aclaris® THERAPEUTICS

2022 ANNUAL REPORT

Empowering patients through Kinome Innovation

Dear Fellow Shareholders,

It is my sincere honor to share this correspondence with you, in my first year since my appointment as Chief Executive Officer of Aclaris Therapeutics. Since joining the company last year, our company has continued to progress forward our clinical and development initiatives which position us well not only in 2023, but in the years beyond as well.

Typically, my approach is to segment areas of focus into three key areas: people, process and programs.

PEOPLE

Throughout 2022, as our key development programs, notably zunsemetinib and ATI-1777, continued their maturation, we engaged in a process to build out our internal capabilities by recruiting a number of key leadership individuals to help guide our company as we evolve into a clinical development organization with the right amount of expertise and experience to successfully conduct multiple global clinical development programs. Gail Cawkwell, M.D. joined our company as Chief Medical Officer in the second half of 2022 and has hit the ground running bringing her nearly two decades of pharmaceutical development expertise into the conduct of our ongoing trials as well as the planning and execution of all future clinical development activities.

Additionally, during 2022, James Loerop joined our team as Chief Business Officer, bringing over 30 years of large pharma and biotech business development expertise into the company, which has already demonstrated positive results through the most recent transaction we entered into with Pediatrix Therapeutics for the development and commercial rights to ATI-1777 in the Greater China Region, which provided additional upfront capital to our balance sheet. Also late in 2022, Robert Doody joined our team to lead our investor relations efforts and has had an immediate impact toward increasing our level of engagement with the investment community.

We are also incredibly proud of the company's ability to foster leadership from within as we promoted Kevin Balthaser to Chief Financial Officer and Matthew Rothman to General Counsel. We also promoted Gary DeCrescenzo, our head of CMC, to the leadership team, as a reflection of his expertise and the criticality of technical operations as we scale for Phase 3 clinical development. All of these individuals are talented within their respective roles and serve as beacons of the corporate culture we've built and continually nurture within Aclaris.

Overall, I believe we have the leadership team and organization to successfully execute our company's objectives in both the short and long term.

PROCESS

Since joining Aclaris, I've been very impressed with the state of our processes. Our focus in this regard is bolstering areas such as compliance, training and security.

Our relatively small company is fortunate to continually benefit from our world-class research and discovery engine, which consists of many of the leading scientific experts in the field of developing drugs targeting the kinome. Their discoveries laid the path to our maturing clinical development programs

such as our MK2 inhibitors ATI-450 and ATI-2231, along with our "soft" JAK 1/3 inhibitor, ATI-1777, and our ITK/JAK3 inhibitor, ATI-2138. Through our KINect® drug discovery platform, we have the ability to continue to replenish our pipeline with novel therapeutic targets which we believe is a driver for long term success and growth for years to come.

PROGRAMS

Zunsemetinib (ATI-450), an Investigational Oral MK2 Inhibitor

As we entered 2023, our company remained poised for a very exciting year with numerous data catalysts expected throughout. For zunsemetinib, we began the year with three ongoing studies: a Phase 2b dose ranging trial in rheumatoid arthritis (RA), a Phase 2a trial in psoriatic arthritis (PSA) and a Phase 2a trial in hidradenitis suppurativa (HS).

We recently announced the topline preliminary results for our trial in HS, and while we did not meet the primary efficacy endpoint for this particularly challenging disease, we were encouraged by the consistent demonstration of zunsemetinib's mechanism of action and the strengthening of our safety database.

ATI-1777, an Investigational Topical "Soft" JAK 1/3 Inhibitor

Following the results of our positive Phase 2a trial of ATI-1777 in atopic dermatitis, we entered into a Phase 2b dose ranging trial which is currently continuing enrollment. We are hopeful that ATI-1777 can provide efficacy results that are comparable to approved topical JAK inhibitors, however, through the soft nature of ATI-1777, avoid the systemic toxicities that have accompanied those therapies.

ATI-2138, an Investigational Oral Covalent ITK/JAK3 Inhibitor

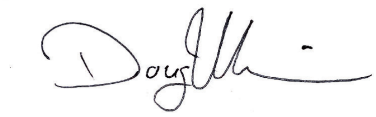
In 2022, we announced results from the Phase 1 single ascending dose study of our ITK/JAK3 inhibitor, ATI-2138, which demonstrated that the drug was not only generally well tolerated, but also resulted in dose-dependent inhibition of both the ITK and JAK3 pathways. We are currently conducting a Phase 1 multiple ascending dose study with ATI-2138. We intend to pursue ulcerative colitis as our first proof of concept indication.

ATI-2231, an Investigational Oral MK2 Inhibitor

Lastly, we plan to explore our second MK2 inhibitor, ATI-2231 in oncology, in collaboration with an academic third party. We look forward to apprising you of our progress with this program as it continues to advance.

As you can see, these are exciting times for Aclaris. We are well positioned, with an experienced and driven team, several novel therapeutic candidates being developed in an emerging immunology and inflammation disease category and a host of important data catalysts expected in the near future. Both myself and our team are humbled by your support and we look forward to engaging with you as we continue our journey.

Warmest regards,



Doug Manion, M.D.
President and Chief Executive Officer
Aclaris Therapeutics, Inc.

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

FORM 10-K

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

For the fiscal year ended December 31, 2022 **Commission file number 001-37581**

ACLARIS THERAPEUTICS, INC.

Incorporated under the Laws of the	I.R.S. Employer Identification No.
State of Delaware	**46-0571712**

640 Lee Road, Suite 200
Wayne, PA 19087
(484) 324-7933

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

Title of Each Class:	Trading Symbol(s)	Name of Each Exchange on which Registered
Common Stock, $0.00001 par value	ACRS	The Nasdaq Stock Market, LLC

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 15(d) of the Exchange Act. Yes ☐ No ☒

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

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

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

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

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

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

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

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

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

As of June 30, 2022, the last business day of the registrant’s last completed second quarter, the aggregate market value of the registrant’s common stock held by non-affiliates of the registrant was approximately $898.4 million based on the closing price of the registrant’s common stock, as reported by the Nasdaq Global Select Market, on such date.

As of January 31, 2023, 66,692,964 shares of common stock, $0.00001 par value, were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Company's definitive proxy statement, to be filed pursuant to Regulation 14A under the Securities Exchange Act of 1934, for its 2023 Annual Meeting of Stockholders are incorporated by reference in Part III of this Form 10-K.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or this Annual Report, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, that involve substantial risks and uncertainties. The forward-looking statements are contained principally in Part I, Item 1. "Business," Part I, Item 1A. "Risk Factors," and Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations," but are also contained elsewhere in this Annual Report. In some cases, you can identify forward-looking statements by the words "may," "might," "can," "will," "to be," "could," "would," "should," "expect," "intend," "plan," "objective," "anticipate," "believe," "estimate," "predict," "project," "potential," "likely," "continue" and "ongoing," or the negative of these terms, or other comparable terminology intended to identify statements about the future. These statements 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 the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report, we caution you that these statements are based on a combination of facts and factors currently known by us and our expectations of the future, about which we cannot be certain. Forward-looking statements include statements about:

- our plans to develop our drug candidates;
- the timing of our planned clinical trials of our drug candidates and the reporting of the results from these trials;
- the clinical utility of our drug candidates;
- our plans and expectations related to manufacturing capabilities and strategy;
- our expectations regarding coverage and reimbursement of our drug candidates, if approved;
- the timing of our regulatory filings and approvals for our drug candidates;
- our intellectual property position;
- our plans to pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates, and earn revenue from such arrangements;
- our expectations regarding competition;
- our expectations regarding our continued reliance on third parties;
- the impacts of macroeconomic conditions on our business;
- our expectations regarding our use of capital; and
- our estimates regarding future revenue, expenses and needs for additional financing.

You should refer to Part I, Item 1A. "Risk Factors" in this Annual Report for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Annual Report will prove to be accurate, and you should not place undue reliance on these forward-looking statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. 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 may cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law. 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.

All brand names or trademarks appearing in this Annual Report, including KINect and RHOFADE are the property of their respective owners. Unless the context requires otherwise, references in this report to "Aclaris," the "Company," "we," "us," and "our" refer to Aclaris Therapeutics, Inc. and its subsidiaries.

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PART I

Item 1. Business

Overview

We are a clinical-stage biopharmaceutical company focused on developing novel drug candidates for immuno-inflammatory diseases. In addition to developing our novel drug candidates, we are pursuing strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our novel drug candidates.

