and other covered entities;
- pharmaceutical companies are required to offer discounts on brand-name drugs to patients who fall within the Medicare Part D coverage gap, commonly referred to as the "donut hole"; and
- pharmaceutical companies are required to pay an annual non-tax deductible fee to the federal government based on each company's market share of prior year total sales of branded products to certain federal healthcare programs. Since we expect our branded pharmaceutical sales to constitute a small portion of the total federal health program pharmaceutical market, we do not expect this annual assessment to have a material impact on our financial condition.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013, which will remain in effect until 2030 unless additional congressional action is taken. These Medicare sequester reductions have been suspended from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic. Proposed legislation, if passed, would extend this suspension until the end of the pandemic. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of

prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal year 2021 includes a \$135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the U.S. government sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. Further, the Trump administration previously released a "Blueprint", or plan, to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. HHS has already started the process of soliciting feedback on some of these measures and, at the same, is immediately implementing others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy, a type of prior authorization, for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. In addition, there has been several changes to the 340B drug pricing program, which imposes ceilings on prices that drug manufacturers can charge for medications sold to certain health care facilities. On December 27, 2018, the District Court for the District of Columbia invalidated a reimbursement formula change under the 340B drug pricing program, and CMS subsequently altered the FYs 2019 and 2018 reimbursement formula on specified covered outpatient drugs ("SCODs"). The court ruled this change was not an "adjustment" which was within the Secretary's discretion to make but was instead a fundamental change in the reimbursement calculation. However, most recently, on July 31, 2020, the U.S. Court of Appeals for the District of Columbia Circuit overturned the district court's decision and found that the changes were within the Secretary's authority. On September 14, 2020, the plaintiffs-appellees filed a Petition for Rehearing En Banc (i.e., before the full court), but was denied on October 16, 2020. It is unclear how these developments could affect covered hospitals who might purchase our future products and affect the rates we may charge such facilities for our approved products in the future, if any.

Further, on July 24, 2020 and September 13, 2020, President Trump signed several Executive Orders aimed at lowering drug pricing that seek to implement several of the administration's proposals. In response, The FDA also released a final rule on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20 2020 CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates will be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. The MFN Model regulations mandate participation by identified Part B providers and will apply in all U.S. states and territories for a seven-year period beginning January 1, 2021 and ending December 31, 2027. The Interim Final Rule has not been finalized and is subject to revision and challenge. Additionally, 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 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. Although a number of these, and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, Congress has indicated that it will continue to seek new legislative measures to control drug costs.

In addition, in September 2007, the Food and Drug Administration Amendments Act of 2007 was enacted giving the FDA enhanced post-marketing authority including the authority to require post-marketing studies and clinical trials, labeling changes based on new safety information and compliance with risk evaluations and mitigation strategies approved by the FDA. The FDA's exercise of this authority could result in delays or increased costs during product development, clinical trials and regulatory review, increased costs to ensure compliance with post-approval regulatory requirements and potential restrictions on the sale and/or distribution of approved products. Other legislative and regulatory initiatives have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. For example, the Drug Supply Chain Security Act of 2013 imposes new obligations on manufacturers of certain pharmaceutical products related to product tracking and tracing. We do not know whether additional legislative changes will be enacted, or whether the FDA regulations, guidance documents or interpretations will be changed, or what the impact of such changes on the marketing approvals of roxalixase, if any, may be. In addition, increased scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

The current presidential administration and U.S. Congress have also recently attempted to repeal or "repeal and replace" the Affordable Care Act. Although those efforts did not succeed, we the presidential administration may continue to seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the Affordable Care Act. There is still uncertainty with

respect to the impact President Trump's administration and the U.S. Congress may have on the Affordable Care Act, if any, and any changes will likely take time to unfold. Additionally, since its enactment, there have been judicial and Congressional challenges to certain aspects of the Affordable Care Act. For example, on December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or Texas District Court Judge, ruled that the entire Affordable Care Act is invalid based primarily on the fact that the Tax Cuts and Jobs Act of 2017 repealed 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, which is commonly referred to as the "individual mandate". The current administration and CMS have both stated that the ruling will have no immediate effect, and on December 18, 2019, the Fifth Circuit U.S. Court of Appeals held that the individual mandate is unconstitutional and remanded the case to the lower court to reconsider its earlier invalidation of the full Affordable Care Act. On March 2, 2020, the United States Supreme Court granted the petitions for writs of certiorari to review this case and has allotted one hour and twenty minutes for oral arguments, which were held on November 10, 2020. We cannot predict what affect further changes to the Affordable Care Act would have on our business. Pending review, the Affordable Care Act remains in effect, but it is unclear at this time what effect the latest ruling will have on the status of the Affordable Care Act. However, we cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on us.

Moreover, we cannot predict what healthcare reform initiatives may be adopted in the future. Further, federal and state legislative and regulatory developments are likely, and we expect ongoing initiatives in the United States to increase pressure on drug pricing. Such reforms could have an adverse effect on anticipated revenues from reloxalase and any other product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

#### **We may fail to comply with evolving European and other privacy laws.**

Since we conduct clinical trials in the European Economic Area, or the EEA, we are subject to additional European data privacy laws. The General Data Protection Regulation, (EU) 2016/679, or GDPR, became effective on May 25, 2018, and deals with the processing of personal data and on the free movement of such data. The GDPR imposes a broad range of strict requirements on companies subject to the GDPR, including requirements relating to having legal bases for processing personal information relating to identifiable individuals and transferring such information outside the EEA, including to the United States, providing details to those individuals regarding the processing of their personal information, keeping personal information secure, having data processing agreements with third parties who process personal information, responding to individuals' requests to exercise their rights in respect of their personal information, reporting security breaches involving personal data to the competent national data protection authority and affected individuals, appointing data protection officers,

conducting data protection impact assessments, and record-keeping. The GDPR increases substantially the penalties to which we could be subject in the event of any non-compliance, including fines of up to 10,000,000 Euros or up to 2% of our total worldwide annual turnover for certain comparatively minor offenses, or up to 20,000,000 Euros or up to 4% of our total worldwide annual turnover for more serious offenses. Given the limited enforcement of the GDPR to date, we face uncertainty as to the exact interpretation of the new requirements on our trials and we may be unsuccessful in implementing all measures required by data protection authorities or courts in interpretation of the new law.

In particular, national laws of member states of the EU are in the process of being adapted to the requirements under the GDPR, thereby implementing national laws which may partially deviate from the GDPR and impose different obligations from country to country, so that we do not expect to operate in a uniform legal landscape in the EEA. Also, as it relates to processing and transfer of genetic data, the GDPR specifically allows national laws to impose additional and more specific requirements or restrictions, and European laws have historically differed quite substantially in this field, leading to additional uncertainty. Further, the impact of the impending "Brexit", (whereby the United Kingdom is planning to leave the EEA in March of 2019), either with or without a "deal" is uncertain and cannot be predicted at this time.

