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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 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)

Delaware	**45-2729920**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
One Newton Executive Park, Suite 202 Newton, MA	**02462**
(Address of principal executive offices)	**(Zip Code)**

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

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

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	ALNA	The Nasdaq Capital Market

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

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

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

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

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

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

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

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

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

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 June 30, 2021, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of Common Stock held by non-affiliates of the registrant computed by reference to the price of the registrant's Common Stock (based on the last reported sale price on the Nasdaq Global Select Market as of such date) was $76,417,879.

As of March 25, 2022 there were 89,774,309 shares of the registrant's Common Stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A within 120 days of the end of the fiscal year ended December 31, 2021. Portions of such definitive proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K.

Allena Pharmaceuticals, Inc.
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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or this Annual Report, 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 on our management's belief and assumptions and on information currently available to our management. These statements relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- our estimates and expectations regarding our capital requirements, cash and expense levels, liquidity sources and our need for additional financing and our ability to continue as a going concern;
- our ability to fund our operating expenses and capital requirements beyond the next several weeks;
- our ability to consummate a strategic or financing transaction, including a possible partnership for ALLN-346;
- in the event we are unable to obtain sufficient funds to continue our operations, our ability to obtain an in-court or out-of-court restructuring of our liabilities;
- our ability to enroll a sufficient number of patients (including as a result of any delays arising from the global outbreak of the coronavirus, or the COVID-19 coronavirus) 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 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 ALLN-346;
- the market acceptance of ALLN-346 or any future product candidates that are approved for marketing in the United States or other countries;
- our ability to successfully commercialize ALLN-346 and any future product candidates with a targeted sales force;
- 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, political unrest in the U.S. and abroad, 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 ALLN-346 and any future product candidates, 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;

This list is not exhaustive. Other sections of this Annual Report on Form 10-K 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 Annual Report, 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 Annual Report and the documents that we reference herein and have filed as exhibits hereto as 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 Annual Report represent our views as of the date of this Annual Report. 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 Annual Report.

PART I

Unless the context otherwise requires, we use the terms "Allena," "the Company," "we," "us," "our" and similar designations in this Annual Report to refer to Allena Pharmaceuticals, Inc. and its wholly owned subsidiaries.

ITEM 1. BUSINESS

Overview

We are a biopharmaceutical company dedicated to developing and commercializing first-in-class, oral enzyme therapeutics to treat patients with rare and severe metabolic and kidney disorders. We are focused on metabolic disorders that result in excess accumulation of certain metabolites that stimulate inflammation, damage the kidney, and potentially lead to chronic kidney disease, or CKD, and end-stage renal disease, or ESRD. We believe our proprietary know-how in enzyme technology allows for the design, development, formulation, and scalable manufacturing of non-absorbed and stable enzymes delivered orally and in sufficient doses for activity in the gastrointestinal tract. This approach enables us to develop enzyme therapies that degrade metabolites within the GI tract, which reduces potentially toxic metabolite levels in the blood and urine, and in turn, diminishes the systemic disease burden including on the kidney over time.

Our product candidate, ALLN-346, is an orally administered, novel, urate degrading enzyme for patients with hyperuricemia and gout in the setting of advanced CKD, for which we have Fast Track designation from the U.S. Food and Drug Administration (FDA). We have conducted a Phase 1 program, including both a single-ascending dose and multiple-ascending dose study in healthy volunteers. In both studies, ALLN-346 was well tolerated with no clinically significant safety signals and no dose-limiting toxicities observed in any cohort up to the highest administered dose. We are currently conducting two Phase 2a studies. Study 201 is a 7-day inpatient study in patients with hyperuricemia, for which we reported initial data in January 2022. Study 202 is a 14-day outpatient study in patients with hyperuricemia, gout and varying degrees of renal insufficiency, for which we expect to report initial data in Q2 2022.

We previously had been developing reloxaliase, a first-in-class, oral enzyme therapeutic for the treatment of hyperoxaluria, a metabolic disorder characterized by markedly elevated urinary oxalate, or UOx, levels and commonly associated with kidney stones, CKD and ESRD. However, in March 2022 we terminated this program following the first of two planned Sample Size Reestimations (SSR1) of the Phase 3 URIROX-2 Trial, which was conducted by an independent data safety monitoring board (DSMB) statistician. SSR1 was designed to assess the effect of reloxaliase vs. placebo on the reduction of urinary oxalate (UOx) levels over the first 28 days of the trial, the primary endpoint to support a potential accelerated approval filing. The trial had been initially sized at 200 subjects, which would provide more than 90% power for the primary UOx endpoint based on an assumption of a 15% greater effect size of reloxaliase over placebo. The DSMB was provided with data for the first 78 subjects enrolled in the trial. Based on the results of its unblinded analysis, the DSMB recommended that the trial size be increased from the initial 200 subjects to the maximum allowed number of 400 subjects under the pre-specified rules. However, even with this maximum recommended sample size increase, the power to detect an effect of reloxaliase vs. placebo would still be less than 80% based on the available data. Based upon this recommendation, we believe that the separation between the reloxaliase and placebo groups for the UOx primary endpoint is lower than expected, and therefore that the likelihood of success for the long term endpoint of reduction in kidney stone disease progression is also lower than expected. As such, we have decided to terminate the URIROX-2 study and have initiated the process of closing the study with the CRO, investigative sites, patients, and business partners. No further clinical studies of reloxaliase are planned at this time.

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. Utilizing our proprietary technological approach, we conceived and developed ALLN-346, which is a novel, oral enzyme therapeutic for the treatment hyperuricemia. Our proprietary and scalable manufacturing capabilities have enabled us to produce sufficient quantities of ALLN-346 to support our clinical development program.

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. Humans lack urate oxidase, an enzyme that degrades uric acid in a wide range of other organisms, including animals, plants, bacteria and fungi. Hyperuricemia is the major predisposing condition for gout, a disease that most commonly manifests with acute flares of arthritis, and can also lead to chronic arthritis, joint damage and palpable deposits of urate crystals in the skin. Hyperuricemia can also lead to increased uric acid excretion in the urine and subsequently to kidney stone formation and kidney damage, also known as urate nephropathy. In addition, hyperuricemia has been linked to hypertension, CKD, glucose intolerance, dyslipidemia, insulin resistance, obesity and cardiovascular disease.

We engineered ALLN-346 to degrade urate in the GI tract and, in turn, reduce the urate burden on the kidney and lower the risk of urate-related complications. ALLN-346 is targeted to lower serum uric acid in patients with CKD, who have

decreased kidney function and diminished capacity for urinary excretion of uric acid. 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. An estimated 375,000 patients in the United States have refractory gout and CKD.

We are currently conducting two Phase 2a studies of ALLN-346: Study 201, a one-week inpatient study being conducted at a clinical pharmacology unit (CPU), and Study 202, a two-week outpatient study being conducted at approximately 20 sites across the U.S. During the first quarter of 2021, we reported initial results from Study 201, which we believe established proof of pharmacology. Subject to securing adequate financing, we expect to report further data from Study 201 and initial data from Study 202 during the second quarter of 2022. In all clinical trials conducted to date ALLN-346 has been well-tolerated with no clinically significant safety signals.

Strategy

Our goal is to advance the development of ALLN-346, an orally administered, novel urate degrading enzyme that has been optimized for stability in the intestinal tract. This proprietary enzyme was designed by our scientists to degrade urate in the intestinal tract and thereby reduce the urate burden on the kidney and lower the risk of urate-related complications. ALLN-346 is targeted to lower serum uric acid in patients with CKD, who have decreased kidney function and diminished capacity for urinary excretion of uric acid. 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.

We have conducted two preclinical proof-of-concept studies in mice and pigs that support the potential of ALLN-346 as an oral therapy for the treatment of hyperuricemia in patients with gout and associated CKD. We received clearance of the IND for ALLN-346 from the FDA in the first quarter of 2020 and completed a Phase 1 program with favorable results during 2020. We are currently conducting two Phase 2a studies of ALLN-346: Study 201, a one-week inpatient study being conducted at a clinical pharmacology unit (CPU), and Study 202, a two-week outpatient study being conducted at approximately 20 sites across the U.S. During the first quarter of 2021, we reported initial results from Study 201, which we believe established proof of pharmacology. Subject to securing adequate financing, we expect to report further data from Study 201 and initial data from Study 202 during the second quarter of 2022. In all clinical trials conducted to date ALLN-346 has been well-tolerated with no clinically significant safety signals.

We are currently exploring financing and strategic alternatives to provide adequate resources to further advance the development of ALLN-346 with the assistance of Stifel.

Competitive Strengths

We believe the following competitive strengths have been and continue to be important to our business:

- Lead product candidate, ALLN-346, which has received Fast Track designation and for which we are currently conducting two Phase 2a clinical trials;
- Therapeutic focus on rare and severe metabolic disorders that affect the kidney and have high unmet medical needs due to the absence of approved or effective therapies;
- Proprietary technological approach that allows us to design, formulate and deliver non-absorbed and stable enzymes orally and in sufficient doses for activity in the GI tract, an approach that enables us to develop enzyme therapies that utilize the GI tract to degrade metabolites, such as urate, reducing plasma and urine levels, and in turn, reducing their disease burden including on the kidney over time;
- Management team with substantial experience in developing and commercializing pharmaceutical products for metabolic and kidney disorders;
- Strong relationships with key opinion leaders and patient advocacy groups focused on metabolic and kidney disorders; and
- Board members with experience in building and operating life science companies.

ALLN-346

Overview of Hyperuricemia & Gout

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. Humans lack urate oxidase, an enzyme that degrades uric acid in a wide range of other organisms, including animals, plants, bacteria and fungi. Hyperuricemia can be a predisposing condition for gout and kidney stones, and is also intricately linked with various metabolic disorders, including hypertension, CKD, glucose intolerance, dyslipidemia, insulin resistance and obesity. Hyperuricemia may also be an independent risk factor for cardiovascular disease.

Gout is an arthritic condition caused by excess uric acid in the blood. When uric acid levels in the blood are too high, hard crystals may form in the joints, causing sudden attacks of burning pain, stiffness, and swelling. These attacks can happen repeatedly unless gout is treated. Over time, they can harm joints, tendons, and other tissues.

There are approximately 850,000 hyperuricemic patients with moderate to severe CKD on urate lowering therapy, of which approximately 375,000 have uncontrolled gout.

Current Therapeutic Options and Their Limitations

There are currently three classes of drugs approved to treat hyperuricemia and gout. The most commonly prescribed medications, xanthine oxidase inhibitors such as allopurinol and febuxostat, are orally available drugs that work by decreasing the production of uric acid. Uricosuric agents, such as probenicid, are also orally available, and exert their effect by increasing the excretion of uric acid in the kidney. Additionally, an injectable recombinant uricase, pegloticase, exerts its effect by breaking down urate in the bloodstream. Because of a number of factors, including its intravenous route of administration, pegloticase is generally reserved for use in patients with severe disease.

We engaged a healthcare strategy consulting firm that estimated the market for urate lowering therapies to be approximately $1 billion in the U.S. and concluded that it was incompletely served by existing therapies. Hyperuricemic and gout patients with renal impairment are more challenging to manage due to limitations of existing therapies. Several of the currently approved drugs for gout raise concerns over lack of efficacy or increased toxicity in patients with reduced kidney function. These limitations include poor tolerability, reduced efficacy, dose restriction and contraindications. Co-morbidities (e.g. cardiovascular disease) are common in this patient population and may also limit urate lowering therapeutic options. Accordingly, there is a significant unmet need for a safe and effective therapy that can be used in gout patients with renal impairment.

Our Solution

We have designed our product candidate, ALLN-346, an orally administered, novel, urate degrading enzyme, for which we have received Fast Track designation from the FDA, for the treatment of patients with hyperuricemia and gout in the setting of 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. Humans lack urate oxidase, an enzyme that degrades uric acid in a wide range of other organisms, including animals, plants, bacteria and fungi. Hyperuricemia is associated with gout, an arthritic condition caused by excess uric acid in the blood that leads to the formation of hard crystals in the joints. Hyperuricemia can also lead to increased uric acid excretion in the urine and subsequently to kidney stone formation and kidney damage, also known as urate nephropathy. In addition, hyperuricemia has been linked to hypertension, CKD, glucose intolerance, dyslipidemia, insulin resistance and obesity.

We engineered ALLN-346 to degrade urate in the GI tract and, in turn, reduce the urate burden on the kidney and lower the risk of urate-related complications. ALLN-346 is targeted to lower serum uric acid in patients with CKD, who have decreased renal function and diminished capacity for urinary excretion of uric acid. Patients with renal impairment who have hyperuricemia and gout are often not optimally managed due to limitations of available therapies, including decreased tolerability, dose restrictions, drug-drug interactions and contraindications.

We have conducted two preclinical proof-of-concept studies in mice and pigs that support the potential of ALLN-346 as an oral therapy for the treatment of hyperuricemia in patients with gout and associated CKD. In June 2018, we announced completion of a preclinical proof-of-concept study and presented the data at the American College of Rheumatology meeting in October 2018. The poster presentation included data demonstrating urate reduction in a urate oxidase knock-out mouse model, a severe animal model of hyperuricemia with advanced CKD and kidney damage due to urate crystal deposition. After one week of treatment, mice treated with ALLN-346 achieved a robust reduction in urate burden on the kidney, as evidenced by normalization in urine uric acid and a significant reduction in plasma urate. We believe this study supports our selection of ALLN-346 as our lead product candidate for the treatment of hyperuricemia in patients with gout and associated CKD. We also presented the results of a pilot study in a pig model with acute hyperuricemia at the American College of Rheumatology meeting in October 2019. A pig model was chosen as a high vertebrate model that closely mimics human gastrointestinal and renal systems. In seven juvenile pigs with severe hyperuricemia induced by intravenous uric acid infusion, enteral administration of ALLN-346 significantly lowered plasma urate levels (AUC) by 38%, along with a significant reduction in

urine urate excretion. The results of this study confirm the role of the small intestine in urate elimination, and further supports the potential of ALLN-346 oral therapy to reduce hyperuricemia and the overall urate burden in patients with gout.

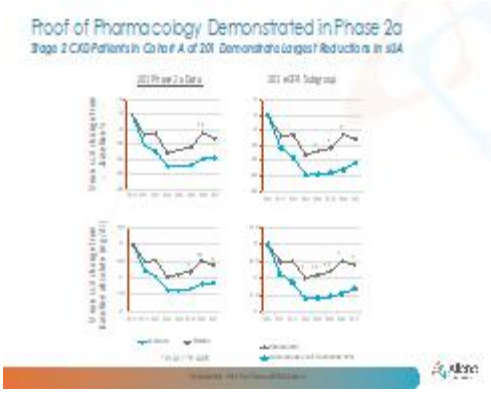
We filed an IND for ALLN-346 with the FDA in the fourth quarter of 2019 and initiated a single ascending dose Phase 1 clinical trial during the second quarter of 2020, for which we reported results during the fourth quarter of 2020. The double-blind, placebo-controlled, SAD study enrolled 24 healthy volunteers. Groups of eight study participants were randomized 3:1 to ALLN-346 or matching placebo in three sequential cohorts dosed orally with three, six, or 12 capsules in one day. Each capsule of ALLN-346 contained a target dose of 90 mg of enzyme, equivalent to 2,250 units. ALLN-346 was well-tolerated with no clinically significant safety signals and no dose-limiting toxicities observed in any cohort up to the highest administered dose. In addition, assay of serum samples by ELISA immunoassay demonstrated that ALLN-346 was not absorbed systemically, supporting that its mechanism of action appears to be restricted to the GI tract.

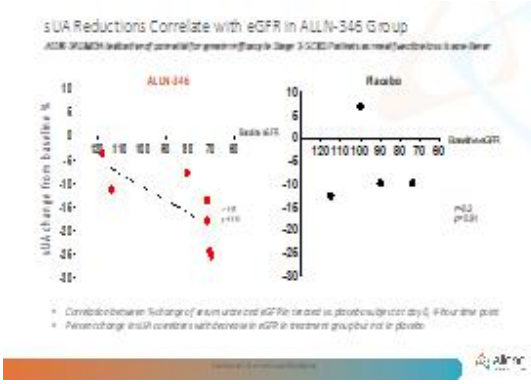
Following the successful completion of the single-ascending dose Phase 1 study, we initiated a multiple-ascending dose Phase 1 study during the second quarter of 2021, for which we reported results during the third quarter of 2021. The study included 18 healthy volunteers, who received either ALLN-346 or placebo (2:1 randomization) for seven days. There were two cohorts consisting of nine subjects each, with the first receiving three capsules of ALLN-346 three times daily, and the second receiving five capsules of ALLN-346 three times daily. ALLN-346 was well tolerated with no evidence of systemic absorption, as confirmed by an enzyme-linked immunosorbent assay (ELISA). Evaluation of clinical and laboratory parameters revealed no clinically significant safety signals and no serious adverse events were reported.

We are currently conducting two Phase 2a studies of ALLN-346. The first of these, Study 201, is a one-week inpatient study being conducted at a clinical pharmacology unit (CPU). In Study 201, patients with hyperuricemia are being randomized (2:1) to receive either five capsules of ALLN-346 or matching placebo three times daily for one week. Planned enrollment in the trial consists of two cohorts, each with approximately 12 patients. Of the 11 patients in the first cohort, seven received ALLN-346 and four received placebo. The majority of these patients had Stage 2 CKD, including five of the seven subjects treated with ALLN-346. The second cohort is currently being enrolled with topline data expected in Q2 2022. Key bioactivity endpoints include serum uric acid level, 24-hour urine uric acid level, and renal clearance of uric acid.

Data from the first cohort of Study 201 demonstrated a statistically significant reduction in serum uric acid (sUA) from baseline ($p<0.05$) in patients treated with ALLN-346. Consistent with the known pathophysiologic adaptation of increased intestinal elimination of uric acid in patients with impaired kidney function and the GI-based mechanism of action of ALLN-346, there was a strong correlation between the effect of ALLN-346 on sUA reduction and the level of kidney function (correlation coefficient $r=0.95$; $p=0.003$). We believe that these results support proof of pharmacology for the gastrointestinal (GI) mechanism of action of ALLN-346. In the first cohort, ALLN-346 was well-tolerated with no clinically significant safety signals and no serious adverse events were reported.

The topline data on sUA from patients in the first cohort during the one-week treatment period are shown graphically below:





The second Phase 2a trial of ALLN-346, Study 202, is a two-week, outpatient study designed to enroll hyperuricemic patients with gout and CKD and is currently being conducted at approximately 20 sites across the U.S. Patients are being randomized (2:1) to receive either five capsules of ALLN-346 or a matching placebo three times daily, with enrollment of up to four planned cohorts, each consisting of approximately 12 patients. Cohort A is currently enrolling patients with an estimated glomerular filtration rate (eGFR) of 60-89 mL/minute (considered to have Stage 2, or mild CKD), and cohort B is

currently enrolling patients with an eGFR of 30-59 mL/minute (considered to have Stage 3, or moderate CKD). Key bioactivity endpoints will include serum uric acid level, 24-hour urine uric acid level, and renal clearance of uric acid. Topline safety and efficacy data from each of these two cohorts is expected to be available in the second quarter of 2022.