In 2017, we acquired Confluence Life Sciences, Inc. (now known as Aclaris Life Sciences, Inc.), or Confluence. The acquisition of Confluence added small molecule drug discovery and preclinical development capabilities, including KINect, a proprietary drug discovery platform. This allowed us to bring early-stage research and development activities in-house that we previously outsourced to third parties. We leverage these capabilities and KINect to identify potential drug candidates that we may develop independently or in collaboration with third parties. As part of the Confluence acquisition we also acquired our investigational drug candidates zunsemetinib, an inhibitor of the mitogen-activated protein kinase-activated protein kinase 2, or MK2, signaling pathway, ATI-1777, a topical "soft" Janus kinase, or JAK, 1/3 inhibitor, and ATI-2138, an inhibitor of interleukin-2-inducible T cell kinase, or ITK. We also earn revenue from Confluence's provision of contract research services to third parties.

Our Drug Candidates

Our pipeline of drug candidates that we are currently developing is summarized in the table below. These investigational drugs were developed internally utilizing our proprietary KINect drug discovery platform.

Drug Candidate / Program	Target	Route of Administration	Indication	Development Phase
Immuno-Inflammatory				
Zunsemetinib	MK2 inhibitor	Oral	Rheumatoid arthritis (moderate to severe)	Phase 2b
			Hidradenitis suppurativa (moderate to severe)	Phase 2a
			Psoriatic arthritis (moderate to severe)	Phase 2a
ATI-1777	"Soft" JAK 1/3 inhibitor	Topical	Atopic dermatitis (moderate to severe)	Phase 2b
ATI-2138	ITK/JAK3 inhibitor	Oral	T cell-mediated autoimmune diseases	Phase 1
Gut-Biased Program	JAK inhibitor	Oral	Inflammatory bowel disease	Discovery
Oncology				
ATI-2231	MK2 inhibitor	Oral	Metastatic breast cancer	Preclinical
			Pancreatic cancer	

Clinical Programs

Zunsemetinib, an Investigational Oral MK2 Inhibitor

We are developing zunsemetinib, an investigational oral MK2 inhibitor, as a potential treatment for rheumatoid arthritis, hidradenitis suppurativa and psoriatic arthritis. MK2 is a key regulator of pro-inflammatory mediators including TNFα, IL1β, IL6, IL8, IL17 and other essential pathogenic signals in chronic immuno-inflammatory diseases, as well as in oncology. As an oral drug candidate, we are developing zunsemetinib as a potential alternative to injectable anti-TNF/IL1/IL6/IL17 biologics and JAK inhibitors for treating certain immuno-inflammatory diseases. Zunsemetinib has been adopted as the nonproprietary name for ATI-450.

Moderate to Severe Rheumatoid Arthritis

In March 2020, we initiated a 12-week, Phase 2a, multicenter, randomized, investigator and patient-blind, sponsor-unblinded, parallel group, placebo-controlled clinical trial to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of zunsemetinib in subjects with moderate to severe rheumatoid arthritis (ATI-450-RA-201). In the trial, which consisted of a 12-week treatment period and a 4-week follow-up period, 19 subjects were randomized in a 3:1 ratio and received either zunsemetinib at 50 mg twice daily or placebo, in combination with methotrexate, for 12 weeks.

The final per-protocol analysis, which consisted of the 17 subjects who completed the treatment period (15 in the treatment arm and two in the placebo arm), showed that zunsemetinib demonstrated durable clinical activity, as defined by a marked and sustained reduction in DAS28-CRP and improvement of American College of Rheumatology 20%/50%/70% (ACR20/50/70) responses over 12 weeks. Zunsemetinib was generally well tolerated. All adverse events were mild to moderate. The most common adverse events (each reported in 2 subjects) were urinary tract infection, or UTI, and ventricular extrasystoles, all of which were determined to be unrelated to treatment except for one UTI. Two subjects withdrew from the trial during the treatment period, one in the treatment arm and one in the placebo arm. The subject in the treatment arm withdrew due to an elevated creatine phosphokinase, or CPK, level, which was determined by the site investigator to be treatment-related; this subject also had palpitations and ventricular extrasystoles, which were unrelated to the trial medication. The subject in the placebo arm withdrew as a result of prohibited medication needed to treat muscle strain. There was also one non-treatment-related serious adverse event (COVID-19) reported in the 4-week follow-up period of the trial in a subject who was no longer receiving treatment; the subject withdrew during the 4-week follow-up period of the trial.

A final analysis, which consisted of the 17 subjects, of ex vivo stimulated cytokines from blood samples taken from the treatment arm showed a marked and durable inhibition of TNFα, IL1β, IL6, and IL8 over the 12-week treatment period. Similarly, analysis of endogenous inflammation biomarkers also demonstrated a marked and sustained inhibition of median concentrations of hsCRP, TNFα, IL6, IL8 and MIP1β in the treatment arm over the 12-week period.

In December 2021, we initiated a Phase 2b randomized, multicenter, double-blind, parallel group, placebo-controlled, dose-ranging trial to investigate the efficacy, safety, tolerability, pharmacokinetics and pharmacodynamics of multiple doses (20 mg and 50 mg twice daily) of zunsemetinib in combination with methotrexate in subjects with moderate to severe rheumatoid arthritis (ATI-450-RA-202). This trial consists of a 12-week treatment period and a 30-day follow-up period, and seeks to enroll approximately 240 subjects in the United States and in multiple countries in Europe. The primary endpoint is the proportion of subjects achieving ACR20 at week 12. We expect topline data in the second half of 2023.

Moderate to Severe Hidradenitis Suppurativa

In December 2021, we initiated a Phase 2a, randomized, multicenter, double-blind, placebo-controlled trial to investigate the efficacy, safety, tolerability, pharmacokinetics and pharmacodynamics of zunsemetinib (50 mg twice daily) in subjects with moderate to severe hidradenitis suppurativa (ATI-450-HS-201). This trial consists of a 12-week treatment period and a 30-day follow-up period. The trial has completed enrollment with 95 subjects randomized in the United States. The primary endpoint is the change in inflammatory nodule and abscess count at week 12. We expect topline data in March of 2023.

Moderate to Severe Psoriatic Arthritis

In June 2022, we initiated a Phase 2a, randomized, multicenter, double-blind, placebo-controlled trial to investigate the efficacy, safety, tolerability, pharmacokinetics and pharmacodynamics of zunsemetinib (50 mg twice daily) in subjects with moderate to severe psoriatic arthritis (ATI-450-PsA-201). This trial consists of a 12-week treatment period and a 30-day follow-up period, and seeks to enroll approximately 70 subjects in the United States and in Poland. The primary endpoint is the proportion of subjects achieving ACR20 at week 12. We expect topline data by the end of 2023.

ATI-1777, an Investigational Topical "Soft" JAK 1/3 Inhibitor

We are developing ATI-1777, an investigational topical "soft" JAK 1/3 inhibitor, as a potential treatment for moderate to severe atopic dermatitis. "Soft" JAK inhibitors are designed to be topically applied and active in the skin, but rapidly metabolized and inactivated when they enter the bloodstream, which may result in low systemic exposure.

In October 2020, we initiated a Phase 2a, multicenter, randomized, double-blind, vehicle-controlled, parallel-group clinical trial to determine the efficacy, safety, tolerability and pharmacokinetics of ATI-1777 in subjects with moderate to severe atopic dermatitis (ATI-1777-AD-201). In the trial, which consisted of a 4-week treatment period and a 2-week follow-up period during which no treatment was given, 50 subjects with moderate to severe atopic dermatitis were randomized in a 1:1 ratio into one of two arms: ATI-1777 topical solution 2.0% w/w or vehicle applied twice daily. In June 2021, we announced that the trial achieved its primary endpoint, which was the percent change from baseline in the modified Eczema Area and Severity Index, or mEASI, score at week 4, with a high degree of statistical significance ($p<0.001$) (one-sided p-value), which corresponded to a 74.4% reduction in mEASI score from baseline at week 4 in subjects applying ATI-1777 compared to a 41.4% reduction in subjects applying vehicle. The final data was based on the full analysis set, or FAS, which was comprised of 48 subjects randomized and documented to have received at least one dose of trial medication. Positive trends in favor of ATI-1777 were observed in key secondary efficacy endpoints, such as improvement in itch, percent of mEASI-50 responders, investigator's global assessment responder analysis, and reduction in body surface area impacted by disease. In addition, the FAS analysis also showed positive trends in favor of ATI-1777 in percent of mEASI-75 responders (65.2% for ATI-1777 compared to 24.0% for vehicle) and mEASI-90 responders (30.4% for ATI-1777 compared to 20.0% for vehicle). These secondary efficacy endpoints were not powered for statistical significance. Based on an analysis of pharmacokinetic plasma samples in the ATI-1777 arm at multiple timepoints, minimal systemic exposure was observed, which supports a "soft" topical JAK inhibitor approach. ATI-1777 was generally well tolerated. No serious adverse events were reported. The most common adverse events (reported in at least 2 subjects in the trial) were increased blood CPK levels and headache in subjects in the ATI-1777 arm and UTI (one in each of the ATI-1777 and the vehicle arm); none of these adverse events in the ATI-1777 arm were determined by the clinical trial investigators to be related to ATI-1777. One treatment-related adverse event, application site pruritus, was reported in one subject in the ATI-1777 arm.