In the event we continue to conduct clinical trials in the EEA, we must also ensure that we maintain adequate safeguards to enable the transfer of personal data outside of the EEA, in particular to the United States, in compliance with European data protection laws. We expect that we will continue to face uncertainty as to whether our efforts to comply with our obligations under European privacy laws will be sufficient. If we are investigated by a European data protection authority, we may face fines and other penalties. Any such investigation or charges by European data protection authorities could have a negative effect on our existing business and on our ability to attract and retain new clients or pharmaceutical partners. We may also experience hesitancy, reluctance, or refusal by European or multi-national clients or pharmaceutical partners to continue to use our products and solutions due to the potential risk exposure as a result of the current (and, in particular, future) data protection obligations imposed on them by certain data protection authorities in interpretation of current law, including the GDPR. Such clients or pharmaceutical partners may also view any alternative approaches to compliance as being too costly, too burdensome, too legally uncertain, or otherwise objectionable and therefore decide not to do business with us. Any of the foregoing could materially harm our business, prospects, financial condition and results of operations.

In addition, California recently enacted the CCPA, which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA will require covered companies to provide certain disclosures to consumers about its data collection, use and sharing practices, and to provide affected California residents with ways to opt-out of certain sales or transfers of personal information. The CCPA went into effect on January 1, 2020, and the California Attorney General has commenced bringing enforcement actions against violators as of July 1, 2020. The California Attorney General has proposed draft regulations, which have not been finalized to date, that may further impact our business activities if they are adopted. The uncertainty surrounding the implementation of CCPA exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information.

**Even if we are able to commercialize any product candidates, such products may become subject to unfavorable pricing regulations, third-party reimbursement practices, or healthcare reform initiatives, which would harm our business.**

The regulations that govern marketing approvals, pricing, and reimbursement for new medicines vary widely from country to country. Some countries require approval of the sale price of a medicine 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 medicine in a particular country, but then be subject to price regulations that delay our commercial launch of the medicine, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the medicine in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any product candidates we may develop obtain marketing approval.

Our ability to commercialize any medicines successfully also will depend in part on the extent to which reimbursement for these medicines and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any medicine that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval. Further, due to the COVID-19 pandemic, millions of individuals have lost/will be losing employer-based insurance coverage, which may adversely affect our ability to commercialize our products.

There may be significant delays in obtaining reimbursement for newly approved medicines, and coverage may be more limited than the purposes for which the medicine is approved by the FDA or comparable foreign regulators. Moreover, eligibility for reimbursement does not imply that any medicine will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, marketing and distribution. Interim reimbursement levels for new medicines, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the medicine and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost medicines and may be incorporated into existing payments for other services. Net prices for medicines may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of medicines from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved medicines we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize medicines, and our overall financial condition.

**Due to the novel nature of our product candidates and the potential for any product candidates we may develop to offer therapeutic benefit, we face uncertainty related to pricing and reimbursement for these product candidates.**

Our initial target patient populations are relatively small, as a result of which the pricing and reimbursement of any product candidates we may develop, if approved, must be adequate to support the necessary commercial infrastructure. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell any such product candidates will be adversely affected. The manner and level at which reimbursement is provided for services related to any product candidates we may develop (e.g. for administration of our product to patients) is also important. Inadequate reimbursement for such services may lead to physician resistance and adversely affect our ability to market or sell our products. In addition, it may be necessary for us to develop new reimbursement models in order to realize adequate value. Payors may not be able or

willing to adopt such new models, and patients may be unable to afford that portion of the cost that such models may require them to bear. If we determine such new models are necessary but we are unsuccessful in developing them, or if such models are not adopted by payors, our business, financial condition, results of operations, and prospects could be adversely affected.

We expect that coverage and reimbursement by government and private payors will be essential for most patients to be able to afford our product candidates. Accordingly, sales of any such product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of any product candidates we may develop will be paid by health maintenance, managed care, pharmacy benefit, and similar healthcare management organizations, or will be reimbursed by government authorities, private health coverage insurers, and other third-party payors. Coverage and reimbursement by a third-party payor may depend upon several factors, including the third-party payor's determination that use of a product is:

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

In the United States, no uniform policy for coverage and reimbursement for products exists among third-party payors. Therefore, coverage and reimbursement for our products can differ significantly from payor to payor. Obtaining coverage and reimbursement for a product from third-party payors is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical, and cost-effectiveness data. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. One payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product. There is significant uncertainty related to third-party coverage and reimbursement of newly approved products. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. If coverage and reimbursement are not available, or are available only at limited levels, we may not be able to successfully commercialize any product candidates we may develop. Even if coverage is provided, the approved reimbursement amount may not be adequate to realize a sufficient return on our investment.

Moreover, the downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products such as ours. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell any product candidates we may develop will be harmed.

**In light of the large population of patients with hyperoxaluria who reside outside the United States, our ability to generate meaningful revenues in those jurisdictions may be limited due to the strict price controls and reimbursement limitations imposed by governments outside of the United States.**

In some countries, particularly those in the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our product candidates is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially, if we are not able to market our product to the large population of patients with hyperoxaluria who reside in outside the United States.

**Currently we plan to seek regulatory approval to market reloxaliase solely for the treatment of enteric hyperoxaluria in adults and, unless we seek regulatory approval for additional indications, we will be prohibited from marketing reloxaliase for any other indication.**

We intend to initially seek approval to market reloxaliase for the treatment of enteric hyperoxaluria in adults. Even if we obtain regulatory approval to market reloxaliase in this indication, we will likely be prohibited from marketing reloxaliase for any other indications. The FDA strictly regulates the promotional claims that may be made about prescription products. While reloxaliase has been studied in patients beyond the enteric subgroup, reloxaliase may not be promoted for uses that are not approved by the FDA as reflected in its approved labeling. Under applicable regulations, the ability of a company to make marketing statements about the effectiveness of its drug outside of the statements made in the label, referred to as "off-label" marketing, is prohibited. If we are found to have promoted such off-label uses, we may become subject to significant liability.



**If we fail to comply or are found to have failed to comply with FDA and other regulations prohibiting the promotion of reloxaliase for unapproved uses, we could be subject to criminal penalties, substantial fines or other sanctions and damage awards.**

The regulations prohibiting the promotion of products for unapproved uses are complex and subject to substantial interpretation by the FDA and other government agencies. If we receive marketing approval for reloxaliase for the treatment of enteric hyperoxaluria in adults, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. We intend to implement compliance and training programs designed to ensure that our sales and marketing practices comply with applicable regulations. Notwithstanding these programs, the FDA or other government agencies may allege or find that our practices constitute prohibited promotion of reloxaliase for unapproved uses. We also cannot be sure that our employees will comply with company policies and applicable regulations regarding the promotion of products for unapproved uses.