If we are able to secure adequate additional financing and subject to a planned protocol amendment, we plan to open two additional cohorts in Study 202 during Q2 2022, consisting of patients with Stage 4 or advanced CKD (Cohort C) and an allopurinol combination therapy cohort in Stage 3 CKD patients (Cohort D).

Our Proprietary Technological Approach

Expertise in Enzyme Technology

We believe our proprietary know-how in enzyme technology allows for the design, development, formulation, and scalable manufacturing of non-absorbed and stable enzymes delivered orally and in sufficient doses for activity in the GI tract. This approach enables us to develop enzyme therapies that degrade metabolites within the GI tract, which reduces potentially toxic metabolite levels in the blood and urine, and in turn, diminishes the disease burden including on the kidney over time. 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. Utilizing our proprietary technological approach, we conceived and are developing ALLN-346, a novel, oral enzyme therapeutic for the treatment of hyperuricemia and gout.

One of the technologies that we use in our lead product candidate, ALLN-346, is protein crystallization, which stabilizes a highly active form of the urate degrading enzyme, uricase, ensuring effective transit through the GI tract, as well as stabilization at room temperature for convenient storage. Crystallized enzymes are more stable, pure and concentrated than enzymes in solution. For example, one enzyme crystal may contain several billion molecules of the underlying enzyme. These characteristics improve storage and delivery, permitting delivery of the enzyme molecules with fewer capsules. Once an enzyme is in the crystallized state, we can formulate it for oral delivery. 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. For example, Renagel and Renvela, marketed by Sanofi, remove excess levels of phosphate in the body in patients with CKD by delivering drug to the GI tract, where it binds to phosphate and removes it from the body through the bowel.

Manufacturing

ALLN-346 is an oral, solid dosage form of crystalline uricase enzyme that is produced using methods of production that have been carefully selected for cost-effectiveness and ease of scaling. We believe our manufacturing technology enables us to produce large quantities of our oral enzyme product candidates, sufficient to support our clinical and planned commercial strategy.

Manufacturing biological products is generally a complex and cost intensive process because they are manufactured in living systems or cells and tend to be large complex molecules. Since the living systems used to produce biologics can be sensitive to minor changes in manufacturing techniques, small process differences can significantly affect the nature of the finished biologic product and, most importantly, the way it functions in the body.

Production of ALLN-346 occurs utilizing scientifically developed know-how, delivering high productivity from host bacterial cells. The entire biomass is harvested and processed through primary recovery and downstream purification unit operations, resulting in the recovery of large quantities of uricase. The purified and concentrated product is dried into a protein powder, and formulated for production as an oral tablet/capsule combination drug product.

Drug product production starts with dried uricase drug substance, then uses tailored pharmaceutical techniques to blend, densify, tablet and enterically coat the product candidate. The final presentation includes four enterically coated tablets contained in a single immediate release capsule. The combination oral capsule-tablet presentation has attractive properties of pharmaceutical activity, product stability and modulation of product release suitable for further development and ultimate commercial use, if approved. While still in early development, detailed plans have been developed for further improvements in product potency, enhanced product release characteristics and reduced pill burden.

The unique gene-engineered nature of ALLN-346 and its expected mechanism of action 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.

We have secured development and supply agreements with premiere global drug product contract manufacturing organizations suited to support our clinical development program for ALLN-346.

Commercialization Strategy

We hold worldwide development and commercialization rights to ALLN-346. Provided that we are able to secure adequate funding to continue the development of ALLN-346, we currently expect that we will enter into one or more strategic partnerships to enable the further development and eventual commercialization of ALLN-346, if approved. We have engaged Stifel to assist us in exploring financing and strategic alternatives to provide for the continued clinical development and commercialization of ALLN-346, including a potential sale of the program.

Competition

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, biotechnology companies and specialty pharmaceutical companies. Key competitive factors affecting the commercial success of 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 are currently 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. According to its 2020 annual report, Horizon reported over $400 million in net sales for KRYSTEXXA in 2020 and, in January 2020, announced it increased its peak annual sales expectations for KRYSTEXXA to more than $1 billion in peak U.S. annual net sales. However, KRYSTEXXA must be administered intravenously and is generally prescribed only for the most severely affected gout patients. In addition to Horizon, a number of other competitors have medicines 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.

Intellectual Property

We strive to protect the proprietary technologies that we believe are important to our business, including seeking and maintaining patents intended to cover the composition of matter of our product candidates, their methods of use and processes for their manufacture, and any other aspects of inventions that are commercially important to the development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will depend on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, defend and enforce our patents, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and patent scope can be reinterpreted by the courts after issuance. Moreover, many jurisdictions permit third parties to challenge issued patents in administrative proceedings, which may result in further narrowing or even cancellation of patent claims. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any or our issued patents will provide sufficient protection from competitors. Any of our patents may be challenged, circumvented, or invalidated by third parties.

Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months or potentially even longer, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. Moreover, we may have to participate in interference proceedings or derivation proceedings declared by the U.S. Patent and Trademark Office, or the USPTO, to determine priority of invention.

Patents

As of March 28, 2022, we own or have rights in one issued U.S. patent, one pending U.S. patent application, and seven pending foreign patent applications relating to our ALLN-346 program. In particular, with regard to ALLN-346, we own one issued U.S. patent with composition of matter claims directed to recombinant uricase enzymes with certain mutations, which is

scheduled to expire in 2038, without taking a patent term extension into account. We also have counterpart patent applications pending in the U.S., Australia, Canada, China, Europe, Hong Kong, Israel and Japan, which, if granted, would be scheduled to expire in 2038, without taking a patent term extension into account.

In the United States, the term of a patent covering an FDA-approved drug may be eligible for a patent term extension under the Hatch-Waxman Act as compensation for the loss of patent term during the FDA regulatory review process. The period of extension may be up to five years beyond the expiration of the patent, but cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent among those eligible for an extension may be extended. Similar provisions are available in Europe and in certain other jurisdictions to extend the term of a patent that covers an approved drug. For example, it is possible that an issued U.S. patent covering ALLN-346 or its use may be entitled to a patent term extension. If ALLN-346 receives FDA approval, we intend to apply for a patent term extension, if available, to extend the term of a patent that covers the approved product. We also intend to seek patent term extensions in any jurisdictions where they are available, however, there is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

In addition to patent protection, we also rely on trade secret protection for our proprietary information that is not amenable to, or that we do not consider appropriate for, patent protection, including, for example, certain aspects of our manufacturing procedures. However, trade secrets can be difficult to protect. Although we take steps to protect our proprietary information, including restricting access to our premises and our confidential information, as well as entering into agreements with our employees, consultants, advisors and potential collaborators, third parties may independently develop the same or similar proprietary information or may otherwise gain access to our proprietary information. As a result, we may be unable to meaningfully protect our trade secrets and proprietary information.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products, including biological products. In addition, some jurisdictions regulate the pricing of pharmaceutical products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Licensure and Regulation of Biologics in the United States

In the United States, our product candidates are regulated as biological products, or biologics, under the Public Health Service Act, or PHSA, and the Federal Food, Drug, and Cosmetic Act, or FDCA, and their implementing regulations. The failure to comply with the applicable U.S. requirements at any time during the product development process, including nonclinical testing, clinical testing, the approval process or post-approval process, may subject an applicant to delays in the conduct of a study, regulatory review and approval, and/or administrative or judicial sanctions. These sanctions may include, but are not limited to, the U.S. Food and Drug Administration's, or FDA's, refusal to allow an applicant to proceed with clinical testing, refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, warning or untitled letters, adverse publicity, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, and civil or criminal investigations and penalties brought by the FDA or the Department of Justice, or DOJ, or other governmental entities.

An applicant seeking approval to market and distribute a new biologic in the United States generally must satisfactorily complete each of the following steps:

- nonclinical laboratory tests, animal studies and formulation studies all performed in accordance with the FDA's Good Laboratory Practice, or GLP, regulations;
- submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials may begin;
- approval of the protocol and related documentation by an institutional review board, or IRB, or ethics committee representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety, potency, and purity of the product candidate for each proposed indication, in accordance with Good Clinical Practices, or GCP, requirements and any additional requirements for the protection of human research subjects and their health information;

- preparation and submission to the FDA of a Biologic License Application, or BLA, for a biologic product requesting marketing for one or more proposed indications, including submission of detailed information on the manufacture and composition of the product candidate in clinical development and proposed labeling;
- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA pre-license inspections of the manufacturing facility or facilities, including those of third parties, at which the biological product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods, and controls are adequate to preserve the biological product's identity, strength, quality, and purity;
- satisfactory completion of any FDA audits of the nonclinical and clinical study sites to assure compliance with GLPs and GCPs, respectively, and the integrity of clinical data in support of the BLA;
- payment of user fees (unless a fee waiver applies) for FDA review of the BLA;
- securing FDA approval of the BLA and licensure of the new biologic product; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and any post-approval studies required by the FDA.

Nonclinical Studies and Investigational New Drug Application

Before testing any biological product candidate in humans, the product candidate must undergo nonclinical testing. Nonclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as animal studies to evaluate the potential for efficacy and toxicity. The conduct of the nonclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations. The results of the nonclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol are submitted to the FDA as part of an IND. An IND is a request for authorization from the FDA to ship an unapproved, investigational product in interstate commerce and to administer it to humans. The IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about the product candidate or conduct of the proposed clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks. In that case, the IND sponsor and the FDA must resolve any outstanding FDA concerns before the clinical trial can begin.

As a result, submission of the IND may result in the FDA not allowing the trial to commence or allowing the trial to commence on the terms originally specified by the sponsor in the IND. If the FDA raises concerns or questions either during this initial 30-day period, or at any time during the IND process, it may choose to impose a partial or complete clinical hold. A complete clinical hold issued by the FDA would delay either a proposed clinical study or cause suspension of an ongoing study, until all outstanding concerns have been adequately addressed and the FDA has notified the company that investigation may proceed. This could cause significant delays or difficulties in completing planned clinical trials in a timely manner. A partial clinical hold places restrictions on a clinical trial, such as limiting the doses administered or the duration of the trial. The FDA may impose clinical holds at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA.

Human Clinical Trials in Support of a BLA

Clinical trials involve the administration of the investigational product candidate to healthy volunteers or patients with the disease to be treated under the supervision of a qualified principal investigator in accordance with GCP requirements. Clinical trials are conducted under study protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

A sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of the BLA so long as the clinical trial is well-designed and well-conducted in accordance with GCP requirements, including review and approval by an independent ethics committee, and the FDA is able to validate the study data through an onsite inspection, if necessary.

Further, each clinical trial must be reviewed and approved by an IRB, either centrally or individually at each institution at which the clinical trial will be conducted. The IRB will consider, among other things, clinical trial design, patient informed consent, ethical factors, and the safety of human subjects. An IRB must operate in compliance with FDA regulations. The FDA, IRB, or the clinical trial sponsor may suspend or discontinue a clinical trial at any time for various reasons, including a

finding that the clinical trial is not being conducted in accordance with FDA requirements or the subjects or patients are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive GCP rules and the requirements for informed consent. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group may recommend continuation of the study as planned, changes in study conduct, or cessation of the study at designated check points based on access to certain data from the study. Information about certain clinical studies must be submitted within specific timeframes to the National Institutes of Health for public dissemination at www.clinicaltrials.gov.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may be required after approval.

- *Phase 1* clinical trials are initially conducted in a limited population to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion, and pharmacodynamics in healthy humans or, on occasion, in patients, such as cancer patients.
- *Phase 2* clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications and determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials.
- *Phase 3* clinical trials proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken within an expanded patient population to further evaluate dosage, provide substantial evidence of clinical efficacy, and further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of a BLA; such Phase 3 studies are referred to as "pivotal."

In some cases, the FDA may approve a BLA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety and effectiveness after approval. Such post-approval trials are typically referred to as Phase 4 clinical trials. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of biologics approved under accelerated approval regulations. If the FDA approves a product while a company has ongoing clinical trials that were not necessary for approval, a company may be able to use the data from these clinical trials to meet all or part of any Phase 4 clinical trial requirement or to request a change in the product labeling. Failure to exhibit due diligence with regard to conducting Phase 4 clinical trials could result in withdrawal of approval for products.

A manufacturer of an investigational product candidate for a serious disease or condition is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for individual patient access to such investigational drug. This requirement applies on the earlier of the first initiation of a Phase 2 or Phase 3 trial of the investigational drug or, as applicable, 15 days after the drug receives a designation as a breakthrough therapy, fast track product, or regenerative advanced therapy.

Compliance with cGMP Requirements

Before approving a BLA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in full compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The PHSA emphasizes the importance of manufacturing control for products like biologics whose attributes cannot be precisely defined. Among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biological product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the biological product candidate does not undergo unacceptable deterioration over its shelf life.

Manufacturers and others involved in the manufacture and distribution of products must also register their establishments with the FDA and certain state agencies. Both domestic and foreign manufacturing establishments must register and provide additional information to the FDA upon their initial participation in the manufacturing process. Any product manufactured by or imported from a facility that has not registered, whether foreign or domestic, is deemed misbranded under the FDCA. Establishments may be subject to periodic unannounced inspections by government authorities to ensure compliance with cGMPs and other laws. Manufacturers may have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA may lead to a product being deemed to be adulterated.

Review and Approval of a BLA

The results of product candidate development, nonclinical testing, and clinical trials, including negative or ambiguous results as well as positive findings, are submitted to the FDA as part of a BLA requesting license to market the product. The BLA must contain extensive manufacturing information and detailed information on the composition of the product and proposed labeling as well as payment of a user fee.

The FDA has 60 days after submission of the application to conduct an initial review to determine whether it is sufficient to accept for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission has been accepted for filing, the FDA begins an in-depth review of the application. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or the PDUFA, the FDA has ten months in which to complete its initial review of a standard application and respond to the applicant, and six months for a priority review of the application. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs. The review process may often be significantly extended by FDA requests for additional information or clarification. The review process and the PDUFA goal date may be extended by three months if the FDA requests or if the applicant otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Under the PHSA, the FDA may approve a BLA if it determines that the product is safe, pure, and potent and the facility where the product will be manufactured meets standards designed to ensure that it continues to be safe, pure, and potent.

On the basis of the FDA's evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities and any FDA audits of nonclinical and clinical study sites to assure compliance with GLPs and GCPs, respectively, the FDA may issue an approval letter, denial letter, or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. If the application is not approved, the FDA may issue a complete response letter, which will contain the conditions that must be met in order to secure final approval of the application, and when possible will outline recommended actions the sponsor might take to obtain approval of the application. Sponsors that receive a complete response letter may submit to the FDA information that represents a complete response to the issues identified by the FDA. Such resubmissions are classified under PDUFA as either Class 1 or Class 2. The classification of a resubmission is based on the information submitted by an applicant in response to an action letter. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has two months to review a Class 1 resubmission and six months to review a Class 2 resubmission. The FDA will not approve an application until issues identified in the complete response letter have been addressed. If an applicant does not resubmit the BLA in response to a complete response letter, the applicant may withdraw the original application or request an opportunity for a hearing. The FDA issues a denial letter if it determines that the establishment or product does not meet the agency's requirements.

The FDA may also refer the application to an advisory committee for review, evaluation, and recommendation as to whether the application should be approved. In particular, the FDA may refer applications for novel biologic products or biologic products that present difficult questions of safety or efficacy to an advisory committee. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates, and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

If the FDA approves a new product, it may limit the approved indications for use of the product. It may also require that contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may call for post-approval studies, including Phase 4 clinical trials, to further assess the product's safety after approval. The agency may also require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, to help ensure that the benefits of the product outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patent registries. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Fast Track, Breakthrough Therapy and Priority Review Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, and priority review designation.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For fast track products, sponsors may have greater

interactions with the FDA and the FDA may initiate review of sections of a fast track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the application is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case- by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

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. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a product, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the product from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

The 21st Century Cures Act

The 21st Century Cures Act, which was signed into law in December 2016, requires the FDA to establish a process for the qualification of drug development tools that may be used to support or obtain licensure of a biological product or support of the investigational use of a biological product. A drug development tool includes a biomarker, a clinical outcome assessment,

and any other method, material, or measure that the FDA determines aids drug development and regulatory review. A biomarker is a characteristic, such as a physiologic, pathologic, or anatomic characteristic or measurement, that is objectively measured and evaluated as an indicator of normal biological processes, pathologic processes, or biological responses to a therapeutic intervention and includes a surrogate endpoint. A clinical outcome assessment is a measurement of a patient's symptoms, overall mental state, or the effects of a disease or condition on how the patient functions and includes a patient-reported outcome.

The 21st Century Cures Act also requires that, for approval of any BLAs submitted after June 12, 2017, the FDA shall make public a brief statement regarding the patient experience data and related information, if any, submitted and reviewed as part of the application. Patient experience data includes data that are collected by any persons, including patients, family members and caregivers of patients, patient advocacy organizations, disease research foundations, researchers and drug manufacturers, and are intended to provide information about patients' experiences with a disease or condition, including the impact of such disease or condition, or a related therapy, on patients' lives and patient preferences with respect to treatment of such disease or condition.

Post-Approval Regulation

If regulatory approval for marketing of a product or new indication for an existing product is obtained, the sponsor will be required to comply with all regular post-approval regulatory requirements as well as any post-approval requirements that the FDA has imposed as part of the approval process. The sponsor will be required to report certain adverse reactions and production problems to the FDA, provide updated safety and efficacy information, comply with applicable tracking and tracing requirements, and comply with requirements concerning advertising and promotional labeling requirements. Manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon manufacturers. Accordingly, the sponsor and its third-party manufacturers must continue to expend time, money, and effort in the areas of production and quality control to maintain compliance with cGMP regulations and other regulatory requirements.

A biologic product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official lot release, the manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency, and effectiveness of pharmaceutical products.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, untitled letters or warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Pharmaceutical products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Orphan Drug Designation

Orphan drug designation in the United States is designed to encourage sponsors to develop products intended for rare diseases or conditions. In the United States, a rare disease or condition is statutorily defined as a condition that affects fewer

than 200,000 individuals in the United States or that affects more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available the biologic for the disease or condition will be recovered from sales of the product in the United States. The FDA has granted Orphan Drug Designation to reloxaliase for the treatment of primary hyperoxaluria and pediatric hyperoxaluria. This includes both children with secondary hyperoxaluria, attributable to excess GI absorption of oxalate, as well as the rare condition primary hyperoxaluria, a genetic defect of one of several liver enzymes.

Orphan drug designation qualifies a company for tax credits and market exclusivity for seven years following the date of the product's marketing approval if granted by the FDA. An application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. A product becomes an orphan when it receives orphan drug designation from the Office of Orphan Products Development, or OOPD, at the FDA based on acceptable confidential requests made under the regulatory provisions. The product must then go through the review and approval process like any other product.

A sponsor may request orphan drug designation of a previously unapproved product or new orphan indication for an already marketed product. In addition, a sponsor of a product that is otherwise the same product as an already approved orphan drug may seek and obtain orphan drug designation for the subsequent product for the same rare disease or condition if it can present a plausible hypothesis that its product may be clinically superior to the first drug. More than one sponsor may receive orphan drug designation for the same product for the same rare disease or condition, but each sponsor seeking orphan drug designation must file a complete request for designation.