In May 2022, we initiated a Phase 2b, multicenter, randomized, double-blind, vehicle-controlled, parallel-group trial to determine the efficacy, safety, tolerability and pharmacokinetics of ATI-1777 in subjects with moderate to severe atopic dermatitis (ATI-1777-AD-202). In this trial, we are exploring multiple concentrations of twice daily treatment with ATI-1777 and a single concentration of once daily treatment with ATI-1777, in patients 12 years and older. This trial consists of a 4-week treatment period and a 2-week follow-up period, and seeks to enroll approximately 240 subjects in the United States. The primary endpoint is the percentage change from baseline in EASI score at week 4. We expect topline data mid-2023.

ATI-2138, an Investigational Oral Covalent ITK/JAK3 Inhibitor

We are developing ATI-2138, an investigational oral covalent ITK/JAK3 inhibitor, as a potential treatment for T cell-mediated autoimmune diseases. The ITK/JAK3 compound interrupts T cell signaling through the combined inhibition of ITK/JAK3 pathways in lymphocytes. We have selected ulcerative colitis as the intended first clinical development target for ATI-2138. We are also exploring additional indications that are relevant to the mechanism of action.

In October 2021, we submitted an Investigational New Drug application, or IND, for ATI-2138 for the treatment of psoriasis. The IND was allowed by the U.S. Food and Drug Administration, or FDA, in November 2021.

In December 2021, we initiated a Phase 1 randomized, observer-blind, placebo-controlled, single ascending dose (SAD) trial to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of ATI-2138 in healthy subjects (ATI-2138-PKPD-101). In this trial, 64 male and female healthy volunteer subjects were randomized in a 3:1 ratio into seven doses in eight cohorts. Each cohort consisted of eight randomized subjects, with six receiving ATI-2138 and two receiving placebo. Single dose levels were 1 mg, 3 mg, 5 mg, 15 mg, 25 mg, 50 mg and 80 mg. Data from this trial showed that ATI-2138 was generally well tolerated at all doses tested in the trial. No serious adverse events or severe adverse events were reported. The most common adverse events in subjects treated with ATI-2138, headache (four subjects) and lightheadedness (two subjects), were mild and transient. ATI-2138 demonstrated linear pharmacokinetic data and absorption with a favorable pharmacokinetic profile up to the 80 mg single dose. The terminal half-life ranged from 1.5 to 2.5 hours. In addition, no significant food effect at the 15 mg dose (fasted versus fed) was observed, and similar pharmacokinetic data was observed with the capsule versus tablet formulation at the 25 mg dose. We also observed dose-dependent inhibition of both ITK and JAK3 exploratory pharmacodynamic biomarkers, and near complete inhibition of the dual ITK and JAK3-stimulated interferon production at the 15 mg through 80 mg doses.

In October 2022, we submitted a new IND for ATI-2138 for the treatment of ulcerative colitis, which was allowed in November 2022. In December 2022, we initiated a Phase 1 placebo-controlled, randomized, multiple ascending dose (MAD) trial to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of ATI-2138 in healthy volunteers (ATI-2138-PKDP-102). This trial seeks to enroll approximately 60 healthy volunteers in the United States. We expect topline data in the second half of 2023.

Preclinical Programs

ATI-2231, an Investigational Oral MK2 Inhibitor

We are exploring the use of ATI-2231, an investigational oral MK2 inhibitor designed to have a long half-life, as a potential treatment for pancreatic cancer and metastatic breast cancer as well as in preventing bone loss in patients with metastatic breast cancer. We expect clinical development activities to be initiated in 2023, which we expect to advance as a collaboration with an academic third party.

Discovery Programs

We are developing oral gut-biased JAK inhibitors with limited systemic exposure as potential treatments for inflammatory bowel disease. In addition, we are engaged in research to identify brain penetrant kinase inhibitor candidates as potential treatments for neurodegenerative diseases.

Manufacturing and Supply

We do not have any manufacturing facilities. We rely on third parties for the manufacture of preclinical and clinical supplies for our drug candidates.

Competition

The pharmaceutical industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary drugs. While we believe that our knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, biotechnology and specialty pharmaceutical companies, academic institutions and governmental agencies and public and private research institutions. Our drug candidates, if approved, will compete with existing treatments and new treatments that may become available in the future.

With respect to zunsemetinib as a potential treatment for immuno-inflammatory diseases such as rheumatoid arthritis, hidradenitis suppurativa and psoriatic arthritis, there are several different types of therapies in the market. Medications for the treatment of rheumatoid arthritis and psoriatic arthritis currently fall into two categories: drugs that ease symptoms such as nonsteroidal anti-inflammatory drugs and drugs that slow disease activity. Drugs that slow disease activity include corticosteroids and disease-modifying anti-rheumatic drugs, or DMARDs. DMARDs include (i) conventional synthetic DMARDs, such as methotrexate, sulfasalazine, leflunomide and hydroxychloroquine, (ii) biologic DMARDs (monoclonal antibodies which inhibit targets such as TNFα, IL1β, IL6, IL17 and costimulatory signaling mechanisms), and (iii) targeted synthetic DMARDs such as JAK inhibitors. Hidradenitis suppurativa is currently treated

with antibiotics, corticosteroids and surgery, as well as anti-TNF therapy. Drugs for the treatment of immuno-inflammatory diseases such as rheumatoid arthritis, hidradenitis suppurativa and psoriatic arthritis, are produced and sold, or are approved for marketing, by large pharmaceutical companies, including AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Johnson & Johnson, Pfizer, Novartis, UCB, Regeneron Pharmaceuticals, and Roche. In addition, we are aware of a number of companies developing and conducting clinical trials for investigational drug candidates, including biosimilars, that, if approved, could compete with zunsemetinib, if approved, for the treatment of immuno-inflammatory diseases.

With respect to ATI-1777 as a potential treatment for moderate to severe atopic dermatitis, there are several different types of therapies in the atopic dermatitis market, such as biologics, oral and topical corticosteroids, injectable and oral methotrexate products, oral and topical calcineurin inhibitors, oral mycophenolate products, other JAK inhibitors, other oral antibiotics and antihistamines and phototherapy. There are also several prescription, non-prescription and over-the-counter, or OTC, topical products, including PDE4 inhibitors, utilized to treat atopic dermatitis. These types of drugs are produced and sold, or are approved for marketing, by large pharmaceutical companies, including AbbVie, Incyte, LEO Pharma A/S, Pfizer, and Sanofi and Regeneron Pharmaceuticals. In addition, we are aware of a number of companies including large pharmaceutical companies, such as Eli Lilly, Novartis, LEO Pharma A/S, Pfizer, and Dermavant Sciences developing and conducting clinical trials for investigational drug candidates, that, if approved, could compete with ATI-1777, if approved, for the treatment of atopic dermatitis.

The commercial opportunity for our drug candidates, if approved, could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any drug we may develop. Our competitors also may obtain FDA or other regulatory approval for their drug candidates more rapidly than our potential third-party partners may obtain approval for our drug candidates, which could result in our competitors establishing a strong market position before our drug candidates are able to enter the market.

Many of the companies against which we are competing, or against which we may compete in the future, have significantly greater financial resources and expertise in research and development, manufacturing, and preclinical and clinical development than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and subject registration for clinical trials, as well as in acquiring technologies complementary to, or that may be necessary for, our development programs.

Intellectual Property

Our success depends in large part upon our ability to obtain and maintain proprietary protection for our drug candidates and to operate without infringing the proprietary rights of others. We seek to avoid the latter by monitoring patents and publications that may affect our business, and to the extent we identify such developments, evaluating and taking appropriate courses of action. Our policy is to protect our proprietary position by, among other methods, filing patent applications on inventions that are important to the development and conduct of our business with the U.S. Patent and Trademark Office, or USPTO, and its foreign counterparts.