Over the past several years, a significant number of pharmaceutical and biotechnology companies have been the target of inquiries and investigations by various federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including the Department of Justice and various U.S. Attorneys' Offices, the OIG, the FDA, the Federal Trade Commission and various state Attorneys General offices. These investigations have alleged violations of various federal and state laws and regulations, including claims asserting antitrust violations, violations of the Federal Food, Drug, and Cosmetic Act, the False Claims Act, the Prescription Drug Marketing Act, anti-kickback laws, and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement. Many of these investigations originate as "qui tam" actions under the False Claims Act. Under the False Claims Act, any individual can bring a claim on behalf of the government alleging that a person or entity has presented a false claim, or caused a false claim to be submitted, to the government for payment. The person bringing a qui tam suit is entitled to a share of any recovery or settlement. Qui tam suits, also commonly referred to as "whistleblower suits," are often brought by current or former employees. In a qui tam suit, the government must decide whether to intervene and prosecute the case. If it declines, the individual may pursue the case alone.

If the FDA or any other governmental agency initiates an enforcement action against us or if we are the subject of a qui tam suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects and reputation.

**Inadequate funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.**

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the FDA, the SEC and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new therapies to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. Separately, in response to the COVID-19 pandemic, on March 10, 2020 the FDA announced its intention to postpone most inspections of foreign manufacturing facilities and products while local, national and international conditions warrant. On March 18, 2020, the FDA announced its intention to temporarily postpone routine surveillance inspections of domestic manufacturing facilities and provided guidance regarding the conduct of clinical trials which the FDA continues to update. As of June 23, 2020, the FDA noted it was continuing to ensure timely reviews of applications for medical products during the COVID-19 pandemic in line with its user fee performance goals and conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. However, the FDA may not be able to maintain this pace and delays, or setbacks are possible in the future. On July 10, 2020, the FDA announced its goal of restarting domestic on-site inspections during the week of July 20, but such activities will depend on data about the virus' trajectory in a given state and locality and the rules and guidelines that are put in place by state and local governments. The FDA has developed a rating system to assist in determining when and where it is safest to conduct prioritized domestic inspections. Should FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, FDA has stated that it generally intends to issue a complete response letter. Further, if there is inadequate information

to make a determination on the acceptability of a facility, FDA may defer action on the application until an inspection can be completed. In 2020, several companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. If global health concerns or a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, upon completion of this offering and in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

### Risks Related to Litigation

**If successful product liability claims are brought against us, we may incur substantial liability and costs. If the use of our product candidates harms patients, or is perceived to harm patients even when such harm is unrelated to our product candidates, our regulatory approvals could be revoked or otherwise negatively impacted and we could be subject to costly and damaging product liability claims.**

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, participants in our clinical trials, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. There is a risk that our product candidates may induce adverse events. 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;
- withdrawal of clinical trial participants;
- costs due to related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- increased FDA warnings on product labels;
- the inability to commercialize our product candidates; and
- decreased demand for our product candidates, if approved for commercial sale.

We carry product liability insurance in amounts that we believe are sufficient in light of our current clinical programs; however, 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. If and when we obtain marketing approval for product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. On occasion, large judgments have been awarded in class action lawsuits based on drugs or medical treatments 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 exceed our insurance coverage, could adversely affect our results of operations and business.

During the course of treatment, patients may suffer adverse events, including death, for reasons that may or may not be related to our product candidates. Such events could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market our product candidates, if approved, or require us to suspend or abandon our commercialization efforts of any approved product candidates. Even in a circumstance in which we do not believe that an adverse event is related to our products, the investigation into the circumstance may be time-consuming or inconclusive. These investigations may interrupt our sales efforts, delay our regulatory approval process in other countries, or impact and limit the type of regulatory approvals our product candidates receive or maintain. As a result of these factors, a product liability claim, even if successfully defended, could have a material adverse effect on our business, financial condition or results of operations.

### **Risks Related to Our Dependence on Third Parties**

**\* The third parties upon whom we rely for the supply of the drug product and drug substance used in our product candidates are our sole source of supply, and the loss of any of these suppliers could significantly harm our business.**

We do not currently operate manufacturing facilities for clinical or commercial production of any product candidates. We have limited personnel experienced in drug manufacturing and formulation, and we lack the resources and the capabilities to

manufacture reloxaliase or ALLN-346 on a clinical or commercial scale. We do not intend to develop facilities for the manufacture of drug product candidates for clinical trials or products for commercial purposes in the foreseeable future. The drug product and drug substance used in our product candidates are supplied to us from single-source suppliers. Our ability to successfully develop our product candidates, to supply the drug required for our planned clinical trials, and to ultimately supply our commercial drugs in quantities sufficient to meet the market demand, depends in part on our ability to obtain the drug product and drug substance for these drugs in accordance with regulatory requirements and in sufficient quantities for commercialization and clinical testing. We do not currently have arrangements in place for a redundant or second-source supply of any such drug product or drug substance in the event any of our current suppliers of such drug product and drug substance cease their operations for any reason.

For all of our product candidates, we intend to identify and qualify additional manufacturers to provide such drug product and drug substance prior to submission of a BLA to the FDA and/or an MAA to the EMA. We are not certain, however, that our single-source suppliers will be able to meet our demand for their products, either because of the nature of our agreements with those suppliers, our limited experience with those suppliers or our relative importance as a customer to those suppliers. It may be difficult for us to assess their ability to timely meet our demand in the future based on past performance. While our suppliers have generally met our demand for their products on a timely basis in the past, they may subordinate our needs in the future to their other customers. If we were to experience an unexpected loss of supply of any of our product candidates or any of our future product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we would need to find additional or replacement suppliers and as a result could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing preclinical studies or clinical trials. For example, the extent to which the COVID-19 pandemic impacts our ability to procure sufficient supplies for the development of our products and product candidates will depend on the severity and duration of the spread of the virus, and the actions undertaken to contain COVID-19 or treat its effects. Three vaccines for COVID-19 have been granted Emergency Use Authorization by the FDA since late 2020, and more are likely to be authorized in the coming months. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our preclinical studies and clinical trials, which could lead to delays in these studies and trials.

Establishing additional or replacement suppliers for the drug product and drug substance used in our product candidates, if required, may not be accomplished quickly. If we are able to find a replacement supplier, such replacement supplier would need to be qualified and may require additional regulatory approval, which could result in further delay. While we seek to maintain adequate inventory of the drug product and drug substance used in our product candidates, any interruption or delay in the supply of components or materials, or our inability to obtain such drug product and drug substance from alternate sources at acceptable prices in a timely manner could impede, delay, limit or prevent our development efforts, which could harm our business, results of operations, financial condition and prospects.