The period of orphan drug exclusivity begins on the date that the marketing application is approved by the FDA and applies only to the indication for which the product has been designated. The FDA may approve a second application for the same product for a different use or a second application for a clinically superior version of the product for the same use. The FDA cannot, however, approve the same product made by another manufacturer for the same indication during the market exclusivity period unless it has the consent of the sponsor or the sponsor is unable to provide sufficient quantities.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, as amended, a BLA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Generally, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six month exclusivity may be granted if a BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Biosimilars and Exclusivity

The Affordable Care Act, which was signed into law in March 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA. The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars.

Under the BPCIA, a manufacturer may submit an application for licensure of a biologic product that is "biosimilar to" or "interchangeable with" a previously approved biological product or "reference product." In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity, and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and (for products administered multiple times) that the biologic and the reference biologic may be switched

after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. Even if a product is considered to be a reference product eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor's own nonclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity, and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

Patent Term Restoration and Extension

A patent claiming a new biologic product may be eligible for a limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments, which permits a patent restoration of up to five years for patent term lost during product development and FDA regulatory review. The restoration period granted on a patent covering a product is typically one-half the time between the effective date of an IND and the submission date of a marketing application, plus the time between the submission date of a marketing application and the ultimate approval date, provided the sponsor acted with diligence. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Regulation and Procedures Governing Approval of Medicinal Products in Europe

In order to market any product outside of the United States, a company also must comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, an applicant will need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the European Union generally follows the same lines as in the United States. It entails satisfactory completion of nonclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires the submission to the relevant competent authorities of a marketing authorization application and granting of a marketing authorization by these authorities before the product can be marketed and sold in the European Union.

Clinical Trial Approval

In April 2014, the new Clinical Trials Regulation, (EU) No 536/2014 was adopted, and it came into effect on January 31, 2022, repealing the current Clinical Trials Directive 2001/20/EC. The Clinical Trials Regulation is directly applicable in all the European Union Member States meaning no national implementing legislation in each European Union Member State is required. The transitory provisions of the new Clinical Trials Regulation offer sponsors the possibility to choose between the requirements of the previous Clinical Trials Directive and the Clinical Trials Regulation if the request for authorization of a clinical trial is submitted in the year after the new Clinical Trials Regulation became applicable. If the sponsor chooses to submit under the Clinical Trials Directive, the clinical trial continues to be governed by the Directive until three years after the new Clinical Trials Regulation became applicable. If a clinical trial continues for more than three years after the Clinical Trials Regulation became applicable, the Clinical Trials Regulation will at that time begin to apply to the clinical trial.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the European Union. The main characteristics of the regulation include: a streamlined application procedure via a single-entry point through the Clinical Trials Information System, or CTIS; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts (Part I contains scientific and medicinal product documentation and Part II contains the national and patient-level documentation). Part I is assessed by a coordinated review by the competent authorities of all European Union Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned) of a draft report prepared by a Reference Member State. Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned European Union Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

Marketing Authorization

To obtain a marketing authorization for a product in the European Union, an applicant must submit a marketing authorization application, either under the centralized procedure administered by the EMA or one of the procedures administered by competent authorities in European Union Member States (decentralized procedure, national procedure, or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the European Economic Area, or EEA (comprising the EU Member States plus Norway, Iceland and Liechtenstein). Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the European Union, an applicant must demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, class waiver, or a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid throughout the EEA. Pursuant to Regulation (EC) No. 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products (gene therapy, somatic cell therapy and tissue-engineered product) and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. For products with a new active substance not yet authorized in the European Union indicated for the treatment of other diseases and products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health, the centralized procedure is optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the EMA is responsible for conducting an initial assessment of a product. The maximum timeframe for the evaluation of a marketing authorization application by the EMA is 210 days, excluding clock stops when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Clock stops may extend the timeframe of evaluation of a MA application considerably beyond 210 days. Where the CHMP gives a positive opinion, the EMA provides the opinion together with supporting documentation to the European Commission, who make the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's recommendation. Accelerated evaluation may be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation. If the CHMP accepts such a request, the time limit of 210 days will be reduced to 150 days (excluding clock stops), but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that it is no longer appropriate to conduct an accelerated assessment.

Now that the UK (which comprises Great Britain and Northern Ireland) has left the EU, Great Britain will no longer be covered by centralized marketing authorizations (under the Northern Ireland Protocol, centralized marketing authorizations will continue to be recognized in Northern Ireland). All medicinal products with a current centralized marketing authorization were automatically converted to Great Britain marketing authorizations on January 1, 2021. For a period of two years from January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, the UK medicines regulator, may rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a new Great Britain marketing authorization. A separate application will, however, still be required.

Regulatory Data Protection

In the European Union, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Regulation (EC) No 726/2004, as amended, and Directive 2001/83/EC, as amended. Data exclusivity prevents generic or biosimilar applicants from referencing the innovator's pre-clinical or clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization, for a period of eight years from the date on which the reference product was first authorized in the European Union. During the additional two-year period of market exclusivity, a generic or biosimilar application can be submitted, and the innovator's data may be referenced, but no generic or biosimilar medicinal product can be marketed until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on marketing authorization application with a complete independent data package of pharmaceutical tests, nonclinical tests and clinical trials.

Periods of Authorization and Renewals

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk benefit balance by the EMA (for centralized marketing authorizations) or by the competent authority of the authorizing Member State (for national marketing authorizations). To that end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy,

including all variations introduced since the marketing authorization was granted, at least six months before expiry of the initial five year period. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any authorization that is not followed by the placement of the drug on the EEA (for centralized marketing authorizations) or on the market of the authorizing Member State within three years after authorization ceases to be valid.

Regulatory Requirements after Marketing Authorization

Following approval, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of the medicinal product. These include compliance with the European Union's stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed. In addition, the manufacturing of authorized products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the EMA's GMP requirements and comparable requirements of other regulatory bodies in the European Union, which mandate the methods, facilities, and controls used in manufacturing, processing and packing of drugs to assure their safety and identity. Finally, the marketing and promotion of authorized products, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union under Directive 2001/83EC, as amended.

Orphan Drug Designation and Exclusivity

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan drug by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition that either (i) affects not more than five in ten thousand persons in the European Union when the application is made, or (ii) without incentives it is unlikely that the marketing of the drug in the European Union would generate sufficient return to justify the necessary investment in its development. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention, or treatment of the condition in question that has been authorized in the European Union or, if such method exists, the drug will be of significant benefit to those affected by that condition.

An orphan drug designation provides a number of benefits, including fee reductions, regulatory assistance, and the possibility to apply for a centralized marketing authorization. Marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. During this market exclusivity period, neither the EMA nor the European Commission or the Member States can accept an application or grant a marketing authorization for a "similar medicinal product." A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The market exclusivity period for the authorized therapeutic indication may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation because, for example, the product is sufficiently profitable not to justify market exclusivity. Otherwise, during the period of market exclusivity, marketing authorization may only be granted to a "similar medicinal product" for the same therapeutic indication if: (i) a second applicant can establish that its product, although similar to the authorized product, is safer, more effective or otherwise clinically superior; (ii) the marketing authorization holder for the authorized product consents to a second orphan medicinal product application; or (iii) the marketing authorization holder for the authorized product cannot supply enough orphan medicinal product. Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The aforementioned European Union rules are generally applicable in the EEA.

Brexit and the Regulatory Framework in the United Kingdom

In June 2016, the electorate in the UK voted in favor of leaving the EU (commonly referred to as "Brexit") and the UK formally left the European Union on January 31, 2020. There was a transition period during which European Union pharmaceutical laws continued to apply to the UK, which expired on December 31, 2020. However, the European Union and the UK have concluded a trade and cooperation agreement, or TCA, which was provisionally applicable since January 1, 2021 and has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and European Union pharmaceutical regulations. At present, Great Britain has implemented European Union legislation on the marketing, promotion and sale of medicinal products through the Human Medicines Regulations 2012 (as amended) (under the Northern Ireland Protocol, the European Union regulatory framework will continue to apply in Northern Ireland). The regulatory regime in Great Britain therefore currently largely aligns with European Union regulations, however it is possible that these regimes will diverge in future now that Great Britain's regulatory system is independent from the European Union and the TCA does not provide for mutual recognition of UK and

EU pharmaceutical legislation. For example, the new European Union Clinical Trials Regulation is not applicable in the UK and a separate application for a UK clinical trial will be required.

Coverage, Pricing, and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we may seek regulatory approval by the FDA or other government authorities. In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use any product candidates we may develop unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of such product candidates. Even if any product candidates we may develop are approved, sales of such product candidates will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers, and managed care organizations, provide coverage, and establish adequate reimbursement levels for, such product candidates. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover any product candidates we may develop could reduce physician utilization of such product candidates once approved and have a material adverse effect on our sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, 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, and the level of coverage and reimbursement can differ significantly from payor to payor. Third-party reimbursement and coverage may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of pharmaceuticals have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement, and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Further, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the Biden administration have each indicated that it will continue to pursue new legislative and/or administrative measures to control drug costs. Individual state legislatures have become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing. Some of these measures include price or patient reimbursement constraints, discounts, restrictions on certain product access, marketing cost disclosure and transparency measures, and, in some cases, measures designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for any product candidates we may develop will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of any product candidates we may develop to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost effectiveness of a particular product candidate to currently available therapies (so called health technology assessments, or HTAs) in order to obtain reimbursement or pricing approval. For

example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic, and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU Member States, and parallel trade (arbitrage between low-priced and high-priced member states), can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products, if approved in those countries.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of pharmaceutical products that are granted marketing approval. Arrangements with providers, consultants, third-party payors, and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching physicians and patient privacy laws and regulations and other healthcare laws and regulations that may constrain our business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, 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 a federal healthcare program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things: knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent; 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. 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 of fraudulent claim for purposes of the False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- the anti-inducement law which 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 know 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;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information;
- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively the ACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the U.S. Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these

reporting obligations extend to include transfers of value made to certain non-physician providers (physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists and anesthesiologist assistants, and certified-nurse midwives); and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

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 pharmaceutical manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the United States Congress enacted the ACA, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the ACA of importance to our potential product candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic products, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for products that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable products to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient products to be covered under Medicare Part D;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription product spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Some of the provisions of the ACA have yet to be fully implemented, while certain provisions have been subject to judicial and Congressional challenges. For example, the Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Further, the Bipartisan Budget Act of 2018, among other things, amends the ACA, effective January 1, 2019, to reduce the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." Congress may consider other legislation to modify, repeal, or replace elements of the ACA. Thus, the full impact of the ACA, or any law replacing elements of it, on our

business remains unclear. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results. We continue to evaluate the effect that the ACA and its possible repeal and replacement could have on our business.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, in August 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 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year. These reductions went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030 unless additional action is taken by Congress. Pursuant to the Coronavirus Aid, Relief, and Economic Security Act, also known as the CARES Act, as well as subsequent legislation, these reductions have been suspended from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic. Following the suspension, a 1% payment reduction will occur beginning April 1, 2022 through June 30, 2022, and the 2% payment reduction will resume on July 1, 2022. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers, and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

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. Furthermore, on January 31, 2019, the Department of Health and Human Services, or HHS, and HHS Office of Inspector General, or OIG, proposed an amendment to one of the existing Anti-Kickback safe harbors (42 C.F.R. 1001.952(h)) which would prohibit certain pharmaceutical manufacturers from offering rebates to pharmacy benefit managers, or PBMs, in the Medicare Part D and Medicaid managed care programs. The proposed amendment would remove protection for "discounts" from Anti-Kickback enforcement action, and would include criminal and civil penalties for knowingly and willfully offering, paying, soliciting, or receiving remuneration to induce or reward the referral of business reimbursable under federal health care programs. At the same time, HHS also proposed to create a new safe harbor to protect point-of-sale discounts that drug manufacturers provide directly to patients, and adds another safe harbor to protect certain administrative fees paid by manufacturers to PBMs. If this proposal is adopted, in whole or in part, it could affect the pricing and reimbursement for any products for which we receive approval in the future. Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal, and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. Such reforms could have an adverse effect on anticipated revenues from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop product candidates.

Additional regulation

In addition to the foregoing, state, and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservation and Recovery Act, and the Toxic Substances Control Act, affect our business. These and other laws govern the use, handling, and disposal of various biologic, chemical, and radioactive substances used in, and wastes generated by, operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. Equivalent laws have been adopted in third countries that impose similar obligations.

Human Capital

Following the workforce reduction on March 31, 2021, we had 21 full-time employees, including 7 employees with Ph.D. or M.D. degrees. 13 of our employees are engaged in research and development activities and 8 are engaged in general and administrative activities. On March 31, 2022, in connection with the termination of the URIROX-2 study, we completed a workforce reduction to reduce our workforce by approximately 40%. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Facilities

We occupy approximately 6,055 square feet of office space in Newton, MA under a lease that terminates on the last day of the month following the month either party notifies the other party that the term of the lease shall end. In addition, we occupy approximately 11,691 square feet of office and laboratory space in Sudbury, MA under a lease that expires in February

2026. We do not own any real property. We have a one-time option to cancel the lease in February 2023 for any reason or no reason at all. We believe that this office and laboratory space is sufficient to meet our current needs and that suitable additional space will be available as and when needed.

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.

Corporate Information

We were incorporated under the laws of the State of Delaware and commenced business operations in 2011. Our principal executive offices are located at One Newton Executive Park, Suite 202, Newton, MA 02462 and our telephone number is (617) 467-4577. Our website address is www.allenapharma.com. The information contained on our website, or that can be accessed through our website, is not a part of this prospectus and is not incorporated by reference into this prospectus. You should not rely on any such information in deciding whether to purchase our common stock.

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an emerging growth company until the earlier of: (i) the last day of the fiscal year (a) following the fifth anniversary of the completion of the IPO, (b) in which we have total annual gross revenue of at least $1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of the prior June 30th, and (ii) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

Available Information

Our Internet address is www.allenapharma.com. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, proxy and information statements and amendments to those reports filed or furnished pursuant to Sections 13(a), 14, and 15(d) of the Securities Exchange Act of 1934, as amended, are available through the "Investors" portion of our website free of charge as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information on our website is not part of this Annual Report or any of our other securities filings unless specifically incorporated herein by reference. Our filings with the SEC may be accessed through the SEC's Interactive Data Electronic Applications system at http://www.sec.gov. All statements made in any of our securities filings, including all forward-looking statements or information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

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 Annual Report 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.

Summary of the Material Risks Associated with Our Business

- **We have identified conditions and events that raise substantial doubt about our ability to continue operations in the near-term. We may need to seek an in-court or out-of-court restructuring of our liabilities.**
- **If we are able to continue our operations beyond the near term, 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 may need to seek an in-court or out-of-court restructuring of our liabilities.**
- **Our existing and any future indebtedness could adversely affect our ability to operate our business.**
- **We are heavily dependent on the clinical development program for ALLN-346, which is our only clinical program.**
- **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.**
- **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.**
- **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.**
- **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.**
- **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.**
- **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.**
- **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.**

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 operations in the near-term. We may need to seek an in-court or out-of-court restructuring of our liabilities.

We may be forced to amend, delay, limit, reduce or terminate the scope of our development program for ALLN-346 and/or limit or cease our operations if we are unable to obtain additional funding. As of March 31, 2022, we had cash and cash equivalents totaling $9.0 million. We do not believe that our cash and cash equivalents as of March 31, 2022 will enable us to fund our operating expenses and capital requirements beyond the next several weeks. The failure to obtain sufficient additional funds on commercially acceptable terms to fund our operations may have a material adverse effect on our business, results of operations and financial condition and jeopardize our ability to continue operations in the near-term. We will likely need to consider additional cost reduction strategies, which may include, among others, amending, delaying, limiting, reducing, or terminating the development program for ALLN-346, and we may need to seek an in-court or out-of-court restructuring of our liabilities. In the event of such future bankruptcy proceeding, holders of the company's common stock and other securities will likely suffer a total loss of their investment.

If we are able to continue our operations beyond the near term, 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 may need to seek an in-court or out-of-court restructuring of our liabilities.

We do not have sufficient cash and cash equivalents to fund our operating expenses and capital expenditures in the near-term. If we are able to raise funds 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 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 Phase 2a clinical program and any subsequent clinical development of ALLN-346, 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 ALLN-346;
- our ability to successfully commercialize ALLN-346, if approved;
- the selling and marketing costs associated with ALLN-346, including the cost and timing of building our sales and marketing capabilities, if approved;
- the amount of sales and other revenues from ALLN-346, 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 debt obligations, particularly the outstanding balance of our debt owed to Pontifax, which is subject to acceleration upon certain conditions;
- 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 our clinical development program for ALLN-346 and cease operations.

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

As of March 31, 2022, we had $5.0 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.

Because of our limited cash resources and the recent termination of our Phase 3 clinical trial of reloxaliase, we have had discussions with Pontifax regarding potential repayment of the outstanding borrowing. In March 2022, we made voluntary repayments of $2.0 million and $3.0 million, reducing the loan balance to $5.0 million. The Pontifax Agreement contains a provision for the acceleration of the principal balance under certain conditions. We have therefore classified the Pontifax loan balance as a current liability.

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 do not currently have sufficient funds to satisfy our current and future debt service obligations and our operating expenses. 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, and, if we are able to finance our continuing operations, expect that we would incur significant and increasing losses for at least the next several years. Moreover, we 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. If we are able to continue our operations, we expect that we would continue to incur significant and increasing net operating losses for at least the next several years. Our net losses were $48.7 million, $32.8 million and $47.3 million for the years 2021, 2020 and 2019, respectively. As of December 30, 2021, we had an accumulated deficit of $246.5 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 March 31, 2022 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 $8.2 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, the development of which has now been terminated, 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.
If we are able to continue our operations, we anticipate that our expenses will increase substantially if and as we:

- advance the development of ALLN-346;
- seek to identify and develop additional product candidates, if we resume our research efforts;
- 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, which we do not expect to occur for at least the next several years, if ever. 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.

If we are able to continue our operations, 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 clinical development program for ALLN-346, which is our only clinical program.

We are a 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 ALLN-346, our only clinical program. In addition, we have incurred and expect to continue to incur significant expenses as we continue to pursue the clinical development of ALLN-346. The success of ALLN-346 will depend on several factors, including:

- the successful clinical development of ALLN-346, including the successful completion of Phase 3 registrational clinical trials;
- approval of ALLN-346 for marketing by the FDA or EMA;
- execution of an effective sales and marketing strategy for the commercialization of ALLN-346;
- acceptance by patients, the medical community and third-party payors;
- our success in educating physicians and patients about the benefits, administration and use of ALLN-346;
- the incidence and prevalence of patient populations with hyperuricemia and gout in those markets in which ALLN-346 is approved;
- the prevalence and severity of side effects, if any, experienced by patients treated with ALLN-346;
- 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 uricase, the active enzyme in ALLN-346;
- 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 GLPs, 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 any future product candidates. If this were to occur, we would continue to be heavily dependent on the regulatory approval and successful commercialization of ALLN-346, 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 ALLN-346 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 ALLN-346 conducted to date and future studies and trials of ALLN-346, including our pivotal Phase 2a clinical trials, and other product candidates that we may pursue, may not be predictive of the results of subsequent clinical trials. For example, in March 2022 we reported that an interim analysis in our URIROX-2 trial indicated that the trial was unlikely to be successful, despite more favorable results in prior clinical trials. Data, our interpretation of data and results from our Phase 2a clinical trials of ALLN-346 in adults with hyperuricemia and gout do not ensure that we will achieve similar results in subsequent clinical trials. 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.