With respect to our MK2 signaling pathway inhibitor development program, we own numerous issued patents and pending applications to novel MK2 pathway inhibitors, including our lead candidate zunsemetinib, and various methods of use that expire, or would expire, between 2031 and 2041, subject to any applicable patent term adjustment or extension that may be available in a particular country. For example, we own two issued U.S. patents and issued patents and pending applications in the European Union and other foreign countries directed to zunsemetinib and analogs thereof and certain methods of using the same. The U.S. patents expire in 2034 and any claims that may issue from the pending applications expire in 2034, subject to any applicable adjustment or extension. Further, we own numerous pending patent applications in the U.S., European Union and other foreign countries directed to certain methods of using zunsemetinib, methods of manufacturing zunsemetinib and crystal forms of zunsemetinib, which, if issued, would each expire in 2041, subject to any applicable adjustment or extension. We also own pending patent applications in the U.S., European Union and other foreign countries directed to ATI-2231, and methods of use, which, if issued, would expire in 2040, subject to any applicable adjustment or extension.

With respect to our "soft" JAK inhibitor development program, we own one issued U.S. patent and numerous pending applications in the U.S. and foreign countries to novel "soft" JAK inhibitors and various methods of use that expire, or would expire, between 2038 and 2042, subject to any applicable patent term adjustment or extension that may be available in a particular country. For example, we own one U.S. patent and pending applications in the U.S., European Union and other foreign countries directed to various novel inhibitors of JAK1 and/or JAK3, including ATI-1777, and methods of using the same, which, if issued, would expire in 2038, subject to any applicable adjustment or extension. We also own PCT applications directed to crystal forms of ATI-1777 and directed to methods of using ATI-1777 and topical formulations, which, if issued, would expire in 2041 and 2042, respectively, subject to any applicable adjustment or extension.

With respect to our ITK inhibitor development program, we own numerous issued U.S. patents and pending applications in the U.S. and foreign countries directed to novel inhibitors of ITK and methods of use that expire, or would expire, between 2035 and 2039, subject to any applicable patent term adjustment or extension that may be available in a particular country. For example, we own one U.S. patent and pending U.S., European Union and other foreign country applications directed to ATI-2138 and analogs thereof and methods of using the same, which, if issued, would expire in 2039, subject to any applicable adjustment or extension.

Patents extend for varying periods according to the date of patent filing or grant and the legal term of patents in various countries where patent protection is obtained. The actual protection afforded by a patent, which can vary from country to country, depends on the type of patent, the scope of its coverage and the availability of legal remedies in the country. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, a patent term may be shortened if a patent is terminally disclaimed over another patent or as a result of delays in patent prosecution by the patentee, and a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in granting a patent or by patent term extension, which compensates a patentee for delays at the FDA. The patent term of a European patent is 20 years from its filing date; however, unlike in the United States, the European patent does not grant patent term adjustments. The European Union does have a compensation program similar to patent term extension called supplementary patent certificate that would effectively extend patent protection for up to five years.

We also use other forms of protection, such as trademark, copyright, and/or trade secret protection, to protect our intellectual property, particularly where we do not believe patent protection is appropriate or obtainable. We aim to take advantage of all of the intellectual property rights that are available to us and believe that this comprehensive approach will provide us with proprietary positions for our drug candidates, where available.

We also protect our proprietary information by requiring our employees, consultants, contractors and other advisors to execute nondisclosure and assignment of invention agreements upon commencement of their respective employment or engagement. Agreements with our employees also prevent them from bringing the proprietary rights of third parties to us. In addition, we also require confidentiality or service agreements from third parties that receive our confidential information or materials.

Acquisition and License Agreements

Agreement and Plan of Merger with Confluence

In August 2017, we entered into an Agreement and Plan of Merger, or the Confluence Agreement, with Confluence, Aclaris Life Sciences, Inc., our wholly-owned subsidiary, or Merger Sub, and Fortis Advisors LLC, as representative of the former equity holders of Confluence. Pursuant to the terms of the Confluence Agreement, the Merger Sub merged with and into Confluence, with Confluence surviving as our wholly-owned subsidiary, resulting in our acquisition of 100% of the outstanding shares of Confluence.

Under the Confluence Agreement, we agreed to pay the former Confluence equity holders aggregate remaining contingent consideration of up to $75.0 million based upon the achievement of specified regulatory and commercial milestones set forth in the Confluence Agreement. In addition, we have agreed to pay the former Confluence equity holders future royalty payments calculated as a low single-digit percentage of annual net sales, subject to specified reductions, limitations and other adjustments, until the date that all of the patent rights for that product have expired, as determined on a country-by-country and product-by-product basis or, in specified circumstances, ten years from the first commercial sale of such product. In addition to the payments described above, if we sell, license or transfer any of the intellectual

property acquired from Confluence pursuant to the Confluence Agreement to a third party, we will be obligated to pay the former Confluence equity holders a portion of any consideration received from such sale, license or transfer in specified circumstances.

Government Regulation and Product Approval

Governmental authorities in the United States, at the federal, state and local level, and analogous authorities in other countries extensively regulate, among other things, the research, development, testing, manufacture, safety surveillance, efficacy, quality control, labeling, packaging, distribution, record keeping, promotion, storage, advertising, distribution, marketing, sale, export and import, and the reporting of safety and other post-market information of products such as the ones we are developing. A drug candidate must be approved by the FDA before it may be legally promoted in the United States and by comparable foreign regulatory authorities before marketing in other jurisdictions. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by regulatory authorities to approve applications, withdrawal of an approval, imposition of a clinical hold, import/export delays, issuance of warning letters and untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by FDA and the Department of Justice or other governmental entities.

United States Government Regulation

NDA Approval Processes

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The FDA's Center for Drug Evaluation and Research has primary jurisdiction over the premarket development, review and approval of our drug candidates. Accordingly, we are investigating our drug candidates pursuant to IND applications and would expect to seek approval through the New Drug Application, or NDA, pathway.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice regulations;
- submission to the FDA of an IND which must take effect before clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before clinical testing may be initiated at the clinical site;
- performance of adequate and well-controlled clinical trials in accordance with good clinical practice, or GCP, regulations to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of an NDA;
- review of the NDA by an FDA advisory committee, if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product or its components are produced to assess compliance with current good manufacturing practices, or cGMP, and regulations to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- payment of user fees and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including potential requirements for a risk evaluation and mitigation strategy and post-approval studies required by the FDA.

Once a drug candidate is identified for development, it enters the preclinical or nonclinical testing stage. Preclinical studies include laboratory evaluations of product chemistry, pharmacology, toxicity and formulation. An IND sponsor must submit the results of the preclinical studies, together with manufacturing information and analytical data, to the FDA as part of the IND. Some preclinical studies may continue even after the IND is submitted. In addition to including the results of the preclinical studies, the IND will also include a protocol detailing, among other things, the objectives of

the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the first phase lends itself to an efficacy determination. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the IND on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. A clinical hold may occur at any time during the life of an IND, and may affect one or more specific clinical trials or all clinical trials conducted under the IND.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with current GCP regulations. They must be conducted under protocols detailing the objectives of the trial, dosing procedures, research subject selection and exclusion criteria, and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and progress reports detailing the status of the clinical trials must be submitted to the FDA annually, as well as safety reporting. An IRB for each site participating in the clinical trial must review and approve the protocol before the clinical trial commences at that institution and must also approve the information regarding the trial and the consent form that must be provided to each research subject or the subject's legal representative, monitor the study until completed and otherwise comply with IRB regulations.

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

- ***Phase 1.*** The drug is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and elimination. In the case of some products for severe or life-threatening diseases, such as cancer, and especially when the product may be inherently too toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients who already have the condition.
- ***Phase 2.*** Clinical trials are performed on a limited patient population intended to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- ***Phase 3.*** If a drug candidate is found to be potentially effective and to have an acceptable safety profile in Phase 2 clinical trials, the clinical trial program will be expanded to Phase 3 clinical trials to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical trial sites. These trials are intended to establish the overall risk-benefit ratio of the product and provide an adequate basis for product approval and labeling claims.

Phase 4 clinical trials are conducted after approval to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of drugs approved under accelerated approval regulations, or when otherwise requested by the FDA in the form of post-market requirements or commitments. Failure to promptly conduct any required Phase 4 clinical trials could result in withdrawal of approval.