We plan to continue to rely upon contract manufacturers and, potentially, collaboration partners to manufacture commercial quantities of our product candidates if and when approved for marketing by the applicable regulatory authorities. We have not secured commercial supply agreements with any contract manufacturers for reloxaliase or ALLN-346 and can give no assurance that we will enter commercial supply agreements with any contract manufacturers on favorable terms or at all or that we will be able to manufacture our product candidates at commercial scale at the cost we expect. Our contract manufacturers' failure to achieve and maintain high manufacturing standards, in accordance with applicable regulatory requirements, or the incidence of manufacturing errors, could result in patient injury or death, product shortages, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could seriously harm our business. Contract manufacturers often encounter difficulties involving production yields, quality control and quality assurance, as well as shortages of qualified personnel.

#### Risks Related to Third Party Agreements

**\* An element of our strategy is to enter into licensing or collaboration agreements with respect to reloxaliase, ALLN-346 and future product candidates in certain territories. We may not be able to identify suitable collaborators and, even if we do, our dependence on such relationships may adversely affect our business.**

Because we have limited resources, we may seek to enter into collaboration agreements with other pharmaceutical or biotechnology companies. Our strategy for commercializing reloxaliase, ALLN-346 and any future product candidates we may develop outside of the United States may depend on our ability to enter into agreements with collaborators to obtain assistance and funding for the development and potential commercialization of our product candidates in the territories in which we may seek to partner. Despite our efforts, we may be unable to secure collaborative licensing or other arrangements that are necessary for us to further develop and commercialize our product candidates. Supporting diligence activities conducted by potential collaborators and negotiating the financial and other terms of a collaboration agreement are long and complex processes with uncertain results. If we fail to enter into collaborations and do not have sufficient funds or expertise to

undertake the necessary development and commercialization activities ourselves, we may not be able to further develop our product candidates or bring them to market or continue to develop our technology platforms, and our business may be materially and adversely affected. Even if we are successful in entering into one or more collaboration agreements, collaborations may involve greater uncertainty for us, as we may have less control over certain aspects of our collaborative programs than we do over our proprietary development and commercialization programs. All of the risks relating to product development, regulatory approval and commercialization described in this Quarterly Report also apply to the activities of any of our future program collaborators.

Any future collaborations that we enter into may not be successful. Any failure by our partners to perform their obligations or any decision by our partners to terminate these agreements could negatively impact our ability to successfully develop, obtain regulatory approvals for and commercialize our product candidates. In addition, partners may not properly obtain, maintain or, defend or enforce our intellectual property rights, may infringe, misappropriate or otherwise violate third-party intellectual property rights, may misappropriate our trade secrets or may otherwise use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to litigation and potential liability. In the event we grant exclusive rights to such partners, we could be precluded from potential commercialization of our product candidates within the territories in which we have a partner. Furthermore, any termination of our collaboration agreements will terminate any funding we may receive under the relevant collaboration agreement and may impair our ability to fund further development efforts and our progress in our development programs.

Further, our potential future collaborators may develop alternative products or pursue alternative technologies either on their own or in collaboration with others, including our competitors, and the priorities or focus of our collaborators may shift such that our product candidates receive less attention or resources than we would like, or they may be terminated altogether. Any such actions by our potential future collaborators may harm our business prospects and ability to earn revenues. In addition, we could have disputes with our potential future collaborators, such as the interpretation of terms in our agreements. Any such disagreements could lead to delays in the development or commercialization of our product candidates or could result in time-consuming and expensive litigation or arbitration, which may not be resolved in our favor.

**\* We have relied, and will rely in the future, on third parties to conduct our nonclinical studies and clinical trials. If these third parties do not appropriately carry out their contractual duties, fail to conduct high-quality studies or meet expected deadlines, regulatory approval and commercialization of reloxaliase, ALLN-346 or any future candidates we may develop could be delayed or not obtained at all.**

We do not have the ability to conduct all of our clinical trials independently. We have relied and will continue to rely on third parties, including clinical investigators, third-party CROs, patients and consultants, to monitor, manage data for, participate in and execute our ongoing nonclinical and planned clinical programs for reloxaliase, ALLN-346 and other product candidates, and we control only some aspects of their activities. For example, in both our completed Phase 2 and Phase 3 clinical trials and ongoing Phase 3 clinical trial of reloxaliase we relied and are relying heavily on the efforts and contributions of investigative clinical sites and study patients to comply with a strict treatment regimen (e.g. three capsules per day with meals) and accurate timing of 24 hour urine collection, with the complete collection of all of the patient's urine during a given 24 hour period and with the proper handling of collected urine specimens, including storage, documentation, sample handling and shipping to the testing laboratory. Any failure of these third parties to meet their obligations has had or may in the future have an adverse effect on the results of clinical trials we have conducted or will conduct.

The COVID-19 pandemic and various governments' measures taken in response have also had a significant impact on our CROs, and we expect that they will face further disruption which may affect our ability to initiate and complete our preclinical studies and clinical trials.

Because we rely on third parties, our internal capacity to perform these functions is limited. We currently have a small number of employees, which limits the internal resources we have available to identify and monitor our third-party providers. Nevertheless, we are responsible for ensuring that each of our nonclinical studies and clinical trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific requirements and standards, including, for example, GLP, the Animal Welfare Act and GCPs. Our reliance on third parties does not relieve us of our regulatory responsibilities. Regulatory authorities enforce GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the relevant regulatory authorities may require us to perform additional clinical trials in support of our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements. We are also required to register clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to comply with these regulations may require us to repeat nonclinical studies and clinical trials, which would delay the regulatory approval process.

The third parties conducting our nonclinical studies and clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time, skill and resources to our ongoing clinical and nonclinical programs. To the extent we are unable to identify and successfully manage the performance of third-party service providers in the future, our business may be adversely affected. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our protocols, regulatory requirements or for other reasons, our nonclinical studies and clinical trials may be extended, delayed or terminated and we may not be able to obtain, or may be delayed in obtaining, regulatory approval of or successfully commercialize reloxaliase and any other product candidates we may develop. As a result, our results of operations and the commercial prospects for our product candidates could be harmed, our costs could increase and our ability to generate revenues could be delayed, impaired or foreclosed.

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

Because we rely on third parties to manufacture reloxaliase and ALLN-346 and conduct other aspects of our clinical development activities, we must, at times, share trade secrets and other confidential information with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with any collaborators, CROs, manufacturers and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. However, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or other confidential information. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets and confidential information become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's or other third party's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of certain collaborators, CROs, manufacturers and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. Despite our efforts to protect our trade secrets, our competitors or other third parties may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication. Discovery of our trade secrets by a competitor or other third party would impair our competitive position and have an adverse impact on our business.