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 ALLN-346 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.

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 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 2a clinical program for ALLN-346 consists of two Phase 2a clinical trials in adult patients with hyperuricemia and gout. 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 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 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 ALLN-346 or our other product candidates, our business will be substantially harmed.

We are not permitted to market ALLN-346 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 ALLN-346 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 ALLN-346 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 ALLN-346 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

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 only clinical development program, 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 had invested substantially all of our efforts and financial resources in the identification and development of reloxaliase for the treatment of hyperoxaluria, the development program for which we recently terminated. To a lesser extent, we have invested in our clinical development program for ALLN-346 for the treatment of hyperuricemia and 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 ALLN-346 and any future product candidates we may develop. The success of ALLN-346 and any 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;
- 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 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. ALLN-346 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 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 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 ALLN-346 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 ALLN-346 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 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 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. 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 recently terminated URIROX-2 study of reloxaliase was proceeding at a slower rate than we had originally projected. Accordingly, we significantly revised our plans for the interim analysis of this trial, both with regard to its scope and its timing.
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. If a significant number of patients withdraw from any of our clinical trials 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 ALLN-346.

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 ALLN-346 has thus far been well-tolerated without significant safety concerns in the clinical trials conducted to date, these trials are early and involve a relatively small number of subjects. It is possible that the current Phase 2a trials or future clinical trials we conduct may not demonstrate a favorable safety profile. In addition, while we have not observed ALLN-346 to be absorbed into the bloodstream in our clinical trials to date, it is possible absorption could occur in subsequent clinical trials. We may also need to conduct additional clinical trials or other testing for, among other things, drug-drug interactions 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 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 ALLN-346 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 ALLN-346 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 ALLN-346, 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 ALLN-346 and willing to do so. We may not be able to identify or secure contracts with manufacturers with suitable capability to manufacture ALLN-346 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 ALLN-346.

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 ALLN-346, 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 ALLN-346 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 any potential future BLA submission for ALLN-346 and in support of any scale up of commercial supply of ALLN-346 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.

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.

The unique crystalline nature of ALLN-346 and its expected mechanism of action involving the breakdown of urate 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.

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), political unrest in the U.S. and abroad, 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 ALLN-346, if approved.

Risks Related to Sales, Marketing and Competition

The incidence and prevalence for target patient populations of our product candidate have not been established with precision. If the market opportunities for our product candidate 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.

Our research and product development efforts are currently focused on a treatment for hyperuricemia and gout. The precise incidence and prevalence for this disease are unknown. Our projections of both the number of people who have this disease, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidate, are based on estimates. For example, we estimate there are approximately 375,000 patients in the United States who 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 our product candidate may be limited or may not be amenable to treatment with our product candidate, 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 our product candidate, because our potential target population is limited, we may never achieve profitability despite obtaining such significant market share.

Even if our product candidate 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 our product candidate may be smaller than we estimate.

We have never obtained marketing approval for a product candidate or commercialized a product. Even if our product candidate 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 candidate may require significant resources and may not be successful. If our product candidate 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 our product candidate, 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 opportunity for our product candidate is difficult to estimate precisely. Our estimates of the potential market opportunity 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 market for our product candidate could be smaller than our estimates of the potential market opportunity, 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 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 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 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 uricase, the active enzyme in ALLN-346. 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 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 candidate.

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 ALLN-346 for hyperuricemia and gout 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 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 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 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 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 ALLN-346 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 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 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 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 ALLN-346 for hyperuricemia and gout. 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 ALLN-346 for hyperuricemia and gout, 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.

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.

As a result of the COVID-19 pandemic we may experience further disruptions that could severely impact our business, preclinical studies and clinical trials. For example, the COVID-19 pandemic adversely affected the execution and enrollment progress of the URIROX-2 clinical trial of reloxaliase prior to our decision to terminate this program. Additional impacts of the Covid-19 pandemic may include:

- 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 first quarter of 2022, 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 March 2022, we implemented a workforce restructuring to conserve cash as we pursue financing and strategic alternatives. 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, provided that we are able to secure adequate financing to continue our operations, 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, and we may need to implement a further reduction of our workforce. 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 candidate. 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.

In addition, if we are not able to secure adequate financing, we may need to implement a further workforce reduction in the near future. 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 March 31, 2022, we had 22 full-time, part-time, or short-term employees. Our focus on the development of ALLN-346 requires us to optimize cash utilization and to manage and operate our business in a highly efficient manner. If we are able to secure additional financing to continue our operations, 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 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, provided we are able to secure adequate financing to continue our operations, 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 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 ALLN-346 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 renumeration 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. These reductions went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030 unless additional action is taken by Congress. Pursuant to the Coronavirus Aid, Relief, and Economic Security Act, also known as the CARES Act, as well as subsequent legislation, these reductions have been suspended from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic. Following the suspension, a 1% payment reduction will occur beginning April 1, 2022 through June 30, 2022, and the 2% payment reduction will resume on July 1, 2022.. 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. 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. Plaintiffs-appellees filed a petition for a writ of certiorari at the Supreme Court on February 10, 2021. On Friday July 2, 2021, the Supreme Court granted the petition. 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, at a federal level, President Biden signed an Executive Order on July 9, 2021 affirming the administration's policy to (i) support legislative reforms that would lower the prices of prescription drug and biologics, including by allowing Medicare to negotiate drug prices, by imposing inflation caps, and, by supporting the development and market entry of lower-cost generic drugs and biosimilars; and (ii) support the enactment of a public health insurance option. Among other things, the Executive Order also directs HHS to provide a report on actions to combat excessive pricing of prescription drugs, enhance the domestic drug supply chain, reduce the price that the Federal government pays for drugs, and address price gouging in the industry; and directs the FDA to work with states and Indian Tribes that propose to develop section 804 Importation Programs in accordance with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, and the FDA's implementing regulations. FDA released such implementing regulations 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. On September

25, 2020, CMS stated drugs imported by states under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for "best price" or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. If implemented, importation of drugs from Canada may materially and adversely affect the price we receive for any of our product candidates. 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 would have been 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. However, on December 29, 2021 CMS rescinded the Most Favored Nations rule. Additionally, on November 30, 2020, HHS published 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. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed and recent legislation imposed a moratorium on implementation of the rule until January 1, 2026. 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, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs..

We do not know whether additional legislative changes will be enacted, including to the Federal Food, Drug, and Cosmetic Act, or whether the FDA regulations, guidance documents or interpretations will be changed, or what the impact of such changes on the marketing approvals of ALLN-346, 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.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an Executive Order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The Executive Order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures of the Biden administrations or other efforts, if any, to challenge repeal or replace the ACA, will impact our business. 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 ALLN-346 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. Switzerland has passed similar laws, and, following Brexit, the United Kingdom has transposed the GDPR into UK domestic law with effect from January 2021. 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 addition, the GDPR provides that EEA member states may introduce specific or additional requirements related to the Processing of special categories of personal data such as health data that we may process in connection with clinical trials or otherwise. In the UK, the UK Data Protection Act 2018 complements the UK GDPR in this regard. This fact may lead to

greater divergence on the law that applies to the Processing of such personal data across the EEA and/or UK, which may increase our costs and overall compliance risk.

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 hyperuricemia and gout 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 hyperuricemia and gout who reside outside the United States.

Provided that we are able to successfully develop ALLN-346 through registrational clinical trials, we plan to seek regulatory approval to market ALLN-346 solely for the treatment of hyperuricemia and gout in adults and, unless we seek regulatory approval for additional indications, we will be prohibited from marketing ALLN-346 for any other indication.

We are developing ALLN-346 for the treatment of hyperuricemia and gout in adults, and intend to initially seek approval to market ALLN-346 for these indications. Even if we obtain regulatory approval to market ALLN-346 in these indications, we will likely be prohibited from marketing ALLN-346 for any other indications. The FDA strictly regulates the promotional claims that may be made about prescription products. 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 ALLN-346 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 ALLN-346 for the treatment of hyperuricemia and gout 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 ALLN-346 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. Since that time, the FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. Since April 2021, the FDA has conducted limited inspections and employed remote interactive evaluations, using risk management methods, to meet user fee commitments and goal dates. Ongoing travel restrictions and other uncertainties continue to impact oversight operations both domestic and abroad and it is unclear when standard operational levels will resume. The FDA is continuing to complete mission-critical work, prioritize other higher-tiered inspectional needs (e.g., for-cause inspections), and carry out surveillance inspections using risk-based approaches for evaluating public health. 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, and the FDA does not determine a remote interactive evaluation to be adequate, the agency has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. During the COVID-19 public health emergency, a number of 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 ongoing 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, 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, if approved; 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 candidate 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 ALLN-346. We have limited personnel experienced in drug manufacturing and formulation, and we lack the resources and the capabilities to manufacture 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 ALLN-346 and any product candidate we may develop in the future, 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 manufacturer for 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 ALLN-346 and any 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 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 Annual 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 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 ALLN-346 and other product candidates, and we control only some aspects of their activities. 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 ALLN-346 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 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. 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.

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 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, providing 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 our product candidates, 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 our common stock from The Nasdaq Global Select Market.

In accordance with Nasdaq Listing Rule 5810(c)(3)(A) (the "Compliance Period Rule"), we were 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. Since we had not regained compliance within the specified time period, we applied for, and were granted, an additional 180 calendar day compliance period. We were able to do so by transferring to The Nasdaq Capital Market, where we met 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 by providing written notice to Nasdaq of our intention to cure the deficiency during the additional compliance period.

If, at any time during this additional 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 Capital Market. 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 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 $0.22 per share and as high as $17.56 per share through March 30, 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 Capital 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:

- our ability to secure additional funding to continue operations in the near term;
- the outcome of the strategic review process that we are conducting with the assistance of Stifel;
- results from our ongoing Phase 2a clinical trials of ALLN-346, and any potential future clinical trials we may undertake;
- 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 March 25, 2022, we had 89,774,309 outstanding shares of common stock, assuming no exercise of outstanding options or warrants. In addition, the 6,765,837 shares subject to outstanding options under our stock option plans as of December 31, 2021, the 1,606,476 shares reserved for future issuance under our stock option plans, the 306,527 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 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 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 Annual 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, 2021, we had federal net operating loss carryforwards of approximately $188.2 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 our 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 Annual 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, as occurred following our decision to terminate the development of reloxaliase, 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 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

We occupy approximately 6,055 square feet of office space in Newton, MA under a lease that terminates on the last day of the month following the month either party notifies the other party that the term of the lease shall end. In addition, we occupy approximately 11,691 square feet of office and laboratory space in Sudbury, MA under a lease that expires in February 2026. We have a one-time option to cancel the lease in February 2023 for any reason or no reason at all. We do not own any real property. We believe that this office and laboratory space is sufficient to meet our current needs and that suitable additional space will be available as and when needed.

ITEM 3. 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 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our common stock commenced trading under the symbol "ALNA" on the NASDAQ Global Select Market on November 2, 2017. Beginning February 28, 2022, our common stock trades under the symbol "ALNA" on the NASDAQ Capital Market. Prior to November 2,2017, there was no public market for our common stock.

As of March 25, 2022, there were approximately 16 holders of record of our common stock. However, because many of our outstanding shares are held in accounts with brokers and other institutions, we believe we have more beneficial owners.

Dividend Policy

We have never declared or paid any dividends on our capital stock. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. In addition, pursuant to our loan and security agreement with Pontifax, we are prohibited from paying cash dividends without the prior written consent of Pontifax. Moreover, any future indebtedness that we may incur could preclude us from paying dividends. Any future determination to pay dividends will be made at the discretion of our board of directors. Investors should not purchase our common stock with the expectation of receiving cash dividends.

Equity Compensation Plan Information

For information regarding securities authorized for issuance under equity compensation plans, see Part III "Item 12—Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters."

Individual Compensation Plan Information

For information regarding individual compensation plans, see Part III "Item 12—Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters." **Unregistered Sales of Equity Securities and Use of Proceeds**

Recent Sales of Unregistered Equity Securities

None.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

ITEM 6. RESERVED

Not applicable.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Overview

You should read the following discussion and analysis of our financial condition and results of operations together with our "Selected Consolidated Financial Data" and our consolidated financial statements and the related notes included elsewhere in this Annual Report. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a biopharmaceutical company dedicated to developing and commercializing first-in-class, oral enzyme therapeutics to treat patients with rare and severe metabolic and kidney disorders. We are focused on metabolic disorders that result in excess accumulation of certain metabolites that can stimulate inflammation, damage the kidney, and potentially lead to chronic kidney disease, or CKD, and end-stage renal disease, or ESRD. We believe our proprietary know-how in enzyme technology allows for the design, development, formulation, and scalable manufacturing of non-absorbed and stable enzymes delivered orally and in sufficient doses for activity in the gastrointestinal tract. This approach enables us to develop enzyme therapies that degrade metabolites within the GI tract, which reduces potentially toxic metabolite levels in the blood and urine, and in turn, diminishes the disease burden including on the kidney over time.

Our product candidate, ALLN-346, is an orally administered, novel, urate degrading enzyme for patients with hyperuricemia and gout in the setting of advanced CKD. We have conducted a Phase 1 program, including both a single-ascending dose and multiple-ascending dose study in healthy volunteers. In both studies, ALLN-346 was well tolerated with no clinically significant safety signals and no dose-limiting toxicities observed in any cohort up to the highest administered dose. We are currently conducting two Phase 2a studies. Study 201 is a 7-day inpatient study in patients with hyperuricemia, for which we reported initial data in January 2022. Study 202 is a 14-day outpatient study in patients with hyperuricemia, gout and varying degrees of renal insufficiency, for which we expect to report initial data in Q2 2022.

We previously had been developing reloxaliase, a first-in-class, oral enzyme therapeutic for the treatment of hyperoxaluria, a metabolic disorder characterized by markedly elevated urinary oxalate, or UOx, levels and commonly associated with kidney stones, CKD and ESRD. However, in March 2022 we terminated this program following the first of two planned Sample Size Reestimations (SSR1) of the Phase 3 URIROX-2 Trial, which was conducted by an independent data safety monitoring board (DSMB) statistician. Based on the results of its unblinded analysis, the DSMB recommended that the trial size be increased from the initial 200 subjects to the maximum allowed number of 400 subjects under the pre-specified rules. However, even with this maximum recommended sample size increase, the power to detect an effect of reloxaliase vs. placebo would still be less than 80% based on the available data. Based upon this recommendation, we believe that the separation between the reloxaliase and placebo groups for the UOx primary endpoint is lower than expected, and therefore that the likelihood of success for the long term endpoint of reduction in kidney stone disease progression is also lower than expected. We have therefore decided to terminate the URIROX-2 study. No further clinical studies of reloxaliase are planned at this time.

In July 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.

In March 2021, we entered into an At Market Issuance Sales Agreement with B. Riley Securities, Inc. ("B. Riley ATM Agreement"). During the year ended December 31, 2021, we issued and sold a total of 4,081,338 shares of our common stock under the B. Riley ATM Agreement at a weighted average price of $1.11 per share for net proceeds of approximately $4.2 million.

In December 2021, we entered into an updated At Market Issuance Sales Agreement with B. Riley Securities, Inc. ("Updated B. Riley ATM Agreement"), which was essentially identical to the initial agreement, but utilized a shelf registration statement that we also filed at that time. During the first quarter of 2022 through the filing date of this Annual Report, we issued and sold 6,804,888 shares of our common stock under the Updated B. Riley ATM Agreement at a weighted average price of $0.62 per share for net proceeds of $4.1 million. The B. Riley ATM Agreement was terminated at the time we entered into the Updated B. Riley ATM Agreement.

During the first quarter of 2021, we issued and sold 6,058,318 shares of our 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 we entered into the B. Riley ATM Agreement.

In December 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.

In July 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.

In June 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 December 31, 2021, we had cash and cash equivalents totaling $30.0 million, and as of March 31, 2022 we had cash and cash equivalents of $9.0 million.

We have incurred significant net operating losses in every year since our inception and, provided we are able to secure adequate financing to continue our operations, 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 $48.7 million, $32.8 million and $47.3 million for the years ended December 31, 2021, 2020 and 2019, respectively. As of December 31, 2021, we had an accumulated deficit of $246.5 million. If we are able to secure adequate financing to continue our operations, we anticipate that our expenses will increase significantly as we:

- 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 impact our ability to continue as a going concern.

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 our common stock from The Nasdaq Global Select Market.

In accordance with Nasdaq Listing Rule 5810(c)(3)(A) (the "Compliance Period Rule"), we were 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. On February 22, 2022 we applied to transfer our securities to Nasdaq Capital Market and requested a second 180-day period to regain compliance with the Minimum Bid Price Requirement. On February 24, 2022, Nasdaq approved our request for a second 180-day period, or until August 22, 2022, 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 Capital Market.

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 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 ALLN-346 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.

We are developing ALLN-346 for patients with hyperuricemia and CKD. We began incurring external research and development costs for this program in 2016. We recently terminated development of reloxaliase, which we had been developing for the treatment of enteric hyperoxaluria and which had accounted for the substantial majority of our research and development expenses over the past three years.

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):

	For the Year Ended December 31,		
	2021	2020	2019
Reloxaliase external costs	$ 15,493	$ 8,431	$ 18,393
ALLN-346 external costs	7,752	2,366	5,697
Employee compensation and benefits	8,659	7,908	10,187
Other	3,068	1,678	2,967
Total research and development expenses	$ 34,972	$ 20,383	$ 37,244

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 $107.3 million of external research and development costs for reloxaliase and $18.2 million of external research and development costs for ALLN-346. Provided that we are able to secure sufficient capital to continue our operations, we expect that our research and development costs will increase in future years as we advance our ALLN-346 program, including initiating additional clinical trials and scaling our manufacturing processes.

The successful development of 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 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.

Restructuring Charges

Restructuring charges consist of severance, bonus and other related costs incurred as a result of a reduction of our workforce completed in December 2019.

Interest Income (Expense), Net

Interest income (expense), net, primarily consists of interest income earned on our cash and cash equivalents, interest expense incurred on our credit facility, amortized debt discount related to the fair value of the warrants issued in conjunction with the advances under our former credit facility with Silicon Valley Bank, or SVB, and related debt issuance costs.

Other Income (Expense), Net

Other income (expense), net, primarily consists of a success fee paid to Pacific Western Bank, or PWB, during the year ended December 31, 2020 associated with our loan agreement with PWB, or PWB Loan Agreement, 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 accounting principles generally accepted in the United States, or 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.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report, we believe the following accounting policies used in the preparation of our financial statements require the most significant judgments and estimates.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing purchase orders and open contracts, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the services when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met; however, some require advance payments. We make estimates of our accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by CROs and CMOs in connection with research and development activities for which we have not yet been invoiced.