Clinical trials are inherently uncertain, and Phase 1, Phase 2 and Phase 3 testing may not be successfully completed. The FDA or the sponsor may suspend a clinical trial at any time for a variety of reasons, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. In some cases, clinical trials are overseen by an independent group of qualified experts organized by the trial sponsor, which is called the clinical monitoring board or data safety monitoring board. This group provides authorization for whether or not a trial may move forward at designated check points. These decisions are based on the limited access to data from the ongoing trial.

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

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

The results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests and other control mechanisms, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of user fees, but a waiver of such fees may be obtained under specified circumstances. The FDA reviews all NDAs submitted for a period of 60 days to ensure that they are sufficiently complete for substantive review before it accepts them for filing. It may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing.

During the approval process, the FDA also will determine whether a risk evaluation and mitigation strategy, or REMS, is necessary to assure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS, and the FDA will not approve the application without an approved REMS, if required. A REMS can substantially increase the costs of obtaining approval. The FDA could also require a special warning, known as a boxed warning, to be included in the product label in order to highlight a particular safety risk.

Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant. The FDA may refer the NDA to an advisory committee for review and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. NDAs receive either standard or priority review. A drug representing a significant improvement in treatment, prevention or diagnosis of disease may receive priority review. A priority review 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 the NDA from ten months to six months from filing of the NDA. After the FDA evaluates the NDA and conducts inspections of manufacturing facilities where the drug product and/or its active pharmaceutical ingredient will be produced, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete, and the application is not ready for approval. A Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. Even if such data and information are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval.

Post-approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA and other governmental agencies, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion, and reporting of adverse experiences with the product. Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further FDA review and approval. There are also continuing annual user fee requirements for products, as well as new application fees for certain supplemental applications. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products that have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs.

Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and some state agencies for compliance with GMP regulations and other laws. The FDA has promulgated specific requirements for drug cGMPs. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Failure to comply with the applicable U.S. requirements at any time during the product development process or approval process, or after approval, may subject us to administrative or judicial sanctions, any of which could have a material adverse effect on us. These sanctions could include:

- refusal to approve pending applications;
- withdrawal of an approval;
- imposition of a clinical hold;
- warning letters;
- product seizures or detention, or refusal to permit the import or export of products;
- restrictions on the marketing or manufacturing of the product;
- total or partial suspension of production or distribution or product recalls; or
- injunctions, fines, disgorgement, or civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of drug products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. However, companies may share truthful and not misleading information that is otherwise consistent with the product's FDA approved labeling. 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. However, physicians may, in their independent medical judgment, prescribe legally available products for off-label uses. The FDA does not regulate the behavior of physicians in their choice of treatments but the FDA does restrict sponsor communications on the subject of off-label use.

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

Non-patent Exclusivity

The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity, or NCE. A drug is an NCE if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. If market exclusivity is granted for an NCE, during the exclusivity period, the FDA may not accept for review or approve an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder.

The FDCA also provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages, dosage forms or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and prohibits the FDA from approving an ANDA or a 505(b)(2) NDA submitted by another company with overlapping conditions associated with the new clinical investigations for the three-year period. Clinical investigation exclusivity does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of an NDA for the same drug. However, an applicant submitting an NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Regulation Outside of the United States

Even if we obtain FDA approval for a drug candidate, we must obtain approval by the comparable regulatory authorities of countries outside of the United States before we can commence clinical trials in such countries, and our potential third-party partners must obtain approval of the regulators of such countries or economic areas, such as the

European Union, before they may market any of our drug candidates in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing and promotion, pricing and reimbursement vary greatly by geographic region, and the time may be longer or shorter than that required for FDA approval.

In the European Economic Area, or EEA, which is composed of the Member States of the European Union plus Norway, Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA.

There are two types of MAs:

- The Community MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the European Union. Under the Centralized Procedure, the maximum timeframe for the evaluation of a marketing authorization application is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP). Accelerated evaluation might be granted by the CHMP in exceptional cases, when the authorization of a medicinal product is of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation. Under the accelerated procedure, the standard 210 days review period is reduced to 150 days.
- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member State through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure.

In the EEA, upon receiving marketing authorization, NCEs generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the EEA from referencing the innovator's data to assess a generic application. During the additional two-year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator's data may be referenced, but no generic product can be marketed until the expiration of the market exclusivity. However, there is no guarantee that a product will be considered by the EEA's regulatory authorities to be an NCE, and products may not qualify for data exclusivity.

Other Health Care Laws

Health care providers, physicians and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any of our drug candidates for which marketing approval is obtained. Our potential third-party partners' arrangements with third-party payors, health care professionals and customers may expose them to broadly applicable fraud and abuse and other health care laws and regulations, including, without limitation, the federal Anti-Kickback Statute and the federal civil False Claims Act, that may constrain the business or financial arrangements and relationships through which they sell, market and distribute any drug candidates for which marketing approval is obtained. In addition, we and our potential third-party partners may be subject to transparency laws and patient privacy regulation by the federal government and by the U.S. states and foreign jurisdictions in which we or they conduct business.

The federal Anti-Kickback Statute makes it illegal for any person or entity, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully, directly or indirectly, solicit, receive, offer, or pay any remuneration that is intended to induce the referral of business, including the purchase, order, or lease of any good, facility, item or service for which payment may be made under a federal health care program, such as Medicare or Medicaid. The term "remuneration" has been broadly interpreted to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, formulary managers, and beneficiaries on the other. Although there are a number of statutory exceptions and

regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal health care covered business, the Anti-Kickback Statute has been violated. Violations of this law are punishable by up to ten years in prison, and can also result in criminal fines, civil monetary penalties, administrative penalties and exclusion from participation in federal health care programs.

Additionally, the intent standard under the Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the Affordable Care Act, to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the Affordable Care Act codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act.

Federal false claims and false statement laws, including the federal civil False Claims Act, prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, for payment to, or approval by, federal programs, including Medicare and Medicaid, claims for items or services, including drugs, that are false or fraudulent or not provided as claimed. Entities can be held liable under these laws if they are deemed to "cause" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers, promoting a product off-label, or for providing medically unnecessary services or items. In addition, activities relating to the sale and marketing of products are subject to scrutiny under this law. Penalties for federal civil False Claims Act violations may include up to three times the actual damages sustained by the government, plus mandatory civil penalties for each separate false claim, the potential for exclusion from participation in federal health care programs, and, although the federal civil False Claims Act is a civil statute, False Claims Act violations may also implicate various federal criminal statutes.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, prohibits among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any health care benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a health care benefit program, willfully obstructing a criminal investigation of a health care offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services. Like the Anti-Kickback Statute, the Affordable Care Act amended the intent standard for the health care fraud statute under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

The civil monetary penalties statute imposes penalties against any person or entity that, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

Also, many states have similar fraud and abuse statutes or regulations that may be broader in scope and may apply regardless of payor, in addition to items and services reimbursed under Medicaid and other state programs. Additionally, to the extent that a product is sold in a foreign country, the seller may be subject to similar foreign laws.

In addition, legislation imposing marketing restrictions and transparency requirements on pharmaceutical manufacturers has been enacted at the state and federal levels. For example, the Affordable Care Act imposed, among other things, annual reporting requirements to the Centers for Medicare & Medicaid Services, or CMS, for covered manufacturers for certain payments and other transfers of value provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other health care professionals (such as physician assistants and nurse practitioners) and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members. Failure to submit timely, accurately and completely the required information for all payments, transfers of value and ownership or investment interests may result in civil monetary penalties for "knowing failures." Certain states also mandate implementation of compliance programs, impose restrictions on drug manufacturer marketing practices, require registration of certain employees engaged in marketing activities in the

location, and/or require the tracking and reporting of gifts, compensation and other remuneration to health care professionals, including physicians.

We have developed a comprehensive compliance program that establishes internal controls to facilitate adherence to the rules and program requirements to which we are subject. Although the development and implementation of compliance programs designed to establish internal controls and facilitate compliance can mitigate the risk of investigation, prosecution, and penalties assessed for violations of these laws, or any other laws that may apply to us, the risks cannot be entirely eliminated. If our operations are found to be in violation of any such laws or any other governmental regulations, we may be subject to significant penalties, including, without limitation, administrative, civil, and criminal penalties, damages, fines, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits and future earnings, the curtailment or restructuring of our operations, exclusion from participation in federal and state health care programs, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws and individual imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, including the final omnibus rule published on January 25, 2013, mandates, among other things, the adoption of uniform standards for the electronic exchange of information in common health care transactions, as well as standards relating to the privacy and security of individually identifiable health information, which require the adoption of administrative, physical and technical safeguards to protect such information. Among other things, HITECH makes HIPAA's security standards directly applicable to "business associates", namely independent contractors or agents of HIPAA covered entities that create, receive or obtain protected health information in connection with providing a service for or on behalf of a covered entity and their subcontractors that use, disclose, access, or otherwise process protected health information. HITECH also increased the civil and criminal penalties that may be imposed against covered entities and 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. In addition, certain state laws govern the privacy and security of health information in certain circumstances, some of which are more stringent than HIPAA and many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties.