## **Risks Related to Intellectual Property**

### Risks Related to Protecting Our Intellectual Property

**If we are unable to obtain and maintain sufficient patent protection for our product candidates, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to commercialize our product candidates successfully may be adversely affected.**

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary product candidates. If we do not adequately protect or enforce our intellectual property, competitors may be able to erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. To protect our proprietary position, we file patent applications in the United States and abroad related to our novel product candidates that are important to our business. The patent application and approval process is expensive, complex and time-consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. In addition, the determination of patent rights with respect to biological and pharmaceutical products commonly involves complex legal and factual questions, which has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending patent applications cannot be enforced against third parties practicing the technology claimed in such

applications unless and until a patent issues from such applications. Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

Moreover, because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, our patents or pending patent applications may be challenged in the courts or patent offices in the United States and abroad. For example, we may be subject to a third party preissuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or become involved in post-grant review procedures, oppositions, derivations, reexaminations, *inter partes* review or interference proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized.

Our pending and future patent applications may not result in patents being issued which protect our product candidates, in whole or in part, or which effectively prevent others from commercializing competitive products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. In addition, the laws of foreign countries may not protect our rights to the same extent or in the same manner as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may also seek approval to market their own products similar to or otherwise competitive with our products, for example, reloxaliase. Alternatively, our competitors may seek to market generic versions of any approved products by submitting abbreviated BLAs to the FDA during which process they may claim that patents owned or licensed by us are invalid, unenforceable or not infringed. In these circumstances, we may need to defend or assert our patents, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid or unenforceable, or that our competitors are competing in a non-infringing manner. Thus, even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

**We heavily rely on certain in-licensed patents and other intellectual property rights in connection with our development of reloxaliase and, if we fail to comply with our obligations under our existing and any future intellectual property licenses with third parties, we could lose license rights that are important to our business.**

Our ability to develop and commercialize our lead product candidate, reloxaliase, is heavily dependent on licenses to patent rights and other intellectual property granted to us by third parties. For example, we are party to a license agreement with Althea Technologies, Inc. (now known as Ajinomoto Althea, Inc.), or Althea, under which we received an exclusive, worldwide, royalty-bearing, sublicensable, and, except under certain circumstances, non-transferable license under certain of the patent rights to develop, use, make, have made, market, offer to sell, sell, have sold, distribute, import or otherwise exploit reloxaliase. We may enter into additional license agreements in the future. Our license agreement with Althea imposes, and we expect that future license agreements will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with our obligations under these licenses, our licensors, including Althea, may have the right to terminate these license agreements, in which event we might not be able to market our lead product candidate, reloxaliase. Similarly, other licensors may convert an exclusive license to a non-exclusive license, which could adversely affect the value of a product candidate developed under a given license agreement. Termination of any of our license agreements or reduction or elimination of our licensed rights may also result in our having to negotiate new or reinstated licenses with less favorable terms.

Further, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. For example, pursuant to our license agreement with Althea, Althea controls such activities for certain patents licensed to us under such agreement. Therefore, we cannot be certain that these patents will be prosecuted, maintained and enforced in a manner consistent with the

best interests of our business. If our current or future licensors or collaboration partners fail to obtain, maintain or protect any patents or patent applications licensed to us, our rights to such patents and patent applications may be reduced or eliminated and our right to develop and commercialize any of our product candidates that are the subject of such licensed rights could be adversely affected.

**Patent term may be inadequate to protect our competitive position on our products for an adequate amount of time.**

Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the normal expiration of the patent, which is limited to the approved indication (or any additional indications approved during the period of extension). However, a patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of the product's approval by the FDA, only one patent applicable to an approved drug is eligible for the extension, and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. In the future, if and when our product candidates, for example, reloxaliase, receive FDA approval, we intend to apply for patent term extensions on patents covering those products in any jurisdiction where these are available. However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. Moreover, we may not receive an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

Risks Related to Intellectual Property Litigation

**We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time consuming and unsuccessful.**

Competitors and other third parties may infringe, misappropriate or otherwise violate our patents and other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management, business and scientific personnel. In addition, many of our adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can.

A court may disagree with our allegations and may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the third-party technology in question. Furthermore, the other party could counterclaim that we infringe their intellectual property or counterclaim that a patent we have asserted against them is invalid or unenforceable, or both. In patent litigation in the United States, counterclaims challenging the validity, enforceability or scope of asserted patents are commonplace. Similarly, third parties may initiate legal proceedings against us seeking a declaration that certain of our intellectual property rights are non-infringed, invalid, or unenforceable. The outcome of any such proceeding is generally unpredictable.

Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement, or written description. In addition, validity challenges may, under certain circumstances, be based upon non-statutory obviousness-type double patenting and associated rules related to common ownership, which, if successful, could result in a finding that the patent claims at issue are invalid and unenforceable or a loss of patent term, including a patent term adjustment granted by the USPTO. Furthermore, patents may be held unenforceable if someone connected with prosecution of the patent in question withheld relevant information from the USPTO or made a misleading statement during prosecution of the patent. It is possible that prior art of which we and the patent examiner were unaware during prosecution exists, which could render our patents invalid. It is also possible that prior art may exist that we are aware of but do not believe is relevant to our current or future patents, but that could nevertheless be determined to render our patents invalid.

An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. If a defendant were to prevail on a legal assertion of invalidity or unenforceability of our patents covering one of our product candidates, we would lose at least part, and perhaps all, of the patent protection covering such product candidate. Competing drugs may also be sold in other countries in which our patent coverage might not exist or be as strong. If we lose a foreign patent lawsuit, alleging our infringement of a competitor's patents, we could be prevented from marketing our drugs in one or more foreign countries. Any of these outcomes would have a material adverse effect on our business.

Because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. There could also be public announcements of the results of hearing, motions, or other interim developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of shares of our common stock. Even if we ultimately prevail, a court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may not be an adequate remedy. Furthermore, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our business.

**If we are sued for infringing intellectual property of third parties, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates.**

Our commercial success depends, in part, upon our ability to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the proprietary rights and intellectual property of third parties. We may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates and technologies we use in our business. Our competitors or other third parties may assert infringement claims against us, alleging that our product candidates are covered by their patents. We cannot be certain that we do not infringe existing patents or that we will not infringe patents that may be granted in the future. For example, we are aware of companies that have filed patent applications directed to oxalate and uric acid degrading enzymes, some of which have already been allowed or issued, and others may issue in the future. It is possible that additional patent applications are filed and additional patents directed to these enzymes are granted in the future. Furthermore, because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of our product candidates. If a patent holder believes our product candidate infringes its patent rights, the patent holder may sue us even if we have received patent protection for our technology. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant drug revenue and against whom our own patent portfolio may thus have no deterrent effect.