We contract with CROs and CMOs to conduct clinical and manufacturing and other research and development services on our behalf. We base our expenses related to CROs and CMOs on our estimates of the services received and efforts expended pursuant to quotes and contracts with them. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our CROs or CMOs will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or amount of prepaid expense accordingly. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Stock-Based Compensation

We apply the fair value recognition provisions of ASC 718, *Compensation—Stock Compensation*, or ASC 718, for stock-based awards granted to employees, directors non-employees. We estimate the fair value of each stock option grant using the Black-Scholes option-pricing model. We recognize the corresponding stock-based compensation expense on a straight-line basis over the requisite service period, which is generally the vesting period of the respective award.

The Black-Scholes option-pricing model uses the following inputs: the fair value of our common stock, the expected volatility of our common stock, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield. Due to the lack of a public market for our common stock prior to our IPO and a lack of company-specific historical and implied volatility data, we have based our computation of expected volatility on the historical volatility of a representative group of public companies with similar characteristics to us, including stage of product development, life science industry focus, length of trading history and similar vesting provisions. The historical volatility data is calculated based on a period of time commensurate with the expected term assumption. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available or until circumstances change, such that the identified entities are no longer representative companies. In the latter case, more suitable, similar entities whose share prices are publicly available would be utilized in the calculation. We weigh our own historical volatility of our own stock price and the historical volatility of a representative group of public companies for the computation of expected volatility used for estimating the fair value of option grants. We will increase the weighting on the historical volatility of our own stock price over the historical volatility of a representative group of public companies until such time as we have a sufficient amount of historical information regarding the volatility of our own stock. We use the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, *Share-Based Payment*, to calculate the expected term for options granted to employees as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. Under this approach, the weighted-average expected option term is presumed to be the average of the contractual term (ten years) and the vesting term (generally four years) of our stock options. We utilize this method due to lack of historical exercise data and the "plain-vanilla" nature of our stock-based awards. The expected term is applied to the stock option grant group as a whole, as we do not expect substantially different exercise or post-vesting termination behavior among our employee population. For options granted to non-employees, we utilize the contractual term of the arrangement as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the stock options. The expected dividend yield is assumed to be zero as we have never paid dividends and have no current plans to pay any dividends on our common stock. We recognize forfeitures as they occur.

The fair value of stock options granted to employees and directors for their services on the board of directors was estimated on the date of grant using the Black-Scholes option-pricing model, with the following range of assumptions for the years ended December 31, 2021, 2020 and 2019:

	Years Ended December 31,		
	2021	2020	2019
Risk-free interest rate	0.4% – 1.4%	0.4% – 0.5%	1.4% – 2.6%
Expected dividend yield	—%	—%	—%
Expected term (in years)	5.0 – 7.0	5.5 – 6.1	5.5 – 6.8
Expected volatility	92% – 95%	94% – 95%	80% – 83%

The following table summarizes the classification of our stock-based compensation expense recognized in our statements of operations and comprehensive loss (in thousands):

	Years Ended December 31,		
	2021	2020	2019
Research and development	$ 1,128	$ 1,286	$ 1,175
General and administrative	2,543	2,765	1,814
Total	$ 3,671	$ 4,051	$ 2,989

As of December 31, 2021, we had $5.1 million of unrecognized compensation expense related to stock option awards, which is expected to be recognized over weighted-average remaining vesting periods of approximately 2.5 years. As of December 31, 2021, we did not have any unrecognized compensation expense related to restricted stock units remaining to be recognized. Provided we are able to secure adequate funding to continue operations, we expect stock-based compensation expense to increase, due in part to our existing unrecognized stock-based compensation expense, potential increases in the value of our common stock and expected additional stock-based awards to continue to attract and retain our employees.

Results of Operations

Comparison of Years Ended December 31, 2021 and 2020

The following table summarizes our results of operations for the years ended December 31, 2021 and 2020 (in thousands):

	For the Year Ended December 31,		Dollar
	2021	2020	Change
Operating expenses:			
Research and development	$ 34,972	$ 20,383	$ 14,589
General and administrative	12,677	11,603	1,074
Total operating expenses	47,649	31,986	15,663
Loss from operations	(47,649)	(31,986)	(15,663)
Other income (expense):			
Interest income (expense), net	(976)	(510)	(466)
Other income (expense), net	(38)	(349)	311
Other income (expense), net	(1,014)	(859)	(155)
Net loss	$ (48,663)	$ (32,845)	$ (15,818)

Research and Development Expenses

Research and development expense increased by $14.6 million from $20.4 million for the year ended December 31, 2020 to $35.0 million for the year ended December 31, 2021. The following table summarizes our research and development expenses for the years ended December 31, 2021 and 2020 (in thousands):

	For the Year Ended December 31,		Dollar
	2021	2020	Change
Clinical development external costs	$ 17,565	$ 7,247	$ 10,318
Manufacturing external costs	5,461	3,153	2,308
Employee compensation and benefits	8,659	7,908	751
Other	3,287	2,075	1,212
Total research and development expenses	$ 34,972	$ 20,383	$ 14,589

The $14.6 million increase in research and development expense was primarily attributable to the following:

- Our clinical development external costs increased by $10.3 million from $7.2 million for the year ended December 31, 2020 to $17.6 million for the year ended December 31, 2021:
  - Our URIROX-2 costs increased $6.3 million from $5.4 million for the year ended December 31, 2020 to $11.7 million for the year ended December 31, 2021. During the year ended December 31, 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. 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 during the year ended December 31, 2021;
  - Our URIROX-1 costs decreased $0.3 million from $0.5 million for the year ended December 31, 2020 to $0.2 million for the year ended December 31, 2021. This study was completed in the fourth quarter of 2019 and we released top-line data in November 2019; and
  - Our ALLN-346 costs increased $4.3 million from $0.6 million for the year ended December 31, 2020 to $4.9 million for the year ended December 31, 2021:
    - During the year ended December 31, 2021, we initiated dosing in two Phase 2a studies. We incurred $3.7 million of costs for the Phase 2a program during the year ended December 31, 2021, for which there were no comparable costs during the year ended December 31, 2020; and
    - We incurred costs for our Phase 1 program of $1.1 million and $0.6 million for the year ended December 31, 2021 and 2020, respectively.
- Our manufacturing external costs increased by $2.3 million from $3.2 million for the year ended December 31, 2020 to $5.5 million for the year ended December 31, 2021;
  - Reloxaliase formulation and development related costs increased $1.1 million from $0.7 million for the year ended December 31, 2020 to $1.8 million for the year ended December 31, 2021;
  - ALLN-346 formulation and development related costs increased $0.7 million from $0.9 million for the year ended December 31, 2020 to $1.6 million for the year ended December 31, 2021; and
  - Our manufacturing consulting costs to support our programs increased $0.5 million from $0.3 million for the year ended December 31, 2020 to $0.8 million for the year ended December 31, 2021;
- Our employee compensation and benefits costs increased by $0.8 million for the year ended December 31, 2021. Increased compensation and benefits costs due to an increase in headcount from 22 employees at December 31, 2020 to 35 employees at December 31, 2021 were partially offset by the decision not to pay annual bonuses .

Provided that we are able to secure sufficient capital to continue our operations, we expect that our research and development expenses will increase in future periods as we continue our clinical development and scale our manufacturing processes in our ALLN-346 program.

General and Administrative Expenses

General and administrative expense increased by $1.1 million from $11.6 million for the year ended December 31, 2020 to $12.7 million for the year ended December 31, 2021. The following table summarizes our general and administrative expenses for the years ended December 31, 2021 and 2020 (in thousands):

	For the Year Ended December 31,		Dollar
	2021	2020	Change
Employee compensation and benefits	$ 5,942	$ 6,510	$ (568)
Consulting and professional services	3,593	2,795	798
Market research and commercialization planning	133	35	98
Other	3,009	2,263	746
Total general and administrative expenses	$ 12,677	$ 11,603	$ 1,074

The $1.1 million increase in general and administrative expense was primarily due to the following:

- Our consulting and professional services costs increased by $0.8 million for the year ended December 31, 2021. The increase was primarily due to increased costs for consulting, recruiting, accounting, investor relations and website design and maintenance;
- Our other costs increased by $0.7 million for the year ended December 31, 2021, primarily due to an increase in directors' and officers' insurance costs; and
- These increased costs were partially offset by a decrease of $0.6 million in our employee compensation and benefits costs for the year ended December 31, 2021, primarily due to the decision not to pay annual bonuses.

Provided that we are able to secure sufficient capital to continue our operations, we expect that our general and administrative expense will increase in future periods as we expand our operations and incur additional costs to support our clinical development programs and prepare for potential commercialization.

Interest Income (Expense), net

Interest income (expense), net consists of interest income earned on our cash and cash equivalents, interest expense charged on our outstanding debt, and amortization of our debt discount. Net interest expense increased $0.5 million for the year ended December 31, 2021 due to increased interest expense associated with amounts outstanding under the Pontifax Agreement.

Other Income (Expense), net

Other expense, net consists gain (loss) on foreign currency transactions. Included in other expense, net for year ended December 31, 2020 was a success fee of $0.3 million paid to PWB.

Comparison of Years Ended December 31, 2020 and 2019

The following table summarizes our results of operations for the years ended December 31, 2020 and 2019 (in thousands):

	For the Year Ended December 31,		Dollar
	2020	2019	Change
Operating expenses:			
Research and development	$ 20,383	$ 37,244	$ (16,861)
General and administrative	11,603	9,676	1,927
Restructuring charges	—	605	(605)
Total operating expenses	31,986	47,525	(15,539)
Loss from operations	(31,986)	(47,525)	15,539
Other income (expense):			
Interest income (expense), net	(510)	270	(780)
Other income (expense), net	(349)	(84)	(265)
Other income (expense), net	(859)	186	(1,045)
Net loss	$ (32,845)	$ (47,339)	$ 14,494

Research and Development Expenses

Research and development expense decreased by $16.9 million from $37.2 million for the year ended December 31, 2019 to $20.4 million for the year ended December 31, 2020. The following table summarizes our research and development expenses for the years ended December 31, 2020 and 2019 (in thousands):

	For the Year Ended December 31,		Dollar
	2020	2019	Change
Clinical development external costs	$ 7,247	$ 14,689	$ (7,442)
Manufacturing external costs	3,153	8,823	(5,670)
Employee compensation and benefits	7,908	10,187	(2,279)
Other	2,075	3,545	(1,470)
Total research and development expenses	$ 20,383	$ 37,244	$ (16,861)

The $16.9 million decrease in research and development expense was primarily attributable to the following:

- Our clinical development external costs decreased by $7.4 million from $14.7 million for the year ended December 31, 2019 to $7.2 million for the year ended December 31, 2020:
  - Our URIROX-1 costs decreased $4.5 million from $5.0 million for the year ended December 31, 2019 to $0.5 million for the year ended December 31, 2020. This study was completed in the fourth quarter of 2019 and we released top-line data in November 2019. The costs incurred during the year ended December 31, 2020 were related to closeout activities;
  - Our URIROX-2 costs decreased $1.6 million from $7.0 million for the year ended December 31, 2019 to $5.4 million for the year ended December 31, 2020. 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. A significant portion of the proceeds from sales of our common stock during 2020 were used to activate additional clinical trial sites and increase investment in the URIROX-2 trial. During the second half of 2020 we began expanding URIROX-2 to additional geographies and clinical trial sites;
  - During 2019, we incurred costs of $0.4 million with an independent third party to perform an independent analysis of the results of the URIROX-1 study to assist in the assessment of revisions and redesign of the URIROX-2 study;
  - Costs related to our study 206 of reloxaliase decreased $0.8 million from $1.3 million for the year ended December 31, 2019 to $0.5 million for the year ended December 31, 2020. This study was also completed in the fourth quarter of 2019 and we reported top-line data in November 2019. The costs incurred during the year ended December 31, 2020 were related to closeout activities;
  - We incurred consulting costs of $0.4 million during the year ended December 31, 2019 to support our URIROX-1, URIROX-2 and 206 studies. In conjunction with the completion of the URIROX-1 study and 206 Study in the fourth quarter of 2019 and reduced activity in the URIROX-2 study while we pursued additional financing, we did not require the additional consulting services during the year ended December 31, 2020; and
  - Partially offsetting the decrease in clinical costs related to our reloxaliase program was $0.6 million of costs for our Phase 1 single-ascending dose clinical trial of ALLN-346, which we completed in the fourth quarter of 2020.
- Our manufacturing external costs decreased by $5.7 million from $8.8 million for the year ended December 31, 2019 to $3.2 million for the year ended December 31, 2020;
  - ALLN-346 formulation and development related costs decreased $3.4 million from $4.3 million for the year ended December 31, 2019 to $0.9 million for the year ended December 31, 2020. Included in the formulation and development related costs for the year ended December 31, 2019 was $2.5 million of costs for the production of engineering and clinical batches of drug substance, for which there were no comparable costs for the year ended December 31, 2020;
  - Reloxaliase formulation and development related costs decreased $1.2 million from $1.9 million for the year ended December 31, 2019 to $0.7 million for the year ended December 31, 2020; and
  - Reloxaliase consumables and raw materials costs for engineering and clinical batches decreased $0.9 million from $1.2 million for the year ended December 31, 2019 to $0.3 million for the year ended December 31, 2020;
- Our employee compensation and benefits costs decreased by $2.3 million for the year ended December 31, 2020 due to decreases in average headcount, benefits and stock-based compensation costs as a result of our reduction of workforce completed in December 2019.

General and Administrative Expenses

General and administrative expense increased by $1.9 million from $9.7 million for the year ended December 31, 2019 to $11.6 million for the year ended December 31, 2020. The following table summarizes our general and administrative expenses for the years ended December 31, 2020 and 2019 (in thousands):

	For the Year Ended December 31,		Dollar
	2020	2019	Change
Employee compensation and benefits	$ 6,510	$ 4,277	$ 2,233
Consulting and professional services	2,795	3,173	(378)
Market research and commercialization planning	35	534	(499)
Other	2,263	1,692	571
Total general and administrative expenses	$ 11,603	$ 9,676	$ 1,927

The $1.9 million increase in general and administrative expense was primarily due to the following:

- Our employee compensation and benefits costs increased by $2.2 million for the year ended December 31, 2020, primarily due to an increase in employee salaries, wages, benefit costs and stock-based compensation. Stock-based compensation increased $1.0 million from $1.8 million for the year ended December 31, 2019 to $2.8 million for the year ended December 31, 2020;
- Our consulting and professional services costs decreased by $0.4 million for the year ended December 31, 2020. The decrease was primarily due to decreased recruiting costs and investor and public relations costs;
- Our market research and commercialization planning costs decreased by $0.5 million for the year ended December 31, 2020. During the year ended December 31, 2019, we incurred costs of $0.4 million for a study with an independent third party to perform a market assessment for enteric hyperoxaluria. There were no comparable costs for the year ended December 31, 2020; and
- Our other costs increased by $0.6 million for the year ended December 31, 2020, primarily due to an increase in directors' and officers' insurance costs.

Restructuring Charges

Restructuring charges consist of severance, bonus and other related costs incurred as a result of a reduction of our workforce completed in December 2019.

Interest Income (Expense), net

Interest income (expense), net consists of interest income earned on our cash and cash equivalents, interest expense charged on our outstanding debt, and amortization of our debt discount. We had net interest expense of $0.5 million for the year ended December 31, 2020 and net interest income of $0.3 million for the year ended December 31, 2019. The change was primarily attributable to a decrease in interest earned as a result of lower average balances of cash and cash equivalents for the year ended December 31, 2020 as compared to average balances of cash and cash equivalents for the year ended December 31, 2019.

Other Income (Expense), net

Other income (expense), net consists of a success fee paid to PWB and gain (loss) on foreign currency transactions. Included in other expenses, net for the year ended December 31, 2020 was a success fee of $0.3 million paid to PWB. The conditions required to meet the obligation were fulfilled at the time we completed our registered direct offering on June 5, 2020 and we expensed the success fee at this time.

Liquidity and Capital Resources

Sources of Liquidity

We have funded our operations from inception through December 31, 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 $4.2 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 $30.0 million as of December 31, 2021.

We entered into an updated At Market Issuance Sales Agreement with B. Riley Securities, Inc. ("Updated B. Riley ATM Agreement") on December 23, 2021. During the first quarter of 2022 through the filing date of this Annual Report, we issued and sold 6,804,888 shares of our common stock under the Updated B. Riley ATM Agreement at a weighted average price of $0.62 per share for net proceeds of $4.1 million. The shares were issued and sold pursuant to a shelf registration statement on Form S-3 we filed on May 6, 2021, 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 Annual Report on Form 10-K, we have not offered any other securities pursuant to this shelf registration. The initial B. Riley ATM Agreement was terminated at the time we entered into the Updated B. Riley ATM Agreement.

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 65th 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. We did not withdraw any amounts available through the Third Installment Loan prior to expiration of the availability period.

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. During the first quarter of 2022, we prepaid $5.0 million of the outstanding principal balance. In light of our recent termination of the reloxaliase development program and certain acceleration provisions in the Pontifax Agreement, we have classified the amounts due under the Pontifax loan as a current liability.

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 years ended December 31, 2021, 2020 and 2019 (in thousands):

	For the Year Ended December 31,		
	2021	2020	2019
Net cash used in operations	$ (45,678)	$ (28,159)	$ (43,632)
Net cash used in investing activities	(667)	(632)	(122)
Net cash provided by financing activities	41,291	33,826	12,118
Net increase (decrease) in cash and cash equivalents	$ (5,054)	$ 5,035	$ (31,636)

Net Cash Used in Operating Activities

The 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 $45.7 million for the year ended December 31, 2021 compared to $28.2 million for the year ended December 31, 2020. The increase in cash used in operating activities of $17.5 million was attributable to:

- An increase in net loss of $15.8 million;
- A decrease in non-cash items of $0.4 million resulting primarily from increases in stock-based compensation expense; and
- A decrease of $1.3 million due to changes in the components of working capital.

Net cash used in operating activities was $28.2 million for the year ended December 31, 2020 compared to $43.6 million for the year ended December 31, 2019. The decrease in cash used in operating activities of $15.4 million was attributable to:

- A decrease in net loss of $14.4 million;
- An increase in non-cash items of $1.2 million resulting primarily from increases in stock-based compensation expense; and
- A decrease of $0.2 million due to changes in the components of working capital.

Net Cash Used in Investing Activities

Net cash used in investing activities was $0.7 million, $0.6 million and $0.1 million for the years ended December 31, 2021, 2020 and 2019, respectively. Cash used in investing activities related to net purchases of property and equipment.

Net Cash Provided by Financing Activities

Net cash provided by financing activities of $41.3 million for the year ended December 31, 2021 primarily consisted of net proceeds of $11.7 million and $4.2 from the sale of common stock under the Cowen ATM Agreement and the B. Riley ATM Agreement, respectively, 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. .

Net cash provided by financing activities of $33.9 million for the year ended December 31, 2020 was primarily attributable to net proceeds of $34.0 million from the issuance and sale of our common stock through the registered direct offering completed in June 2020 and our public underwritten offerings completed in July 2020 and December 2020.