Health Care Reform

In the United States, there have been and continue to be a number of significant legislative initiatives to contain health care costs. For example, in March 2010, the Affordable Care Act was passed, which has had, and is expected to continue to have, a significant impact on the health care industry. The Affordable Care Act was designed to expand coverage for the uninsured and at the same time contain overall health care costs. With regard to pharmaceutical products, among other things, the Affordable Care Act expanded and increased industry rebates for drugs covered under Medicaid programs; addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; extended the rebate program to individuals enrolled in Medicaid managed care organizations; established annual fees and taxes on manufacturers of certain branded prescription drugs; made changes to the coverage requirements under the Medicare prescription drug benefit; and established a new Medicare Part D coverage gap discount program, in which manufacturers, as a condition for their outpatient drugs to be covered under Medicare Part D, must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period. Moreover, the Affordable Care Act provided incentives to programs that increase the federal government's comparative effectiveness research and implemented payment system reforms including a national pilot program on payment bundling meant to encourage hospitals, physicians and other providers to improve the coordination, quality and efficiency of certain health care services.

There have been executive branch, judicial and Congressional challenges to certain aspects of the Affordable Care Act. While Congress has not passed comprehensive repeal legislation, several bills affecting the implementation of certain taxes under the Affordable Care Act have been signed into law. On June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace. 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 Affordable Care Act. Further, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or IRA, into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in Affordable Care Act marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and through a newly established manufacturer discount program. It is possible that the Affordable Care Act will be subject to judicial or Congressional challenges in the future. It is unclear how such challenges and any additional health care reform measures of the Biden administration will impact the Affordable Care Act and our business.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. For example, in August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee on Deficit Reduction did not achieve a targeted deficit reduction of at least $1.2 trillion for fiscal years 2012 through 2021, triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions in Medicare payments to providers of 2% per fiscal year, which went into effect beginning on April 1, 2013 and, due to subsequent legislative amendments to the statute, including the Bipartisan Budget Act of 2018, or the BBA, and the Infrastructure Investment and Jobs Act, will stay in effect through 2031 unless additional Congressional action is taken. Under current legislation the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. Additionally, in January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, cancer treatment centers and imaging centers. Moreover, the Drug Supply Chain Security Act imposes new obligations on manufacturers of pharmaceutical products related to product tracking and tracing. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products.

There has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. In July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, the Department of Health and Human Services, or HHS, released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles In addition, the IRA, among other things, (1) directs HHS to negotiate the price of certain single-source drugs and biologics covered under Medicare and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is unclear how the IRA will be implemented in the future, but it is likely to have a significant impact on the pharmaceutical industry. Further, the Biden administration released an additional executive order on October 14, 2022, directing HHS to submit a report on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. It is unclear whether this executive order or similar policy initiatives will be implemented in the future. The effect of reducing prices and reimbursement for certain of our drug candidates, if approved, could significantly impact our business and consolidated results of operations. In addition, the IRA may meaningfully influence our and pharmaceutical industry business strategies. In particular, it may reduce the attractiveness of investment in small molecule and biologic innovation. At the state level, legislatures have become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

The Affordable Care Act, as well as other federal and state health care reform measures that have been and may be adopted in the future, could harm our future revenue. Additional legislative actions may be taken in the future which may change current regulations, guidance and interpretations. The impact of such actions on our business, if any, cannot presently be determined.

The Hatch Waxman Amendments to the FDCA

Orange Book Listing

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent whose claims cover the applicant's product or a method of using the product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an ANDA or an application covered by Section 505(b)(2) of the FDCA. An ANDA provides for marketing of a drug product that has the same active ingredients, generally in the same strengths and dosage form, as the listed drug and has been shown through pharmacokinetic, or PK, testing to be bioequivalent to the listed drug. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are generally not required to conduct, or submit results of, preclinical studies or clinical tests to prove the safety or effectiveness of their drug product. Section 505(b)(2) applications provide for marketing of a drug product that may have the same active ingredients as the listed drug and contains full safety and effectiveness data as an NDA, but at least some of this information comes from studies not conducted by or for the applicant. This alternate regulatory pathway enables the applicant to rely, in part, on the FDA's findings of safety and efficacy for an existing product, or published literature, in support of its application. The FDA may then approve the new drug candidate for all or some of the labeled indications for which the referenced product has been approved, as well as for any new indication sought by the 505(b)(2) applicant.

The ANDA or Section 505(b)(2) applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA or Section 505(b)(2) applicant may also elect to submit a statement certifying that its proposed ANDA label does not contain, or carves out, any language regarding a patented method of use rather than certify to such listed method of use patent. If the applicant does not challenge the listed patents by filing a certification that the listed patent is invalid or will not be infringed by the new product, the ANDA or Section 505(b)(2) application will not be approved until all the listed patents claiming the referenced product have expired.

A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA or Section 505(b)(2) applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA or Section 505(b)(2) application has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA or Section 505(b)(2) application until the earliest of 30 months, expiration of the patent, settlement of the lawsuit, and a decision in the infringement case that is favorable to the ANDA or Section 505(b)(2) applicant. This prohibition is generally referred to as the 30-month stay. Thus, approval of an ANDA or 505(b)(2) NDA could be delayed for a significant period of time depending on the patent certification the applicant makes and the reference drug sponsor's decision to initiate patent litigation.

The ANDA or Section 505(b)(2) application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired.

Patent Term Extension

In the United States, after NDA approval, owners of relevant drug patents may apply for up to a five year patent extension, which provides patent term restoration as compensation for the patent term lost during the FDA regulatory review process for the first permitted commercial marketing of a drug product. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration of the patent. The allowable patent term extension is calculated as half of the drug's testing phase, which is the time between the IND submission becoming effective and the NDA submission, and all of the review phase, which is the time between NDA submission and approval, up to a maximum extension of five years. The time can be shortened if the FDA determines that the applicant did not pursue approval with due diligence. Patent extension cannot extend the

remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended.

Similar provisions are available in the European Union and other foreign jurisdictions to extend the term of a patent that covers an approved drug. For example, in Japan, it may be possible to extend the patent term for up to five years and in the European Union, it may be possible to obtain a supplementary patent certificate that would effectively extend patent protection for up to five years.

Coverage and Reimbursement

We believe the success of our drug candidates, if approved, will depend on obtaining and maintaining coverage and adequate reimbursement as a prescription treatment or in the absence of coverage and adequate reimbursement, on the extent to which patients will be willing to pay out of pocket for our prescription drug products.

Third-party payors determine which prescription drug products they will cover and establish reimbursement levels. Reimbursement by a third-party payor may depend upon a number of factors, including: the third-party payor's determination that a product is safe, effective, and medically necessary; appropriate for the specific patient; cost-effective; supported by peer-reviewed medical journals or current clinical practice guidelines; and whether there are competitive products, either branded or generic, and the pricing of those products. Many private third-party payors, such as managed care plans, manage access to drug products' coverage partly to control costs for their plans, and may use drug formularies and medical policies to limit their exposure. Obtaining and maintaining favorable reimbursement can be a time-consuming and expensive process, and our potential third-party partners may not be able to negotiate or continue to negotiate reimbursement or pricing terms for our drug candidates, if approved, with third-party payors at levels that are profitable to us, or at all. Further 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 which receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In addition to uncertainties surrounding coverage policies, there are periodic changes to reimbursement. Third-party payors regularly update reimbursement amounts and also from time to time revise the methodologies used to determine reimbursement amounts. Accordingly, these updates could impact the demand for our drug candidates, if approved. Our drug candidates, if approved, may not be considered cost effective, and government and third-party private health insurance coverage and reimbursement may not be available to patients or sufficient to allow our potential third-party partners to sell our drug candidates, if approved, on a competitive and profitable basis. Our results of operations could be adversely affected by the Affordable Care Act and by other health care reforms that may be enacted or adopted in the future. In addition, increasing emphasis on managed care in the United States will continue to put pressure on the pricing of pharmaceutical products. Cost control initiatives could decrease the price that our potential third-party partners could receive for any of our drug candidates, if approved, and could adversely affect our profitability. We cannot predict how pending and future health care legislation will impact our business, and any changes in coverage and reimbursement that further restricts coverage of our drug candidates could harm our business.