If we were sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable. However, proving invalidity and unenforceability is difficult. In the United States, for example, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm our business and operating results. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our product candidates and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain such a license, it could be granted on non-exclusive terms, thereby providing our competitors and other third parties access to the same technologies licensed to us. Without such a license, we could be forced, including by court order, to cease developing and commercializing the infringing technology or product candidates. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed such third-party patent rights. A finding of infringement could significantly harm our business and operating results.

Risks Related to Enforcement of Our Intellectual Property Rights

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

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly in developing countries.

Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, the patent laws of some foreign countries do not afford intellectual property protection 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, for example, India and China, do not favor the enforcement of patents and other intellectual property rights. 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, certain foreign countries have compulsory licensing laws under which a patent owner must grant licenses



to third parties. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States.

Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, if our ability to enforce our patents to stop infringing activities is inadequate. These products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in the major markets for our product candidates, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

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

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. In addition, periodic maintenance fees on issued patents often must be paid to the USPTO and foreign patent agencies over the lifetime of the patent. While an unintentional lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, 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. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our drugs or procedures, we may not be able to stop a competitor from marketing drugs that are the same as or similar to our product candidates, which would have a material adverse effect on our business.

**If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.**

Although we have obtained composition of matter patents covering reloxaliase and its use in therapy, we also rely on trade secrets, including confidential and unpatented know-how important to the maintenance of our competitive position. We protect our trade secrets and confidential and unpatented know-how, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to such knowledge, such as our employees, outside scientific collaborators, advisors, contractors, contract manufacturers and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants that obligate them to maintain confidentiality and assign their inventions to us. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts in the United States and certain foreign jurisdictions are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be harmed.

**We may be subject to claims by third parties asserting that our employees or we have misappropriated or otherwise violated their intellectual property rights, or claiming ownership of what we regard as our own intellectual property.**

Many of our consultants, advisors and employees, including our senior management, were previously employed at other biotechnology or pharmaceutical companies. Some of these individuals, including certain members of our senior management, may have executed proprietary rights, non-disclosure and non-competition agreements, or similar agreements, in connection with such previous employment. Although we try to ensure that our consultants, advisors and employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such third party. Litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our senior management and scientific personnel. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Risks Related to Intellectual Property Laws

**Changes to the patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.**

As is the case with other biotechnological and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnological and pharmaceutical industries involve both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Recent patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act, or Leahy-Smith Act, signed into law on September 16, 2011, could increase those uncertainties and costs. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the Leahy-Smith Act has transformed the U.S. patent system into a “first to file” system. The first-to-file provisions, however, only became effective on March 16, 2013. It is still not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could harm our business, results of operations and financial condition.

In addition, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

## Risks Related to Our Common Stock

### Risks Related to Investments in Our Securities

**\* If we fail to maintain the listing of our common stock with a United States national securities exchange, the liquidity of our common stock could be adversely affected.**

On August 25, 2021, we received a letter from the Listing Qualifications Department (the “Staff”) of the Nasdaq Stock Market (“Nasdaq”) notifying us that, for the 30 consecutive business day period between July 14, 2021 through August 24, 2021, our common stock had not maintained a minimum closing bid price of \$1.00 per share (the “Minimum Bid Price Requirement”) required for continued listing on The Nasdaq Global Select Market pursuant to Nasdaq Listing Rule 5550(a)(2). The Nasdaq letter does not result in the immediate delisting of the Company’s common stock from The Nasdaq Global Select Market.

In accordance with Nasdaq Listing Rule 5810(c)(3)(A) (the “Compliance Period Rule”), we have been provided an initial period of 180 calendar days, or until February 21, 2022 (the “Compliance Date”), to regain compliance with the Minimum Bid Price Requirement. If, at any time during this 180-day period, the closing bid price for our common stock closes at \$1.00 or more per share for a minimum of 10 consecutive business days, as required under the Compliance Period Rule, the Staff will provide written notification to us that we comply with the Minimum Bid Price Requirement and the common stock will continue to be eligible for listing on The Nasdaq Global Select Market.

If we do not regain compliance with the Minimum Bid Price Requirement by the Compliance Date, we may be eligible for an additional 180 calendar day compliance period. To qualify, we would be required to transfer to The Nasdaq Capital Market and meet the continued listing requirement for the market value of publicly held shares and all other initial listing standards for The Nasdaq Capital Market, with the exception of the Minimum Bid Price Requirement, and would need to provide written notice to Nasdaq of our intention to cure the deficiency during the additional compliance period.

If it appears to the Staff that we will not be able to cure the deficiency, the Staff will provide written notice to us that our common stock will be subject to delisting. At that time, we may appeal the Staff’s delisting determination to a Nasdaq Hearing Panel (the “Panel”). We expect that our stock would remain listed pending the Panel’s decision. There can be no assurance that, if we do appeal the Staff’s delisting determination to the Panel, such appeal would be successful.

We intend to monitor the closing bid price of our common stock and may, if appropriate, consider available options to regain compliance with the Minimum Bid Price Requirement, which could include seeking to effect a reverse stock split. However, there can be no assurance that we will be able to regain compliance with the Minimum Bid Price Requirement, secure a second period of 180 days to regain compliance, or maintain compliance with any of the other Nasdaq continued listing requirements.

If our common stock is delisted by Nasdaq, our common stock may be eligible to trade on the OTC Bulletin Board or another over-the-counter market. Any such alternative would likely result in it being more difficult for us to raise additional capital through the public or private sale of equity securities and for investors to dispose of, or obtain accurate quotations as to the market value of, our common stock. In addition, there can be no assurance that our common stock would be eligible for trading on any such alternative exchange or markets.

**\* The price of our common stock may be volatile and fluctuate substantially.**

On November 6, 2017, we completed the sale of 5,333,333 shares of our common stock in our IPO, at a price to the public of \$14.00 per share. Since our common stock began trading on The Nasdaq Global Select Market on November 6, 2017, our stock has traded at prices as low as \$0.53 per share and as high as \$17.56 per share through November 5, 2021. There has been a public market for our common stock for only a short period of time. Although our common stock is listed on The Nasdaq Global Select Market, an active public market for our common stock may not emerge or be sustained, particularly if our stock were to be delisted from Nasdaq.