Net cash provided by financing activities of $12.1 million for the year ended December 31, 2019 was primarily attributable to net proceeds of $12.0 million from the issuance and sale of our common stock through the registered direct offering completed in June 2019 and under our ATM facility completed in December 2019.

Funding Requirements

Provided that we are able to secure adequate financing to continue our operations, we expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development for, initiate later stage clinical trials for, and seek marketing approval for, ALLN-346 and any other product candidates we may develop. 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. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

Going Concern

As of December 31, 2021, we had cash and cash equivalents totaling $30.0 million, and as of March 31, 2022 we had cash and cash equivalents totaling $9.0 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 Annual Report. We do not believe that our cash and cash equivalents as of March 31, 2022 will enable us to fund our operating expenses and capital requirements beyond the next several weeks. We will require additional capital to sustain our operations, including our ALLN-346 development program, beyond that time.

On March 18, 2022, we announced our decision to terminate our URIROX-2 study for reloxaliase and initiated the process of closing the study with our CRO, investigative sites, patients and business partners. In connection with the termination of the reloxaliase program, we completed a workforce reduction of approximately 40% in March 2022.

We are exploring opportunities to secure additional funding through equity or debt financings or through collaborations, licensing transactions or other sources. In January 2022, we initiated a process to explore a range of strategic and financing alternatives to maximize shareholder value and have engaged the investment bank Stifel, Nicolaus & Company, Inc. ("Stifel") to act as strategic advisor for this process. Potential strategic alternatives that may be evaluated include a partnership or sale of ALLN-346, a sale or merger of the Company, or securing additional financing to enable further development of our ALLN-346 program. There can be no assurance that this strategic review process will result in the pursuit of any transaction or that any transaction, if pursued, will be completed. The failure to obtain sufficient additional funds on commercially acceptable terms to fund our operations may have a material adverse effect on our business, results of operations and financial condition and jeopardize our ability to continue operations in the near-term. We will likely need to consider additional cost reduction strategies, which may include, among others, amending, delaying, limiting, reducing, or terminating the development program for ALLN-346, and we may need to seek an in-court or out-of-court restructuring of our liabilities. In the event of such future bankruptcy proceeding, holders of our common stock and other securities will likely suffer a total loss of their investment.

As part of the strategic process, the Compensation Committee of the Board of Directors approved a retention plan on January 28, 2022, available to all employees ("Retention Plan"). Employees were required to execute retention agreements to receive payments and other considerations offered by the Retention Plan. Employees who executed a retention agreement received a salary adjustment equal to 6.5% retroactive to January 1, 2022, a restricted stock unit ("RSU") grant and a lump sum retention payment. A total of 3,163,000 RSUs were granted on February 1, 2022 under the Retention Plan. The RSUs vest over a three-year period ratably on July 15th and January 15th of each year following grant date. Lump sum retention payments totaling $3.0 million were made to employees in February 2022. If an employee resigns from the Company or is terminated for cause prior to June 30, 2022, the employee would be required to fully repay the lump sum retention payment received. If an employee resigns from the Company or is terminated for cause between July 1, 2022 and September 30, 2022, the employee would be required to repay 50% of the lump sum retention payment received.

Market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed. 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. 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 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 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 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.

We do not have any committed external sources of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, 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.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to market risk related to changes in interest rates. As of December 31, 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 years ended December 31, 2021, 2020 and 2019.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Our consolidated financial statements, together with the reports of our independent registered public accounting firms, appear at pages F-1 through F-26 of this Annual Report for the year ended December 31, 2021.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

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 as of December 31, 2021. 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.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as such term is defined in Exchange Act Rule 13a–15(f) or 15d-15(f). Our internal control system was designed to provide reasonable assurance to our management and our board of directors regarding the preparation and fair presentation of published financial statements. All internal control systems, no matter how well designed have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2021. In making this assessment, our management used the criteria set forth in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission in 2013 (COSO criteria). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2021. This Annual Report does not include an attestation report of our independent registered public accounting firm due to a transition period established by rules of the Securities and Exchange Commission for newly public companies.

Changes in Internal Control Over Financial Reporting

There was no change in our internal control over financial reporting that occurred during the three months or the year ended December 31, 2021 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

On March 31, 2022, the company completed a workforce reduction to reduce its workforce by approximately 40%. As a result of the retention program approved in January 2022, the company does not expect to incur material charges in connection with the reduction in force.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2020.

ITEM 11. EXECUTIVE COMPENSATION

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2020.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2020.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2020.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

Our independent registered public accounting firm is Ernst & Young LLP, Boston, MA, Auditor Firm ID: 42
The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2020.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

(1) 1. **Financial Statements.**

For a list of the financial statements included herein, see Index to the Financial Statements on page F-1 of this Annual Report.

2. Financial Statement Schedules.

No financial statement schedules have been submitted because they are not required or are not applicable or because the information required is included in the financial statements or the notes thereto.

3. List of Exhibits.

See the Exhibit Index in Item 15(b) below.

(b) **Exhibit Index.**

Exhibit Number	Description
3.1*	Amended and Restated Certificate of Incorporation of Allena Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 3.1 to the Registrant's Form 10-Q filed on August 12, 2021)
3.2*	Amended and Restated By-Laws of Allena Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 3.2 to the Registrant's Form 8-K filed on November 6, 2017)
4.1*	Form of Common Stock certificate (Incorporated by reference from Exhibit 4.1 to the Registrant's Amendment No. 1 to Form S-1 filed on October 23, 2017)
4.2*	Form of Indenture for Senior Debt Securities and the Related Form of Senior Debt Security (Incorporated by reference to Exhibit 4.5 to the Registrant's Form S-3 filed on May 6, 2021)
4.3*	Form of Indenture for Subordinated Debt Securities and the Related Form of Subordinated Debt Security (Incorporated by reference to Exhibit 4.6 to the Registrant's Form S-3 filed on May 6, 2021)
4.4*	Form of Common Stock Purchase Warrant (Incorporated by reference to Exhibit 4.1 of the Registrant's Form 8-K filed on July 16, 2021)
4.5*	Form of Pre-Funded Common Stock Purchase Warrant (Incorporated by reference to Exhibit 4.2 of the Registrant's Form 8-K filed on July 16, 2021)
4.6*	Second Amended and Restated Investor Rights Agreement, by and between the Registrant and the Investors named therein, dated as November 25, 2015 (Incorporated by reference from Exhibit 4.2 to the Registrant's Form S-1 filed on October 6, 2017)
4.7*	Warrant to Purchase Stock issued to Silicon Valley Bank, dated May 2, 2016 (Incorporated by reference from Exhibit 4.3 to the Registrant's Form S-1 filed on October 6, 2017)
4.8*	Warrant to Purchase Stock issued to Silicon Valley Bank, dated August 18, 2014 (Incorporated by reference from Exhibit 4.4 to the Registrant's Form S-1 filed on October 6, 2017)
4.9*	Description of Securities of the Registrant (Incorporated by reference to Exhibit 4.5 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2020, filed March 16, 2020)
4.10*	Registration Rights Agreement, dated September 29, 2020 by and among Allena Pharmaceuticals, Inc. and the parties named therein (Incorporated by reference to Exhibit 4.1 to the Registrant's Form 8-K filed on October 1, 2020)
10.1*†	2017 Stock Option and Incentive Plan and forms of agreement thereunder (Incorporated by reference from Exhibit 10.2 to the Registrant's Amendment No. 1 to Form S-1 filed on October 23, 2017)
10.2*†	2017 Employee Stock Purchase Plan (Incorporated by reference from Exhibit 10.3 to the Registrant's Amendment No. 1 to Form S-1 filed on October 23, 2017)

10.3*†	2021 Inducement Equity Plan (Incorporated by reference to Exhibit 10.1 to the Registrant's Form 8-K filed on January 28, 2021)
10.4*†	Senior Executive Cash Incentive Bonus Plan (Incorporated by reference from Exhibit 10.4 to the Registrant's Form S-1 filed on October 6, 2017)
10.5*†	Amended and Restated Employment Agreement, dated January 4, 2019 by and between Allena Pharmaceuticals, Inc. and Louis Brenner, M.D. (Incorporated by reference to Exhibit 10.2 to the Registrant's Form 8-K filed on January 4, 2019)
10.6*†	Retention Compensation and Amendment to Employment Agreement, dated January 28, 2022, by and between Allena Pharmaceuticals, Inc. and Louis Brenner, M.D. (Incorporated by reference to Exhibit 10.1 to the Registrant's Form 8-K filed on February 2, 2022)
10.7*†	Employment Agreement dated January 29, 2021 between Allena Pharmaceuticals, Inc. and Richard Katz (Incorporated by reference to Exhibit 10.1 to the Registrant's Form 8-K filed on February 2, 2021)
10.8*†	Retention Compensation and Amendment to Employment Agreement, dated January 28, 2022, by and between Allena Pharmaceuticals, Inc. and Richard D. Katz, M.D. (Incorporated by reference to Exhibit 10.2 to the Registrant's Form 8-K filed on February 2, 2022)
10.9*	Commercial Lease, by and between the Registrant and Cummings Properties, LLC, dated August 18, 2016, as amended (Incorporated by reference from Exhibit 10.10 to the Registrant's Form S-1 filed on October 6, 2017)
10.10*	Amended and Restated Non-Employee Director Compensation Policy (Incorporated by reference from Exhibit 10.11 to the Registrant's Form 10-K filed on March 11, 2021)
10.11*†	Transition Agreement, dated January 4, 2019 by and between Allena Pharmaceuticals, Inc. and Alexey Margolin, Ph.D. (Incorporated by reference to Exhibit 10.1 to the Registrant's Form 8-K filed on January 4, 2019)
10.12*†	Transition Agreement, dated March 31, 2021, by and between Allena Pharmaceuticals, Inc. and Edward Wholihan (Incorporated by reference from Exhibit 10.1 to the Registrant's Form 8-K filed on April 2, 2021)
10.13*	Loan and Security Agreement by and between Allena Pharmaceuticals, Inc. and Pacific Western Bank, dated June 29, 2018, as amended August 1, 2019 (Incorporated by reference to Exhibit 10.1 to the Registrant's Form 10-Q filed on November 13, 2019)
10.14*	Loan and Security Agreement, dated September 29, 2020 by and between Allena Pharmaceuticals, Inc. and the parties named therein (Incorporated by reference to Exhibit 10.1 to the Registrant's Form 8-K filed on October 1, 2020)
21.1*	Subsidiaries (Incorporated by reference from Exhibit 21.1 to the Registrant's Form S-1 filed on October 6, 2017)
23.1**	Consent of Ernst & Young LLP
24.1	Power of Attorney (included on signature page to this Annual Report on Form 10-K)
31.1**	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2**	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1 ***	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
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)

* Previously filed.
** Filed herewith.

*** Furnished herewith.
† Indicates management contract or compensation plan.
# Confidential treatment has been granted with respect to redacted portions of this exhibit. Redacted portions of this exhibit have been filed separately with the Securities and Exchange Commission.

ITEM 16. FORM 10-K SUMMARY

None.

SIGNATURES

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

Dated: March 31, 2022

ALLENA PHARMACEUTICALS, INC.

By: /s/ Louis Brenner
Louis Brenner, M.D.
Chief Executive Officer and Director

SIGNATURES AND POWER OF ATTORNEY

We, the undersigned directors and officers of Allena Pharmaceuticals, Inc. (the "Company"), hereby severally constitute and appoint Louis Brenner and Richard Katz, and each of them singly, our true and lawful attorneys, with full power to them, and to each of them singly, to sign for us and in our names in the capacities indicated below, any and all amendments to this Annual Report on Form 10-K, and to file or cause to be filed the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as each of us might or could do in person, and hereby ratifying and confirming all that said attorneys, and each of them, or their substitute or substitutes, shall do or cause to be done by virtue of this Power of Attorney.

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

Signature	Title	Date
/s/ Louis Brenner Louis Brenner, M.D.	Chief Executive Officer and Director (Principal Executive Officer)	March 31, 2022
/s/ Richard D. Katz Richard D. Katz, M.D.	Chief Financial Officer (Principal Financial and Accounting Officer)	March 31, 2022
/s/ Alexey Margolin, Ph.D. Alexey Margolin, Ph.D.	Chairman	March 31, 2022
/s/ Allene Diaz Allene Diaz	Director	March 31, 2022
/s/ Mark Fitzpatrick Mark Fitzpatrick	Director	March 31, 2022
/s/ Gino Santini Gino Santini	Director	March 31, 2022
/s/ Ann Miller Ann Miller	Director	March 31, 2022

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Allena Pharmaceuticals, Inc. (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2021, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

The Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations, has a working capital deficiency, and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

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

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2012.

Boston, Massachusetts
March 31, 2022

Allena Pharmaceuticals, Inc.

Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31,	
	2021	**2020**
Assets		
Current assets:		
Cash and cash equivalents	$ 29,988	$ 35,042
Prepaid expenses and other current assets	3,018	2,207
Total current assets	33,006	37,249
Property and equipment, net	1,173	881
Operating lease assets	455	678
Other assets	123	123
Total assets	$ 34,757	$ 38,931
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,030	$ 2,410
Loan payable, net of discount	9,852	—
Accrued expenses and other current liabilities	4,480	3,421
Operating lease liabilities	317	291
Total current liabilities	15,679	6,122
Loan payable, net of current portion and discount	—	9,853
Operating lease liabilities, net of current portion	210	387
Total liabilities	15,889	16,362
Commitments and contingencies (Note 7)		
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 December 31, 2021 and 2020, respectively; 82,969,421 and 50,821,361 shares issued and outstanding at December 31, 2021 and 2020, respectively	83	51
Additional paid-in capital	265,237	220,307
Accumulated deficit	(246,452)	(197,789)
Total stockholders' equity	18,868	22,569
Total liabilities and stockholders' equity	$ 34,757	$ 38,931

See accompanying notes.

Allena Pharmaceuticals, Inc.

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

	Years Ended December 31,		
	2021	2020	2019
Operating expenses:			
Research and development	$ 34,972	$ 20,383	$ 37,244
General and administrative	12,677	11,603	9,676
Restructuring charges	—	—	605
Total operating expenses	47,649	31,986	47,525
Other income (expense):			
Interest income (expense), net	(976)	(510)	270
Other expense, net	(38)	(349)	(84)
Loss on extinguishment of debt	—	—	—
Other income (expense), net	(1,014)	(859)	186
Net loss	$ (48,663)	$ (32,845)	$ (47,339)
Net loss per share attributable to common stockholders — basic and diluted	$ (0.72)	$ (1.01)	$ (2.13)
Weighted-average common shares outstanding — basic and diluted	67,956,739	32,506,679	22,180,868
Comprehensive loss	$ (48,663)	$ (32,845)	$ (47,339)

See accompanying notes.

Allena Pharmaceuticals, Inc.

Consolidated Statements of Stockholders' Equity
(in thousands, except share amounts)

	Common stock		Additional paid-in capital	Accumulated deficit	Total stockholders' equity
	Shares	Amount			
Balance at December 31, 2018	20,809,025	21	167,040	(117,605)	49,456
Issuance of common stock, net of issuance costs	3,875,848	4	11,976	—	11,980
Exercise of common stock options	24,399	—	36	—	36
Issuance of common stock through employee stock purchase plan ("ESPP")	25,737	—	76	—	76
Stock-based compensation	—	—	2,989	—	2,989
Net loss	—	—	—	(47,339)	(47,339)
Balance at December 31, 2019	24,735,009	25	182,117	(164,944)	17,198
Issuance of common stock, net of issuance costs	25,343,290	25	34,071	—	34,096
Exercise of common stock options	11,928	—	17	—	17
Issuance of common stock through employee stock purchase plan ("ESPP")	43,095	—	52	—	52
Issuance of common stock through release of restricted stock units ("RSUs")	688,039	1	(1)	—	—
Stock-based compensation	—	—	4,051		4,051
Net loss	—	—	—	(32,845)	(32,845)
Balance at December 31, 2020	50,821,361	51	220,307	(197,789)	22,569
Issuance of common stock and accompanying warrants, net of issuance costs	31,497,400	31	41,242	—	41,273
Issuance of common stock through employee stock purchase plan ("ESPP")	30,383	—	18	—	18
Issuance of common stock through release of restricted stock units ("RSUs")	620,277	1	(1)	—	—
Stock-based compensation	—	—	3,671		3,671
Net loss	—	—	—	(48,663)	(48,663)
Balance at December 31, 2021	82,969,421	83	265,237	(246,452)	18,868

See accompanying notes.

Allena Pharmaceuticals, Inc.

Consolidated Statements of Cash Flows
(in thousands)

	Years Ended December 31,		
	2021	2020	2019
Cash flows from operating activities:			
Net loss	$ (48,663)	$ (32,845)	$ (47,339)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation expense	3,671	4,051	2,989
Depreciation expense	363	166	163
Non-cash interest expense	53	34	8
Non-cash lease expense	372	601	486
Loss (gain) on sale of equipment	9	(7)	—
Changes in assets and liabilities:			
Prepaid expenses and other current assets	(811)	821	(202)
Other assets	—	—	123
Accounts payable	(1,377)	(544)	972
Accrued expenses	1,005	75	(301)
Operating lease liabilities	(300)	(564)	(531)
Other liabilities	—	53	—
Net cash used in operating activities	(45,678)	(28,159)	(43,632)
Cash flows from investing activities:			
Purchases of property and equipment	(667)	(650)	(122)
Sales of property and equipment	—	18	—
Net cash used in investing activities	(667)	(632)	(122)
Cash flows from financing activities:			
Proceeds from (payments of issuance costs related to) the issuance of common stock, net of issuance costs	41,273	33,995	12,035
Proceeds from exercise of stock options	—	17	36
Proceeds from issuance of stock through ESPP	18	52	76
Proceeds from loan payable	—	10,000	—
Repayment of loan payable	—	(10,000)	—
Debt issuance costs paid	—	(214)	—
Other	—	(24)	(29)
Net cash provided by (used in) financing activities	41,291	33,826	12,118
Net increase (decrease) in cash and cash equivalents	(5,054)	5,035	(31,636)
Cash and cash equivalents, beginning of period	35,042	30,007	61,643
Cash and cash equivalents, end of period	$ 29,988	$ 35,042	$ 30,007
Supplemental disclosures:			
Cash paid for interest	$ 953	$ 358	$ 543
Property and equipment purchases included in accounts payable	$ —	$ 7	$ —
Right-of-use assets obtained in exchange of operating lease obligations	$ —	$ 774	$ 992
Issuance costs included in accounts payable and accrued expenses	$ —	$ 101	$ 45

See accompanying notes.

1. Organization and Basis of Presentation

Allena Pharmaceuticals, Inc. (the "Company") is a clinical stage company focused on developing non-absorbed oral enzyme therapeutics to treat metabolic conditions including hyperoxaluria and hyperuricemia. The Company was incorporated under the laws of the State of Delaware on June 24, 2011. The Company's headquarters are 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 $246.5 million at December 31, 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 December 31, 2021, the Company had $30.0 million of cash and cash equivalents.