Foreign governments also have their own health care reimbursement systems, which vary significantly by country and region, and we cannot be sure that coverage and adequate reimbursement will be made available with respect to our drug candidates, if approved, under any foreign reimbursement system. In some foreign countries, including major markets in the European Union and Japan, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take up to 12 months or longer after the receipt of regulatory marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a pharmacoeconomic study that compares the cost-effectiveness of our drug candidate to other available therapies. Such pharmacoeconomic studies can be costly and the results uncertain. Our business could be harmed if reimbursement of our drug candidates, if approved, is unavailable or limited in scope or amount or if pricing is set at unsatisfactory levels.

Employees and Human Capital Resources

As of December 31, 2022, we had 105 total employees, of which 100 were full-time employees. All of our employees are located in the United States. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and new employees, advisors and consultants. The principal purposes of our equity incentive plans

are to attract, retain and reward personnel through the granting of stock-based compensation awards in order to increase stockholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives.

Corporate Information

We were incorporated under the laws of the State of Delaware in July 2012. Our principal executive offices are located at 640 Lee Road, Suite 200, Wayne, PA 19087. Our telephone number is (484) 324-7933. Our common stock is listed on the Nasdaq Global Select Market under the symbol "ACRS."

Available Information

Our internet website address is www.aclaristx.com. In addition to the information contained in this Annual Report, information about us can be found on our website. Our website and information included in or linked to our website are not part of this Annual Report.

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act are available free of charge through our website as soon as reasonably practicable after they are electronically filed with or furnished to the Securities and Exchange Commission, or SEC. The SEC also maintains a website that contains our reports, proxy and information statements and other information. The address of the SEC's website is www.sec.gov.

Item 1A. Risk Factors

Our business is subject to numerous risks. You should carefully consider the following risks and all other information contained in this Annual Report, as well as general economic and business risks, together with any other documents we file with the SEC. If any of the following events actually occur or risks actually materialize, it could have a material adverse effect on our business, operating results and financial condition and cause the trading price of our common stock to decline.

Summary of Risk Factors

- We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability.
- We will need substantial additional funding to meet our financial obligations and to pursue our business objectives. If we are unable to raise capital when needed, we could be forced to curtail our planned operations.
- Our business is dependent on the successful development of our investigational drug candidate, zunsemetinib.
- We have a limited history as a clinical-stage biopharmaceutical company developing and partnering our drug candidates, which may make it difficult to evaluate the success of our business to date and to assess our future viability.
- If we are unable to successfully develop our drug candidates and to pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates, or experience significant delays in doing so, our business will be harmed.
- Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.
- We intend to pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates. If those arrangements are not successful, we may not be able to capitalize on the market potential of these drug candidates.
- If we are unable to obtain and maintain patent protection for our drug candidates, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and drugs similar or identical to ours, and our ability to successfully pursue strategic alternatives, including identifying and consummating transactions with potential third-party partners, to commercialize our technology and drug candidates may be impaired.
- We face substantial competition, which may result in others discovering, developing or commercializing drugs before or more successfully than we do.

Risks Related to Our Business, Our Financial Position and Capital Needs

We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability.

Since inception, we have incurred significant net losses. We incurred net losses of $86.9 million and $90.9 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $682.3 million. We have financed our operations over the last several years primarily from sales of equity securities and incurring indebtedness in the form of loans from commercial lenders.

We have devoted substantially all of our financial resources and efforts to the development of our drug candidates, including preclinical studies and clinical trials. Our net losses may fluctuate significantly from quarter to quarter and year to year. We expect to continue to incur significant expenses and operating losses in the near term as we:

- pursue strategic alternatives, including identifying and seeking to consummate transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates;
- continue the clinical development of zunsemetinib as a potential treatment for moderate to severe rheumatoid arthritis, moderate to severe hidradenitis suppurativa and moderate to severe psoriatic arthritis, ATI-1777 as

a potential treatment for moderate to severe atopic dermatitis, and ATI-2138 as a potential treatment for T cell-mediated autoimmune diseases;
- continue to develop our preclinical drug candidates, including ATI-2231;
- continue to discover and develop additional drug candidates;
- maintain, expand and protect our intellectual property portfolio; and
- incur legal, accounting, investor relations and other administrative expenses in operating as a public company.

To become and remain profitable, we must succeed in a range of challenging activities, including completing preclinical testing and clinical trials of our drug candidates and pursuing strategic alternatives, including identifying and consummating transactions with third-party partners, for the further development and/or commercialization of our drug candidates, as well as discovering and developing additional drug candidates. We are in the early stages of most of these activities. We may never succeed in these activities and, even if we do, may never earn revenue from our drug candidates that is significant enough to achieve profitability.

For any of our drug candidates, our revenue will be dependent, in part, upon our ability to identify and consummate transactions with third-party partners to further develop, obtain marketing approval for and/or commercialize those drug candidates. Further, we will be dependent on our potential third-party partners' ability to obtain marketing approval and successfully commercialize the product, upon the size of the markets in the territories where marketing approval is obtained, the accepted price for the product, and the ability to obtain coverage and reimbursement, if any. If we fail to identify and enter into partnerships with third parties to further develop, obtain marketing approval for and/or commercialize our drug candidates, any partnerships we enter into do not result in the successful development, marketing approval for and commercialization of our drug candidates, the number of addressable patients is not as significant as estimated by our potential third-party partners, the indication approved by regulatory authorities is narrower than expected, or the treatment population is narrowed by competition, physician choice or treatment guidelines, we may not earn significant revenue from agreements with potential third-party partners for such drug candidates, even if the drug candidates are approved for marketing.

Because of the numerous risks and uncertainties associated with drug development, we are unable to accurately predict the timing or amount of expenses or when, or if, we will be able to achieve profitability. If we are required by regulatory authorities to perform studies in addition to those expected, or if there are any delays in the initiation and completion of our clinical trials, the development of any of our drug candidates or the identification and consummation of transactions with third-party partners to further develop, obtain marketing approval for and/or commercialize our drug candidates, our expenses could increase.

Even if we 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 depress the value of our company and could impair our ability to raise capital, expand our business, maintain our development efforts, diversify our offerings or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We will need substantial additional funding to meet our financial obligations and to pursue our business objectives. If we are unable to raise capital when needed, we could be forced to curtail our planned operations.

Identifying potential drug 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 identify and consummate transactions with third-party partners to further develop, obtain marketing approval for and/or commercialize our drug candidates. We expect to incur significant expenses and operating losses for the foreseeable future as we advance our drug candidates from discovery through preclinical and clinical development. In addition, we may not be able to identify and consummate transactions with third-party partners to further develop, obtain marketing approval for and/or commercialize our drug candidates, and our drug candidates, if approved, may not achieve commercial success. Furthermore, we incur and expect to continue to incur significant costs associated with operating as a public company, including legal, accounting, investor relations and other expenses. We also expect to add additional personnel to support our operational plans and strategic direction.

As of December 31, 2022, we had cash, cash equivalents and marketable securities of $229.8 million. We believe that our existing cash, cash equivalents and marketable securities as of the date of this Annual Report will enable us to fund our operating expenses and capital expenditure requirements for a period greater than 12 months from the date of this

report based on our current operating assumptions. These assumptions may prove to be wrong, and we could use our available capital resources sooner than we expect. Changes may occur beyond our control that would cause us to consume our available capital before that time, including changes in and progress of our development activities, acquisitions of additional products or drug candidates, and changes in regulation. Our future capital requirements will depend on many factors, including:

- the number and development requirements of the drug candidates that we may pursue;
- the scope, progress, results and costs of preclinical development, laboratory testing and conducting preclinical and clinical trials for our drug candidates;
- the costs, timing and outcome of regulatory review of our drug candidates;
- the extent to which we in-license or acquire additional drug candidates and technologies;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the impact on the timing of our preclinical studies, on the recruitment, enrollment, conduct and timing of our clinical trials, and on our business, due to the COVID-19 pandemic;
- our ability to identify and consummate transactions with third-party partners to further develop, obtain marketing approval for and/or commercialize our drug candidates; and
- our ability to earn revenue from licenses to, or partnerships or other arrangements with, third parties.

We will require additional capital to complete the clinical development of zunsemetinib, ATI-1777 and ATI-2138, to develop our preclinical compounds and to support our discovery efforts. Additional funds may not be available on a timely basis, on commercially acceptable terms, or at all, and such funds, if raised, may not be sufficient to enable us to continue to implement our long-term business strategy. Our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions caused by a variety of factors including geopolitical tensions, rising interest rates and inflationary pressures. If we are unable to raise sufficient additional capital or generate revenue from transactions with potential third-party partners for the development and/or commercialization of our drug candidates, we could be forced to curtail our planned operations.