In addition, the market price for our common stock may fluctuate significantly in response to a number of factors, including:

- the success of competitive drugs or technologies;
- regulatory actions with respect to our product candidates or our competitors' products and product candidates;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or drugs;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts, and our performance in relation to such estimates;
- variations in our financial results or those of companies that are perceived to be similar to us;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

In addition, the trading prices for common stock of other biopharmaceutical and biotechnology companies have been highly volatile as a result of the COVID-19 pandemic. The COVID-19 pandemic continues to rapidly evolve. The extent to which the outbreak may impact our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence.

**\* A significant portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is otherwise doing well.**

If our existing stockholders sell, or indicate an intent to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline significantly. As of November 5, 2021, we had 82,571,078 outstanding shares of common stock, assuming no exercise of outstanding options or warrants. In addition, the 7,188,457 shares subject to outstanding options and 372,166 outstanding restricted stock units under our stock option plans as of September 30, 2021, the 1,183,856 shares reserved for future issuance under our stock option plans, the 332,704 shares reserved for future issuance under our employee stock purchase plan and the 10,687,912 shares subject to outstanding warrants, including the 10,678,872 warrants issued with the registered direct offering completed in July 2021, will become eligible for sale in the public market in the future, subject to certain legal and contractual limitations. If our existing stockholders sell substantial amounts of our common stock in the public market, or if the public perceives that such sales could occur, this could have an adverse impact on the market price of our common stock, even if there is no relationship between such sales and the performance of our business.

**Volatility in our share price could subject us to securities class action litigation.**

Securities class action litigations have often been brought against companies following a decline in the market price of their securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant share price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

**Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, would result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.**

We will need additional capital in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. 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. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to those of our existing stockholders.

Pursuant to our 2017 Stock Option and Incentive Plan, or the 2017 Plan, we are authorized to grant stock options and other equity-based awards to our employees, directors and consultants. The number of shares available for future grant under the 2017 Plan will automatically increase each year by up to 4% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our board of directors or compensation committee to take action to reduce the size of the increase in any given year. Currently, we plan to register the increased number of shares available for issuance under the 2017 Plan each year. If our board of directors elects to increase the number of shares available for future grant by the maximum amount each year, our stockholders may experience additional dilution, and our stock price may fall.

Risks Related to Operations

**Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.**

We are subject to the periodic reporting requirements of the Exchange Act of 1934, as amended, or the Exchange Act. Our disclosure controls and procedures are designed to reasonably ensure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures as well as internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are and will be met. These inherent limitations include the realities that judgments in decision-making can be faulty and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

Risks Related to Insider Control

**\* Our directors, executive officers and principal stockholders exercise significant control over our company, which will limit your ability to influence corporate matters.**

As of November 5, 2021, our executive officers, directors and principal stockholders collectively controlled approximately 15.2% of our outstanding common stock, excluding any shares of common stock that such persons may have the right to acquire upon exercise of outstanding options or warrants. As a result, these stockholders, if they act together, will be able to influence our management and affairs and all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions.

Risks Related to Our Status as an “Emerging Growth Company”

**We are an “emerging growth company,” and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.**

We are an “emerging growth company,” as defined in the JOBS Act, and may remain an emerging growth company for up to five years from the time of our IPO. For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of SOX Section 404, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. As a result, the information we provide stockholders will be different than the information that is available with respect to other public companies. In this Quarterly Report, we will not include all of the executive compensation related information that would be required if we were not an emerging growth

company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock, and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards, and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

**As a public reporting company, we are subject to rules and regulations established from time to time by the SEC and the Public Company Accounting Oversight Board, or PCAOB, regarding our internal control over financial reporting. We may not complete improvements to our internal control over financial reporting in a timely manner, or these internal controls may not be determined to be effective, which may adversely affect investor confidence in our company and, as a result, the market price of our common stock could decline and you could lose all or part of your investment.**

Upon completion of our IPO, we became a public reporting company subject to the rules and regulations established from time to time by the SEC and the PCAOB. These rules and regulations require, among other things that we establish and periodically evaluate procedures with respect to our internal controls over financial reporting. These reporting obligations are likely to place a considerable strain on our financial and management systems, processes and controls, as well as on our personnel.

We are required to document and test our internal controls over financial reporting pursuant to SOX Section 404, so that our management can certify as to the effectiveness of our internal controls over financial reporting which requires us to document and make significant changes to our internal controls over financial reporting. In addition, our independent registered public accounting firm will be required to provide an attestation report on the effectiveness of our internal control over financial reporting at such time as we cease to be an “emerging growth company,” as defined in the JOBS Act, although, as described in the preceding risk factor, we could potentially qualify as an “emerging growth company” up to five years from the time of our IPO. At such time, our independent registered public accounting firm may issue a report that is adverse in the event it is not satisfied with the level at which our controls are documented, designed or operating.

If our senior management is unable to conclude that we have effective internal control over financial reporting, or to certify the effectiveness of such controls, or if our independent registered public accounting firm cannot render an unqualified opinion on management’s assessment and the effectiveness of our internal control over financial reporting once we cease to be an emerging growth company, or if material weaknesses in our internal controls are identified, we could be subject to regulatory scrutiny and a loss of public confidence, which could have a material adverse effect on our business and our stock price. In addition, if we do not maintain adequate financial and management personnel, processes and controls, we may not be able to manage our business effectively or accurately report our financial performance on a timely basis, which could cause a decline in our common stock price and adversely affect our results of operations and financial condition.

#### Risks Related to Dividends

**We do not intend to pay dividends on our common stock and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our common stock.**

We have never declared or paid any cash dividend on our common stock and do not currently intend to do so in the foreseeable future. Our credit facility with Pontifax also prohibits us from paying cash dividends without the prior written consent of Pontifax. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends in the foreseeable future. Therefore, the success of an investment in shares of our common stock will depend upon any future appreciation in their value. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which you purchased them.

#### Risks Related to Tax

**Changes in tax law could adversely affect our financial condition and results of operations.**

The rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. We urge investors to consult

with their legal and tax advisers regarding the implications of potential changes in tax laws on an investment in our common stock.

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

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 percentage point change (by value) in the ownership of its equity over a three year period), the corporation’s ability to use its pre-change net operating loss carryforwards and certain other pre-change tax attributes to offset its post-change income may be limited. As of June 3, 2020, we did have an ownership change and have adjusted our federal and state tax attributes accordingly to disclose only the amounts that can be utilized annually to offset future taxable income or tax liabilities. We may experience additional ownership changes or subsequent shifts in our stock ownership, some of which are outside our control. As of December 31, 2020, we had federal net operating loss carryforwards of approximately \$140.9 million. However, our ability to utilize those net operating loss carryforwards will be limited by the “ownership change” as described above, which could result in increased tax liability to us. U.S. federal net operating losses generated in taxable years beginning after December 31, 2017 are not subject to expiration and net operating losses generated in taxable years beginning after December 31, 2017 and before January 1, 2021 are permitted to be carried back five years. Additionally, the deductibility of federal net operating loss carryforwards generated in taxable periods beginning after December 31, 2020 is limited to 80% of taxable income in any future taxable year, where taxable income is determined without taking into account the net operating loss.