The Company's available cash and cash equivalents as of December 31, 2021 are not sufficient to fund the Company's current operating plan for at least the next twelve months following the filing of this Annual Report. The Company requires additional capital to sustain its operations, including its 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. In January 2022, the Company initiated a process to explore a range of strategic and financing alternatives to maximize shareholder value and has engaged the investment bank Stifel, Nicolaus & Company, Inc. ("Stifel") to act as strategic advisor for this process. Potential strategic alternatives that may be evaluated include a partnership or sale of ALLN-346, a sale or merger of the Company, or securing additional financing to enable further development of the Company's ALLN-346 program. There can be no assurance that this strategic review process will result in the Company pursuing any transaction or that any transaction, if pursued, will be completed. If the Company is unable to complete a transaction, it may be required to initiate a bankruptcy process.

As part of the strategic process, the Compensation Committee of the Board of Directors approved a retention plan on January 28, 2022, available to all employees ("Retention Plan"). Employees were required to execute retention agreements to receive payments and other considerations offered by the Retention Plan. Employees who executed a retention agreement received a salary adjustment equal to 6.5% retroactive to January 1, 2022, a restricted stock unit ("RSU") grant and a lump sum retention payment. A total of 3,163,000 RSUs were granted on February 1, 2022 under the Retention Plan. The RSUs vest over a three-year period ratably on July 15th and January 15th of each year following grant date. Lump sum retention payments totaling $3.0 million were made to employees in February 2022. If an employee resigns from the Company or is terminated for cause prior to June 30, 2022, the employee would be required to fully repay the lump sum retention payment received. If an employee resigns from the Company or is terminated for cause between July 1, 2022 and September 30, 2022, the employee would be required to repay 50% of the lump sum retention payment received.

During the first quarter of 2022, the Company made principal prepayments of $5.0 million of the $10.0 million that was outstanding as of December 31, 2021 under the loan and security agreement with Pontifax Medison Finance (Israel) L.P. and Pontifax Medison Finance (Cayman) L.P. (together "Pontifax") ("Pontifax Agreement"). The outstanding principal balance as of the filing date of this Annual Report is $5.0 million. The Company also purchased Directors' & Officers' run-off insurance for $6.8 million in March 2022 to provide continued insurance coverage through any bankruptcy process with run off period of six years, which equal to the statute of limitations.

On March 18, 2022, the Company announced that it was terminating its URIROX-2 study and reloxaliase program and initiated the process of closing the URIROX-2 study with the CRO, investigative sites, patients and business

partners. In connection with the termination of the reloxaliase program, the Company completed a workforce reduction of approximately 40% on March 31, 2022. In accordance with the terms of the Retention Plan, the employees terminated by the Company on March 31, 2022 were not required to repay any portion of their lump sum retention payments originally received in February 2022.

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 the Company's 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 year ended December 31, 2021, the Company issued and sold a total of 4,081,338 shares of its common stock under the B. Riley ATM Agreement at a weighted average price of $1.11 per share for net proceeds of approximately $4.2 million.

The Company entered into another At Market Issuance Sales Agreement with B. Riley Securities, Inc. ("Updated B. Riley ATM Agreement") on December 23, 2021. During the first quarter of 2022 through the filing date of this Annual Report, the Company issued and sold 6,804,888 shares of its common stock under the Updated B. Riley ATM Agreement at a weighted average price of $0.62 per share for net proceeds of $4.1 million. The B. Riley ATM Agreement was terminated at the time the Company entered into the Updated B. Riley Agreement.

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.

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 obtain sufficient additional funds on commercially acceptable terms to fund its operations, it will have a material adverse effect on its business, results of operations and financial condition and jeopardize its ability to continue operations. The Company may need to implement additional 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, and the Company may need to seek an in-court or out-of-court restructuring of its liabilities. In the event of such future liquidation or bankruptcy proceeding, holders of the Company's common stock and other securities will likely suffer a total loss of their investment. These factors raise substantial doubt about the Company's ability to continue as a going concern as of the filing date of this Annual Report. The accompanying 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.

Basis of Presentation

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("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 Standard Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

2. Summary of Significant Accounting Policies

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.

Use of Estimates

The preparation of the Company's consolidated financial statements in conformity with 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 judgments of prepaid and accrued research and development expenses, and the valuation of stock-based awards. Actual results could differ from those estimates.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision-maker in deciding how to allocate resources and assess performance. The Company's chief operating decision-maker, the Company's chief executive officer, views the Company's operations and manages its business as a single operating segment, which is the business of discovering and developing non-absorbed oral enzyme therapeutics.

Comprehensive Income (Loss)

Comprehensive income (loss) is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. Comprehensive loss equaled net loss for the years ended December 31, 2021, 2020 and 2019.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of three months or less to be cash equivalents. Cash and cash equivalents include cash held in banks and amounts held in money market funds. Cash equivalents are stated at cost, which approximates fair value.

Cash and cash equivalents consist of the following at December 31, 2021 and 2020 (in thousands):

	December 31,	
	2021	2020
Cash and cash equivalents:		
Cash	$ 13,465	$ 344
Money market funds	16,523	34,698
	$ 29,988	$ 35,042

Investments

The Company classifies its investments in debt securities as available-for-sale. Available-for-sale investments are carried at fair value with unrealized gains and losses included in stockholders' equity. Any premium or discount arising at purchase is amortized and/or accreted to interest income and/or expense. The cost of securities sold is determined on a specific identification basis, and realized gains and losses are included in interest income (expense) within the statement of operations and comprehensive loss. The Company did not hold any investments at December 31, 2021 and 2020.

The Company evaluates its available-for-sale investments with unrealized losses for other-than-temporary impairment. When assessing investments for other-than-temporary declines in value, the Company considers such factors as, among other things, the significance of the decline in value is as a percentage of the original cost, the

length of time that the market value of the investment has been less than its original cost, the Company's ability and intent to retain the investment for a period of time sufficient to allow for any anticipated recovery in fair value and market conditions in general. If any adjustment to fair value reflects a decline in the value of the investment that the Company considers to be "other than temporary", the Company reduces the investment to fair value through a charge to the statement of operations and comprehensive loss. No such adjustments were necessary during the periods presented.

Concentration of Credit Risk and Off-Balance Sheet Risk

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents and investments. The Company maintains all of its cash and cash equivalents at a single accredited financial institution, in amounts that exceed federally insured limits. The Company generally invests its excess cash in money market funds that are subject to minimal credit and market risk. Management has established guidelines relative to credit ratings and maturities intended to safeguard principal balances and maintain liquidity. The investment portfolio is maintained in accordance with the Company's investment policy, which defines allowable investments, specifies credit quality standards and limits the credit exposure of any single issuer.

The Company has no significant off-balance sheet risk such as foreign exchange contracts, option contracts, or other foreign hedging arrangements.

Significant Suppliers

The Company is dependent on third-party manufacturers to supply products for research and development activities of its programs, including preclinical and clinical testing. In particular, the Company relies and expects to continue to rely on a small number of manufacturers to supply the active pharmaceutical ingredients and formulated drugs related to these programs. These programs could be adversely affected by a significant interruption in the supply of active pharmaceutical ingredients and formulated drugs.

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.

Property and Equipment

Property and equipment consists of laboratory equipment, computer equipment, software and leasehold improvements recorded at cost. These amounts are depreciated using the straight-line method over the estimated useful lives of the assets as follows:

Laboratory equipment	4 years
Computer equipment	3 years
Software	5 years
Leasehold improvements	Shorter of useful life or remaining term of related lease

Upon retirement or sale, the cost of the assets disposed of and the related accumulated depreciation are eliminated from the balance sheet and related gains or losses are reflected in the statement of operations and comprehensive loss. Repairs and maintenance costs are expensed as incurred and costs of significant improvements are capitalized.

Impairment of Long-Lived Assets

The Company evaluates long-lived assets for potential impairment when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparing the book values of the assets to the expected future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book values of the assets exceed their fair value. The Company did not recognize any impairment losses for the years ended December 31, 2021, 2020 and 2019.

Leases

The Company determines at the inception of an arrangement whether the arrangement contains a lease. If a lease is identified in an arrangement, the Company recognizes a right-of-use asset and liability on its balance sheet and determines whether the lease should be classified as a finance or operating lease. The Company does not recognize assets or liabilities for leases with lease terms of less than 12 months.

A lease qualifies as a finance lease if any of the following criteria are met at the inception of the lease: (i) there is a transfer of ownership of the leased asset to the Company by the end of the lease term, (ii) the Company holds an option to purchase the leased asset that it is reasonably certain to exercise, (iii) the lease term is for a major part of the remaining economic life of the leased asset, (iv) the present value of the sum of lease payments equals or exceeds substantially all of the fair value of the leased asset, (v) the nature of the leased asset is specialized to the point that it is expected to provide the lessor no alternative use at the end of the lease term. All other leases are recorded as operating leases.

Finance and operating lease assets and liabilities are recognized at the lease commencement date based on the present value of the lease payments over the lease term using the discount rate implicit in the lease. If the rate implicit is not readily determinable, the Company utilizes its incremental borrowing rate at the lease commencement date. Operating lease assets are further adjusted for prepaid or accrued lease payments. Operating lease payments are expensed using the straight-line method as an operating expense over the lease term. Finance lease assets are amortized to depreciation expense using the straight-line method over the shorter of the useful life of the related asset or the lease term. Finance lease payments are bifurcated into (i) a portion that is recorded as imputed interest expense and (ii) a portion that reduces the finance liability associated with the lease.

Effective January 1, 2019, the Company adopted ASC 842. In adopting ASC 842, the Company elected to utilize a package of practical expedients under which an entity need not reassess whether any expired or existing contracts are or contain leases, the lease classification for any expired or existing leases or initial direct costs for any existing leases. The Company also elected a practical expedient whereby an entity can utilize hindsight in determining the lease term, including options to extend or terminate the lease. Finally, although separation of lease and non-lease components is required under ASC 842, the Company elected a practical expedient to not separate lease and non-lease components and rather accounts for lease and non-lease components together as a single lease component.

Variable lease payments are expensed as incurred. If a lease includes an option to extend or terminate the lease, the Company reflects the option in the lease term if it is reasonably certain it will exercise the option.

Operating leases are recorded in "Operating lease assets," "Operating lease liabilities" and "Operating lease liabilities, net of current portion" on the Company's consolidated balance sheet. The Company did not have any finance leases recorded on its consolidated balance sheet as of December 31, 2020 and 2019.

Research and Development

The Company expenses all costs incurred in performing research and development activities. Research and development expenses include salaries and benefits, materials and supplies, preclinical and clinical trial expenses, manufacturing expenses, stock-based compensation expense, depreciation of equipment, contract services and other outside expenses. Costs of certain development activities, such as manufacturing, are recognized based on an evaluation of the progress to completion of specific tasks. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the consolidated financial statements as prepaid or accrued research and development costs. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

Patent Costs

The Company expenses patent application and related legal costs as incurred and classifies such costs as general and administrative expenses in the accompanying consolidated statements of operations and comprehensive loss.

Accounting for Stock-Based Compensation

The Company accounts for its stock-based compensation in accordance with ASC Topic 718, *Compensation—Stock Compensation* ("ASC 718"). ASC 718 requires all stock-based payments to employees, directors, and non-employees, to be recognized as expense in the statements of operations and comprehensive loss based on their grant date fair values. The Company estimates the fair value of options granted using the Black-Scholes option pricing model for stock option grants to both employees and non-employees. The Company believes the fair value of the stock options granted to non-employees is more reliably determinable than the fair value of the services provided.

The Black-Scholes option pricing model requires inputs based on certain subjective assumptions, including (a) the expected stock price volatility, (b) the expected term of the award, (c) the risk-free interest rate and (d) expected dividends. Due to the limited trading history of the Company's common stock and a lack of company-specific historical and implied volatility data that is equal to the length of the expected term of the Company's options, the Company has based its computation of expected volatility on the historical volatility of a representative group of public companies with similar characteristics to the Company, including stage of product development and life science industry focus. The Company weights its own historical volatility of its stock price and the historical volatility of a representative group of public companies for the computation of expected volatility used for estimating the fair value of option grants. The Company increase the weighting on the historical volatility of its stock price over the historical volatility of a representative group of public companies until such time as the Company has a sufficient amount of historical information regarding the volatility of its stock. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The Company uses the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, *Share-Based Payment*, to calculate the expected term for options granted to employees as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The expected term is applied to the stock option grant group as a whole, as the Company does not expect substantially different exercise or post-vesting termination behavior among its employee population. For options granted to non-employees, the Company utilizes the contractual term of the stock-based payment as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the stock options. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock. The Company recognizes forfeitures as they occur.

The Company expenses the fair value of its stock-based compensation awards on a straight-line basis over the requisite service period, which is generally the vesting period.

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 standards. 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. As of December 31, 2021, the Company concluded that the Warrants continue to meet the equity-classification guidance.

Income Taxes

The Company accounts for income taxes using the liability method in accordance with ASC Topic 740, *Income Taxes* ("ASC 740"). The difference between the financial statement and tax basis of the assets and liabilities is determined annually. Deferred income tax assets and liabilities are computed using the tax laws and rates that are expected to apply for periods in which such differences reverse. Valuation allowances are established, if necessary, to reduce the deferred tax asset to the amount that will more likely than not be realized.

The Company recognizes the effect of income tax positions only if those positions are more likely than not of being sustained. Recognized income tax positions are measured at the largest amount that is greater than 50% likely of being realized. Changes in recognition or measurement are reflected in the period in which the change in judgment occurs.

Net Loss Per Share

The Company has reported losses since inception and has computed basic net loss per share attributable to common stockholders by dividing 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 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 anti-dilutive. 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):

	Years Ended December 31,		
	2021	2020	2019
Numerator:			
Net loss	$ (48,663)	$ (32,845)	$ (47,339)
Net loss attributable to common stockholders	$ (48,663)	$ (32,845)	$ (47,339)
Denominator:			
Weighted-average common shares – basic and diluted	67,956,739	32,506,679	22,180,868
Net loss per share attributable to common stockholders –basic and diluted	$ (0.72)	$ (1.01)	$ (2.13)

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):

	Years Ended December 31,		
	2021	2020	2019
Stock options	6,765,837	4,110,691	3,915,591
Restricted stock units	—	620,277	517,750
Warrants	10,687,912	9,040	9,040
Common stock issuable upon conversion of outstanding debt	2,439,024	2,439,024	—
Total	19,892,773	7,179,032	4,442,381

Loss Contingencies

In accordance with ASC 450, *Contingencies*, the Company accrues anticipated costs of settlement, damages, and losses for loss contingencies based on historical experience or to the extent specific losses are probable and estimable. Otherwise, the Company expenses these costs as incurred. If the estimate of a probable loss is a range, and no amount within the range is more likely, the Company accrues the minimum amount of the range.

Guarantees

The Company has identified the guarantees described below as disclosable, in accordance with ASC 460, *Guarantees*.

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

The Company is a party to a number of agreements entered into in the ordinary course of business that contain typical provisions that obligate the Company to indemnify the other parties to such agreements upon the occurrence of certain events. Such indemnification obligations are usually in effect from the date of execution of the applicable agreement for a period equal to the applicable statute of limitations. The aggregate maximum potential future liability of the Company under such indemnification provisions is uncertain.

The Company leases office space under several noncancelable operating leases. The Company has standard indemnification arrangements under these leases that require it to indemnify the landlord against all costs, expenses, fines, suits, claims, demands, liabilities, and actions directly resulting from any breach, violation, or nonperformance of any covenant or condition of the respective lease.

As of December 31, 2021 and 2020, the Company had not experienced any losses related to these indemnification obligations, and no material claims with respect thereto were outstanding. The Company does not expect significant claims related to these indemnification obligations and, consequently, concluded that the fair value of these obligations is negligible, and no related reserves have been established.

Recently Adopted Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies and adopted by the Company as of the specified effective date. Unless otherwise discussed, the Company believes that the impact of recently issued standards that are not yet effective will not have a material impact on its consolidated financial position or results of operations upon adoption.

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 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, 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. The Company adopted ASU 2020-06 on January 1, 2022. The adoption of ASU 2020-06 did not have a material impact on its 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 consolidated financial statements.

3. Fair Value Measurements

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

Description	December 31, 2021	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Assets:				
Money market funds, included in cash and cash equivalents	$ 16,523	$ 16,523	$ —	$ —
Total assets	$ 16,523	$ 16,523	$ —	$ —

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

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

There have been no changes to the valuation methods used during the years ended December 31, 2021 and 2020. There were no transfers within the fair value hierarchy during the years ended December 31, 2021 and 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. The carrying value of the Company's debt therefore approximates its fair value based on Level 3 of the fair value hierarchy.

4. Property and Equipment, Net

Property and equipment includes the following at December 31, 2021 and 2020 (in thousands):

	December 31, 2021	December 31, 2020
Property and equipment:		
Laboratory equipment	$ 1,820	$ 1,368
Computer equipment	20	6
Software	39	39
Leasehold improvements	219	—
Construction in progress	—	54
	2,098	1,467
Less: Accumulated depreciation	(925)	(586)
Property and equipment, net	$ 1,173	$ 881

The Company recognized $363,000, $166,000 and $163,000 of depreciation expense for the years ended December 31, 2021, 2020 and 2019, respectively.

5. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31, 2021	December 31, 2020
Payroll and employee-related expenses	$ 371	$ 1,945
Third-party research and development expenses	3,195	984
Professional fees	677	250
Loan interest	227	242
Other	10	—
Total accrued expenses	$ 4,480	$ 3,421

6. Restructuring Charges

On November 29, 2019, following the completion of a strategic review of its business, the Company's Board of Directors approved a workforce reduction plan, or the Workforce Reduction, to reduce its workforce by approximately 38%. The Company evaluated the related employee severance and other benefits to employees in connection with the Workforce Reduction to determine whether the benefits were within the scope ASC 712, *Compensation - Non-retirement Post-employment Benefits*, or within the scope of ASC 420, *Exit or Disposal Cost Obligations,* depending on the nature of the benefit and whether it is part of an on-going benefit arrangement under ASC 712 or a one-time termination benefit unique to the Workforce Reduction. The Company recorded restructuring expense of $0.6 million at the time of the Workforce Reduction, pursuant to ASC 420 as the Company did not have an on-going benefit arrangement under ASC 712. The Workforce Reduction was complete as of December 31, 2019.

The following table outlines the components of the restructuring charges during the year ended December 31, 2019 included in the consolidated statement of operations, and ending liability recorded in the balance sheet as of December 31, 2019 (in thousands):

	Charges incurred during the year ended December 31, 2019	Amount paid through December 31, 2019	Remaining liability at December 31, 2019
Employee severance, bonus and other	$ 605	$ (232)	$ 373
Total restructuring charges	$ 605	$ (232)	$ 373

The remaining liability at December 31, 2019 was paid during the year ended December 31, 2020. The Company did not record any restructuring charges during the years ended December 31, 2021 and 2020.

7. 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.

Additional Lease Information Related to the Application of ASC 842

Maturities of the Company’s operating lease liabilities in accordance with ASC 842 as of December 31, 2021 are as follows (in thousands):

2022	$ 317
2023	231
Total maturities	$ 548
Less: Amount representing interest	(21)
Present value of operating lease liabilities	$ 527

Lease costs included in the Company’s consolidated statements of operations and comprehensive loss was $0.4 million and $0.5 million for the years ended December 31, 2021 and 2020, respectively. The Company’s operating leases had a weighted average remaining lease term of 1.3 years and 2.3 years and a weighted average discount rate of 5.5% and 5.5% at December 31, 2021 and 2020, respectively.