Risks Related to Our Charter and Bylaws

**Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.**

Provisions in our restated certificate of incorporation and amended and restated by-laws may delay or prevent an acquisition of us or a change in our management. These provisions include a classified board of directors, a prohibition on actions by written consent of our stockholders and the ability of our board of directors to issue preferred stock without stockholder approval. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively provide for an opportunity to obtain greater value for stockholders by requiring potential acquirors to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, 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.

**General Risk Factors**

**Our business and operations would suffer in the event of computer system failures, cyber-attacks on our systems or deficiency in our cyber security.**

Despite the implementation of security measures, our internal computer systems, and those of third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, malware, natural disasters, fire, terrorism, war and telecommunication, electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. For example, companies have experienced an increase in phishing and social engineering attacks from third parties in connection with the COVID-19 pandemic. In addition, our systems safeguard important confidential personal data regarding patients enrolled in our clinical trials. If a disruption event were to occur and cause interruptions in our operations, it could result in a disruption of our drug development programs. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to

our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of reloxaliase and any other product candidates we may develop could be delayed.

**We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to compliance initiatives and corporate governance practices.**

As a public company, and particularly after we are no longer an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Stock Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We expect that we will need to hire additional accounting, finance and other personnel in connection with our efforts to comply with the requirements of being a public company and our management and other personnel will need to devote a substantial amount of time towards maintaining compliance with these requirements. These requirements will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. We are currently evaluating these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act, or SOX Section 404, we are required to furnish a report by our management on our internal control over financial reporting in our Quarterly Report as filed with the Securities and Exchange Commission, or the SEC. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with SOX Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which has been both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

**If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.**

The trading market for our common stock will likely depend, in part, on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. There can be no assurance that analysts will cover us, or provide favorable coverage. If one or more analysts downgrade our stock or change their opinion of our stock, our share price would likely decline. In addition, if one or more analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.



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

**Recent Sales of Unregistered Securities**

None.

**Issuer Purchases of Equity Securities**

In the quarter ended September 30, 2021, we did not repurchase any shares of our common stock.

**Item 3. Defaults Upon Senior Securities.**

None.

**Item 4. Mine Safety Disclosures.**

None.

**Item 5. Other Information.**

None.

**Item 6. Exhibits.**

Furnish the exhibits required by Item 601 of Regulation S-K (§ 229.601 of this chapter).

<b>Exhibit Number</b>	<b>Description</b>
3.1*	<a href="#"><u>Amended and Restated Certificate of Incorporation of Allena Pharmaceuticals, Inc., as amended (incorporated by reference to Exhibit 3.1 to the Company's Form 10-Q filed on August 12, 2021).</u></a>
3.2**	<a href="#"><u>Amended and Restated By-Laws of Allena Pharmaceuticals, Inc. (incorporated by reference to Exhibit 3.2 to the Company's Form 8-K filed on November 6, 2017).</u></a>
4.1**	<a href="#"><u>Form of Indenture for Senior Debt Securities and the Related Form of Senior Debt Security (incorporated by reference to Exhibit 4.5 to the Company's Form S-3 filed on May 6, 2021).</u></a>
4.2**	<a href="#"><u>Form of Indenture for Subordinated Debt Securities and the Related Form of Subordinated Debt Security (incorporated by reference to Exhibit 4.6 to the Company's Form S-3 filed on May 6, 2021).</u></a>
4.3**	<a href="#"><u>Form of Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.1 of the Company's Form 8-K filed on July 16, 2021).</u></a>
4.4**	<a href="#"><u>Form of Pre-Funded Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.2 of the Company's Form 8-K filed on July 16, 2021).</u></a>
31.1*	<a href="#"><u>Certification of Principal Executive Officer pursuant to Exchange Act rules 13a-14 or 15d-14.</u></a>
31.2*	<a href="#"><u>Certification of Principal Financial Officer pursuant to Exchange Act rules 13a-14 or 15d-14.</u></a>
32.1+	<a href="#"><u>Certification of Principal Executive Officer and Principal Financial Officer pursuant to Exchange Act rules 13a-14(b) or 15d-14(b) and 18 U.S.C. Section 1350.</u></a>
101.INS*	Inline XBRL Instance Document.
101.SCH*	Inline XBRL Taxonomy Extension Schema Document.
101.CAL*	Inline XBRL Taxonomy Extension Calculation Document.
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB*	Inline XBRL Taxonomy Extension Labels Linkbase Document.
101.PRE	Inline XBRL Taxonomy Extension Presentation Link Document.
104	Cover page Interactive Data File (embedded within Inline XBRL document)

\* Filed herewith.

\*\* Previously filed.

+ The certification furnished in Exhibit 32.1 hereto is deemed to be furnished with this Quarterly Report on Form 10-Q and will not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

**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.

ALLENA PHARMACEUTICALS, INC.

November 12, 2021

By: /s/ Louis Brenner  
Louis Brenner, M.D.  
*Chief Executive Officer and Director*  
*(Principal Executive Officer)*

November 12, 2021

By: /s/ Richard Katz  
Richard Katz, M.D.  
*Chief Financial Officer*  
*(Principal Financial and Accounting Officer)*

**CERTIFICATION PURSUANT TO  
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,  
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Louis Brenner, certify that:

1. I have reviewed this quarterly report on Form 10-Q for the period ended September 30, 2021 of Allena 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 and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

November 12, 2021

By: /s/ Louis Brenner

Louis Brenner, M.D.

*Chief Executive Officer, President and Director  
(Principal Executive Officer)*

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**CERTIFICATION PURSUANT TO  
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,  
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Richard Katz, certify that:

1. I have reviewed this quarterly report on Form 10-Q for the period ended September 30, 2021 of Allena 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 and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

November 12, 2021

By: /s/ Richard Katz

Richard Katz, M.D.

*Chief Financial Officer*

*(Principal Financial and Accounting Officer)*

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**CERTIFICATION PURSUANT TO  
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO  
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the quarterly report on Form 10-Q of Allena Pharmaceuticals, Inc. (the "Company") for the period ended September 30, 2021, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers hereby certifies, pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, 18 U.S.C. Section 1350, that to his knowledge:

1. the Report which this statement accompanies fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and
2. the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

November 12, 2021

By: /s/ Louis Brenner

Louis Brenner, M.D.

*Chief Executive Officer, President and Director  
(Principal Executive Officer)*

November 12, 2021

By: /s/ Richard Katz

Richard Katz, M.D.

*Chief Financial Officer  
(Principal Financial and Accounting Officer)*

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