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 December 31, 2021 and 2020.

License Agreement

In March 2012, the Company entered into an exclusive license agreement ("License Agreement") with Althea Technologies, Inc. ("Althea") for certain intellectual property. The Company reimbursed Althea for patent related fees and costs incurred by Althea totaling $0.1 million in the aggregate and issued a total of 88,186 shares of common stock to Althea. Under the terms of the License Agreement, the Company agreed to pay annual license maintenance fees, milestone payments and royalties as a percentage of net sales. Annual license maintenance fees are creditable against royalties earned during the same calendar year and are not material to the financial statements. Milestone payments are triggered upon the achievement of specified development, regulatory and commercialization milestones and are not creditable against royalties. Actual amounts due under the License Agreement will vary depending on the number of products developed, the type and development path of the products, and other related factors. Milestone payments could total up to $56.0 million. The Company may terminate the agreement at any time with 60 days prior written notice.

8. 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 during the three months ended June 30, 2020.

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.

9. Convertible Debt Agreement

On September 29, 2020, the Company entered into the 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 65thpatient 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. The availability to withdraw amounts available under the Credit Line expired unused on September 29, 2021 and the availability to withdraw amounts available under the Third Installment Loan expired unused on December 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.

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 December 31, 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 December 31, 2021 and 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.

As part of the strategic process initiated in January 2022, The Company evaluated the repayment of amounts outstanding under the Pontifax Agreement. Taking into consideration the available cash and cash equivalents at December 31, 2021 along with the termination of its reloxaliase program in March 2022 and its inability to raise sufficient capital to sustain its operations as of the date of this Annual Report, the Company determined it was appropriate to classify the full amount outstanding under the Pontifax Agreement as a current liability given the subjective acceleration of payment under the material adverse change clause. During the first quarter of 2022, the Company made prepayments of principal totaling $5.0 million. The principal amount outstanding as of the filing date of this Annual Report is $5.0 million.

The minimum aggregate future loan and interest payments at December 31, 2021 are as follows (in thousands):

Years Ending December 31,		
2022	$	1,927
2023		5,015
2024		4,880
Total minimum payments		11,822
Less: Amount representing interest		(1,822)
Less: Discount		(148)
Less: Current portion		(9,852)
Loan payable, net of current portion	$	—

10. Stockholders' Equity

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 the B. Riley ATM Agreement on March 29, 2021, under which the Company was authorized to issue and sell shares of its common stock having aggregate sales proceeds of up to $50 million from time to time through B. Riley, acting as sales agent and/or principal. The Company agreed to pay B. Riley a commission of 3.0% of the gross proceeds from any sales of shares of its common stock under this facility. During the year ended December 31, 2021, the Company issued and sold a total of 4,081,338 shares of its common stock under the B. Riley ATM Agreement at a weighted average price of $1.11 per share for net proceeds of approximately $4.2 million.

The Company entered into the Updated B. Riley ATM Agreement on December 23, 2021, under which the Company was authorized to issue and sell shares of its common stock having aggregate sales proceeds of up to $50 million from time to time through B. Riley, acting as sales agent and/or principal. During the first quarter of 2022 through the filing date of this Annual Report, the Company issued and sold 6,804,888 shares of its common stock under the Updated B. Riley ATM Agreement at a weighted average price of $0.62 per share for net proceeds of $4.1 million. The B. Riley ATM Agreement was terminated at the time the Company entered into the Updated B. Riley Agreement.

In December 2018, the Company entered into the Cowen ATM Agreement, under which the Company was authorized to issue and sell shares of its common stock having aggregate sales proceeds of up to $50 million from time to time through Cowen, acting as sales agent and/or principal. The Company agreed to pay Cowen a commission of 3.0% of the gross proceeds from any sales of shares of its common stock under this facility. On December 30, 2019, the Company completed an issuance and sale of 1,243,756 shares of common stock under the ATM Agreement. As a result of this issuance and sale of common stock, the Company received approximately $2.6 million in net proceeds after deducting offering costs. 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. The Cowen ATM Agreement was terminated at the time the Company entered into the B. Riley ATM Agreement.

On June 5, 2020, the Company completed another registered direct offering, in which it issued and sold 7,317,074 shares of its 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.

On July 30, 2020, the Company completed a public underwritten offering of 5,894,191 shares of its 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 December 4, 2020, the Company completed another 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.

Common Stock

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 December 31, 2021 and 2020:

	December 31,	
	2021	2020
Stock options and restricted stock units	8,372,313	5,359,736
Warrants	10,687,912	9,040
Common stock issuable upon conversion of outstanding debt	2,439,024	2,439,024
Employee stock purchase plan	306,527	336,910
Total	21,805,776	8,144,710

Warrants

At December 31, 2021, the Company had 10,687,912 warrants outstanding for the purchase of shares of common stock at a weighted average exercise price of $1.26. At December 31, 2020, the Company had 9,040 warrants outstanding for the purchase of shares of common stock at an exercise price of $11.06. 10,678,872 warrants with an exercise price of $1.25 expire on July 16, 2026. 9,040 warrants with an exercise price of $11.06 expire on May 1, 2026.

11. Stock Incentive Plans

Stock Option Plans

The Company adopted the 2017 Stock Option and Incentive Plan ("2017 Plan") on October 31, 2017. Upon adoption of the 2017 Plan, no further grants were 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, any awards outstanding under the 2011 Plan as of the October 31, 2017 that are cancelled, forfeited or otherwise terminated without being exercised, the number of shares underlying such awards are 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 registrant's Board of Directors. On January 1, 2020, 2021 and 2022, the shares available for grant under the 2017 Plan were automatically increased by 989,400, 2,032,854 and 3,318,776 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 stock-based awards under the terms of the 2017 Plan. As of December 31, 2021, 798,476 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 December 31, 2021, 808,000 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. 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. Stock options granted under the 2021, 2017 and 2011 Plans 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):

	Years Ended December 31,		
	2021	2020	2019
Research and development	$ 1,128	$ 1,286	$ 1,175
General and administrative	2,543	2,765	1,814
Total	$ 3,671	$ 4,051	$ 2,989

The fair value of each stock option granted to employees and directors was estimated on the date of grant using the Black-Scholes option-pricing model, with the following range of assumptions for the years ended December 31, 2021, 2020 and 2019:

	Years Ended December 31,		
	2021	2020	2019
Risk-free interest rate	0.4% – 1.4%	0.4% – 0.5%	1.4% – 2.6%
Expected dividend yield	—%	—%	—%
Expected term (in years)	5.0 – 7.0	5.5 – 6.1	5.5 – 6.8
Expected volatility	92% – 95%	94% – 95%	80% – 83%

The expense related to stock options granted to employees and directors for their service on the Board of Directors was $2.9 million, $2.6 million, and $2.9 million for the years ended December 31, 2021, 2020 and 2019, respectively.

The Company did not grant any stock options to non-employees during the years ended December 31, 2021, 2020 or 2019. The expense related to awards granted to non-employees was not material to the consolidated financial statements for the years ended December 31, 2021, 2020 and 2019.

A summary of the stock option activity under the 2021, 2017 and 2011 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	(686,204)	4.72		
Outstanding at December 31, 2021	6,765,837	$ 2.81	7.6	$ 3
Exercisable at December 31, 2021	3,282,830	$ 3.52	6.2	$ 3

The weighted-average fair value of options granted to employees and directors for their service on the Board of Directors during the years ended December 31, 2021, 2020 and 2019 was $1.41, $1.01 and $3.29 per share, respectively.

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had exercise prices lower than the fair value of the Company's common stock. The total intrinsic value of options exercised during the years ended December 31, 2020 and 2019 was $8,000 and $58,000, respectively. There were no options exercised during the year ended December 31, 2021.

As of December 31, 2021, total unrecognized stock-based compensation expense relating to unvested stock options was $5.1 million. This amount is expected to be recognized over a weighted-average period of 2.5 years.

Restricted Stock Units (RSUs)

During the years ended December 31, 2021, 2020 and 2019, the Company made awards of time-based RSUs to certain employees of the Company. The RSUs are generally forfeited if the employment relationship terminates with the Company prior to vesting. The weighted average fair value of RSUs granted to employees during the years ended December 31, 2021, 2020 and 2019 was $1.29, $1.39 and $2.42 per share, respectively. For the years ended December 31, 2021, 2020 and 2019, the Company recognized $0.8 million, $1.5 million and $0.1 million, respectively of stock-based compensation expense related to these awards. As of December 31, 2021, the Company did not have any unrecognized compensation cost related to nonvested remaining to be recognized.

A summary of the status of nonvested RSUs as of December 31, 2021 and the changes during the year then ended are presented below (in thousands, except fair values):

	Shares	Weighted-Average Grant Date Fair Value
Nonvested at December 31, 2020	620,277	$ 1.29
Granted	—	—
Vested	(620,277)	1.29
Forfeited	—	—
Nonvested at December 31, 2021	—	—

Employee Stock Purchase Plan

The Company adopted the 2017 Employee Stock Purchase Plan ("ESPP") on October 31, 2017. The ESPP permits eligible employees to enroll in six-month offering periods. Participants may purchase shares of the Company's common stock, through payroll deductions, at a price equal to 85% of the fair market value of the common stock on the first or last day of the applicable six-month offering period, whichever is lower. Purchase dates under the ESPP occur on or about January 1 and July 1 each year. The ESPP initially reserved 206,284 shares of common stock for issuance. The ESPP also provides that an additional number of shares will automatically be added to the shares authorized for issuance under the ESPP on January 1 of each year. The number of shares added each year will be equal to the lesser of: (i) 1% of the outstanding shares on the immediately preceding December 31 or (ii) such amount as determined by the Compensation Committee of the registrant's Board of Directors. On January 1, 2018, the shares available for grant under the ESPP was automatically increased by 206,946 shares. No shares were added to the ESPP on January 1, 2019, 2020 and 2021.

During the years ended December 31, 2021 and 2020, $18,000 and $52,000, respectively, were withheld from employees, on an after-tax basis, in order to purchase 30,383 and 43,095 shares of the Company's common stock, respectively. As of December 31, 2021, 306,527 shares of Company's common stock remained available for issuance under the ESPP.

12. Income Taxes

The Company records a provision or benefit for income taxes on pre-tax income or loss based on its estimated effective tax rate for the year. During the year ended December 31, 2021, the Company recorded a net loss of $48.7

million and, since it maintains a full valuation allowance on its deferred tax assets, the Company did not record an income tax benefit for the year ended December 31, 2021.

Deferred taxes are recognized for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. The significant components of the Company's deferred tax assets are comprised of the following (in thousands):

	December 31,	
	2021	2020
Deferred tax assets:		
Net operating loss carryforwards	$ 45,592	$ 32,827
Research and development credits	2,489	656
Licenses	13	16
Stock based compensation	1,579	1,205
Operating lease liabilities	143	170
Other	51	512
Total gross deferred tax assets	49,867	35,386
Less: Valuation allowance	(49,744)	(35,216)
Net deferred tax assets	123	170
Deferred tax liabilities:		
Operating lease assets	(123)	(170)
Total gross deferred tax liabilities	(123)	(170)
Net deferred taxes	$ —	$ —

ASC 740 requires a valuation allowance to reduce the deferred tax assets reported if, based on the weight of the evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized. After consideration of all the evidence, both positive and negative, the Company has recorded a valuation allowance against its deferred tax assets at December 31, 2021 and 2020, respectively, because the Company's management has determined that it is more likely than not that the Company will not recognize the benefits of its federal and state deferred tax assets primarily due to its cumulative loss position and, as a result, a valuation allowance of $49.7 million and $35.2 million has been established at December 31, 2021 and 2020, respectively. The valuation allowance increased by $14.5 million for the year ended December 31, 2021 and decreased by $16.6 million for the year ended December 31, 2020. The increase in valuation allowance for the year ended December 31, 2021 was primarily due to the generation of net operating losses while the decrease in valuation allowance for the year ended December 31, 2020 was primarily related to the decrease in net operating loss and tax credit deferred tax assets as a result of a Section 382 limitation.

The following table presents the Company's change in valuation allowance for the year ended December 31, 2020 and 2019:

	December 31,	
	2021	2020
Valuation allowance at the beginning of the year	$ 35,216	$ 51,800
Change for current period	14,528	(16,584)
Valuation allowance at the end of the year	$ 49,744	$ 35,216

A reconciliation of income tax expense computed at the statutory federal income tax rate to income taxes reflected in the financial statements is as follows:

	2021	2020	2019
Income tax computed at federal statutory tax rate	21.0%	21.0%	21.0%
State taxes, net of federal benefit	5.9%	5.7%	6.1%
Research and development and other tax credits	3.8%	3.7%	4.9%
Stock based compensation	(0.6)%	(1.0)%	(0.6)%
Federal net operating loss - Section 382 Limitation	—%	(28.1%)	—%
Federal tax credit - Section 382 Limitation	—%	(19.3%)	—%
State tax net operating loss - Section 382 Limitation	—%	(25.5%)	—%
State tax credit - Section 382 Limitation	—%	(7.0%)	—%
Other	(0.2%)	—%	—%
Change in deferred tax asset valuation allowance	(29.9)%	50.5%	(31.4)%
	0.0%	—%	—%

As of December 31, 2021 and 2020, the Company had U.S. federal net operating loss carryforwards of approximately $188.2 million and $140.9 million, respectively, which may be available to offset future income tax liabilities. Of the $188.2 million net operating loss carryforwards as of December 31, 2021, $154.3 million has an indefinite life and $33.9 million will expire at various dates through 2037. As of December 31, 2021 and 2020, the Company also had U.S. state net operating loss carryforwards of approximately $96.3 million and $51.1 million, respectively, which may be available to offset future income tax liabilities and expire at various dates through 2041.

As of December 31, 2021 and 2020, the Company had federal research and development tax credit carryforwards of approximately $2.1 million and $0.5 million, respectively, available to reduce future tax liabilities which expire at various dates through 2041. As of December 31, 2021 and 2020, the Company had state research and development tax credit carryforwards of approximately $0.5 million and $0.1 million, respectively, available to reduce future tax liabilities which expire at various dates through 2036. The Company has generated research credits but has not conducted a study to document the qualified activity. This study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the deferred tax asset established for the research and development credit carryforwards and the valuation allowance.

Under the provisions of the Internal Revenue Code, the net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. As of June 3, 2020, the Company did have an ownership change as defined by Sections 382 and 383 of the Internal Revenue Code and therefore the Company has adjusted its federal and state tax attributes accordingly to disclose only the amounts that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company completed its Section 382 study through December 31, 2021 and confirmed no additional ownership changes that would trigger a Section 382 limitation has taken place. Subsequent ownership changes may further affect the limitations in future years.

The Company will recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2021 and 2020, the Company had no accrued interest or penalties related to uncertain tax positions and no such amounts have been recognized in the Company's statements of operations and comprehensive loss.

The Company files income tax returns in the United States and various state jurisdictions. The federal, state and foreign income tax returns are generally subject to tax examinations for the tax years ended December 31, 2018 through December 31, 2021. To the extent the Company has tax attribute carryforwards, the tax years in which the

attribute was generated may still be adjusted upon examination by the Internal Revenue Service, state tax authorities to the extent utilized in a future period.

13. Employee Benefit Plan

Effective January 2012, employees of the Company are eligible to participate in the Company's 401(k) retirement plan ("401(k) Plan"). Participants may contribute up to 100% of their annual compensation to the 401(k) Plan, subject to statutory limitations. Through December 31, 2018, the 401(k) Plan did not allow the Company to make matching contributions. Effective January 1, 2019, the Company amended the 401(k) Plan to allow the Company to make matching contributions. The 401(k) Plan matches 100% of employee contributions up to a maximum of 4% of employees' salary. Matching contributions are fully vested at the time of contribution. Matching contribution costs incurred by the Company for each of the years ended December 31, 2021, 2020 and 2019 were $0.3 million.

14. Selected Quarterly Financial Data (Unaudited)

The following table contains quarterly financial information for 2021 and 2020. The Company believes that the following information reflects all normal recurring adjustments necessary for the fair statement of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

	2021				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total
	(in thousands, except per share amounts)				
Total operating expenses	$ 11,410	$ 13,687	$ 12,431	$ 10,121	$ 47,649
Loss from operations	(11,410)	(13,687)	(12,431)	(10,121)	(47,649)
Net loss	(11,636)	(13,972)	(12,692)	(10,363)	(48,663)
Net loss attributable to common stockholders - basic and diluted	$ (0.21)	$ (0.24)	$ (0.17)	$ (0.13)	$ (0.72)

	2020				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total
	(in thousands, except per share amounts)				
Total operating expenses	$ 7,524	$ 6,559	$ 7,918	$ 9,985	$ 31,986
Loss from operations	(7,524)	(6,559)	(7,918)	(9,985)	(31,986)
Net loss	(7,585)	(6,976)	(8,026)	(10,258)	(32,845)
Net loss attributable to common stockholders - basic and diluted	$ (0.31)	$ (0.26)	$ (0.22)	$ (0.24)	$ (1.01)

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

1. Registration Statement (Form S-8 No. 333-221306) pertaining to the 2011 Stock Incentive Plan, the 2017 Stock Option and Incentive Plan, and the 2017 Employee Stock Purchase Plan of Allena Pharmaceuticals, Inc.,

2. Registration Statement (Form S-8 No. 333-223939) pertaining to the 2017 Stock Option and Incentive Plan and the 2017 Employee Stock Purchase Plan of Allena Pharmaceuticals, Inc.,

3. Registration Statements (Form S-3 Nos. 333-228656, 333-250992 and 333-255837) of Allena Pharmaceuticals, Inc.,

4. Registration Statements (Form S-8 Nos. 333-230127, 333-237218 and 333-254121) pertaining to the 2017 Stock Option and Incentive Plan of Allena Pharmaceuticals, Inc., and

5. Registration Statement (Form S-8 No. 333-254125) pertaining to Allena Pharmaceuticals, Inc. 2021 Inducement Equity Plan;

of our report dated March 31, 2022, with respect to the consolidated financial statements of Allena Pharmaceuticals, Inc., included in this Annual Report (Form 10-K) for the year ended December 31, 2021.

/s/ Ernst & Young LLP

Boston, Massachusetts

March 31, 2022

Exhibit 31.1

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 annual report on Form 10-K for the year ended December 31, 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(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

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

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

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

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

5. The registrant's other certifying officer(s) and I have disclosed, based on my 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.

March 31, 2022

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

Exhibit 31.2

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 annual report on Form 10-K for the year ended December 31, 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(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

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

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

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

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

5. The registrant's other certifying officer(s) and I have disclosed, based on my 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.

March 31, 2022

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

Exhibit 32.1

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

In connection with the annual report on Form 10-K of Allena Pharmaceuticals, Inc. (the "Company") for the year ended December 31, 2021, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers hereby certify, 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.

March 31, 2022

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

March 31, 2022

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