Our business is dependent on the successful development of our drug candidate, zunsemetinib.

Our pipeline includes zunsemetinib, our investigational oral, novel, selective MK2 inhibitor compound, which we are developing as a potential treatment for moderate to severe rheumatoid arthritis, moderate to severe hidradenitis suppurativa and moderate to severe psoriatic arthritis. The success of our business will significantly depend on our successful development of and/or our ability to pursue strategic alternatives for, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize, zunsemetinib.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies, intellectual property, potential future revenue streams or drug candidates.

Until such time, if ever, as we can earn substantial revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings and license and partnership agreements. To the extent that we raise additional capital through the sale of equity securities or convertible debt securities, our stockholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of holders of our common stock. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise additional funds through partnerships, strategic alliances or marketing, distribution or licensing arrangements with potential third-party partners, we may be required to relinquish valuable rights to our technologies, intellectual property, potential future revenue streams, or drug candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements with third parties when needed, we may be required to delay, limit, reduce or terminate our drug development efforts or grant rights to third parties to develop technologies, intellectual property, or drug candidates that we would otherwise prefer to develop ourselves.

We have a limited history as a clinical-stage biopharmaceutical company developing and partnering our drug candidates, which may make it difficult to evaluate the success of our business to date and to assess our future viability.

Our operations over the last several years have been largely focused on undertaking preclinical studies and conducting clinical trials, drug discovery, acquiring new drug candidates and related intellectual property, and raising capital. We have had limited time to demonstrate our ability to successfully develop, manufacture and identify and consummate transactions with third-party partners to further develop, obtain marketing approval for and/or commercialize our drug candidates. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer history of being a clinical-stage biopharmaceutical company focused on developing and partnering drugs. We may also encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives.

Our business could be adversely affected by the evolving and ongoing impact of the COVID-19 global pandemic in regions where we or third parties on which we rely have manufacturing facilities, clinical trial sites or other business operations.

The impact of the global COVID-19 pandemic continues to evolve. Clinical site initiation, patient enrollment and recruitment and the supply of materials for our drug candidates may be adversely affected due to the COVD-19 pandemic, including as a result of staffing shortages and COVID-19 infections. Some subjects may not be able to comply with clinical trial protocols if quarantines impede patient movement.

The extent to which the COVID-19 pandemic or a similar health pandemic or epidemic impacts our business, our preclinical and clinical development and our regulatory efforts will depend on future developments that are highly uncertain and cannot be predicted. Accordingly, we do not yet know the full extent of the impacts on our business, our preclinical and clinical development and regulatory activities, healthcare systems or the global economy as a whole. However, these impacts could adversely affect our business, financial condition, results of operations and growth prospects.

In addition, to the extent the ongoing COVID-19 pandemic adversely affects our business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties described herein.

Risks Related to the Development and Potential Commercialization of Our Drug Candidates

If we are unable to successfully develop our drug candidates and to pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates, or experience significant delays in doing so, our business will be harmed.

We have invested significant efforts and financial resources in the development of our drug candidates and the identification of potential drug candidates. Our ability to earn substantial revenue from our drug candidates will depend heavily on our ability to successfully develop and pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize these drug candidates. The success of any drug candidates that we develop, including zunsemetinib, will depend on several factors, including:

- successful completion of preclinical studies and our clinical trials;
- successful development of manufacturing processes;
- receipt of timely approvals from applicable regulatory authorities;
- the identification and consummation of transactions with third-party partners to further develop, obtain marketing approval for and/or commercialize our drug candidates;
- the commercial launch of our drug candidates, if approved, by a potential third-party partner;
- our potential third-party partners' ability to achieve acceptance of our drug candidates, if approved, by patients, the medical community and third-party payors, and willingness of patients to pay out of pocket for our drug candidates when third-party payor coverage and reimbursement is limited or unavailable;
- our potential third-party partners' ability to achieve success in educating physicians and patients about the benefits, administration and use of our drug candidates, if approved;
- the prevalence and severity of adverse events experienced with our drug candidates;

- the availability, perceived advantages, cost, safety and efficacy of alternative treatments for the proposed indications of our drug candidates;
- obtaining and maintaining patent, trademark and trade secret protection and regulatory exclusivity for our drug candidates and otherwise protecting the intellectual property portfolio;
- maintaining compliance with regulatory requirements, including current good manufacturing practices, or cGMPs;
- our potential third-party partners' ability to compete effectively with other treatment procedures; and
- our potential third-party partners' ability to maintain a continued acceptable safety, tolerability and efficacy profile of our drug candidates following marketing approval.

Whether marketing approval will be granted is unpredictable and depends upon numerous factors, including the substantial discretion of the regulatory authorities. Our drug candidates' success in clinical trials will not guarantee marketing approval. Following submission, the NDA for any drug candidate may not be accepted for substantive review, or even if it is accepted for substantive review the FDA or other comparable foreign regulatory authorities may require additional studies or clinical trials, additional data, or additional manufacturing steps, or require other conditions before they will reconsider or approve the application, which could increase costs and cause delays in the marketing approval process and which may require the expenditure of additional resources. These delays would also impact our ability to identify and consummate transactions with third-party partners to further develop, obtain marketing approval for and/or commercialize our drug candidates. In addition, the FDA or other comparable foreign regulatory authorities may not consider sufficient any additional required studies, clinical trials, data or information that we perform and complete or generate, or we may decide to abandon the program.

It is possible that our drug candidates currently in development will never obtain marketing approval. 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 pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates, which would harm our business.

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 of and pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates.

The risk of failure for our drug candidates is high. It is impossible to predict when or if any of our drug candidates will prove effective or safe in humans or will receive marketing approval. Before obtaining regulatory approval for the sale of any drug candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our drug candidates in humans for use in the target indication. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome.

A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their drug candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their drugs.

We may experience numerous unforeseen events during or as a result of clinical trials that could delay or prevent our ability to pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates, including:

- regulators or IRBs 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 clinical trial contracts or clinical trial protocols with prospective trial sites or 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;

- clinical trials of our drug candidates may produce negative or inconclusive results, including failure to demonstrate statistical significance, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon drug development programs;
- the number of patients required for clinical trials of our drug 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;
- the COVID-19 pandemic may impact the recruitment, enrollment, conduct and timing of our clinical trials;
- our drug candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs to suspend or terminate the trials;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators or IRBs may require that we or our investigators suspend or terminate clinical development 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 drug candidates may be greater than we anticipate; and
- the supply or quality of our drug candidates or other materials necessary to conduct clinical trials of our drug candidates may be insufficient or inadequate.

We could also 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 a data safety monitoring board for such trial or by the FDA or other regulatory authorities. 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 or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities 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.

If we experience delays in the completion of, or termination of, any clinical trial of our drug candidates, our costs will increase, our drug candidate development process will be slowed, the commercial prospects of our drug candidates will be harmed, and our ability to pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates will be delayed. Any of these occurrences may harm our business, financial condition and prospects significantly. In addition, 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 marketing approval of our drug candidates. If we are required to conduct additional clinical trials or other testing of our drug candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our drug candidates or other testing, if the results of these trials or tests are not favorable or if there are safety concerns, we may not be able to pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates, and our potential third-party partners may:

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

Our drug development costs will also increase if we experience delays in testing. We do not know whether any of our preclinical studies or 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 our potential third-party partners may have the exclusive right to commercialize our drug candidates or allow competitors to bring drugs to market before such third-party partners do, which would impact our ability to successfully identify and consummate transactions with third-party partners to further develop, obtain marketing approval for and/or commercialize our drug candidates.

If we experience delays or difficulties in the enrollment of subjects in clinical trials, our ability to pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates could be delayed or prevented.

Successful and timely completion of clinical trials will require that we enroll a sufficient number of subjects. Subject enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population. Trials may be subject to delays as a result of subject enrollment taking longer than anticipated or subject withdrawal, including as a result of factors beyond our control, such as the COVID-19 pandemic. We may not be able to initiate or continue clinical trials for our drug 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 similar regulatory authorities outside the United States. We cannot predict how successful we will be at enrolling subjects in future clinical trials. Subject enrollment is affected by other factors including:

- the eligibility criteria for the trial in question;
- the perceived risks and benefits of the drug candidate in the trial;
- the availability of drugs approved to treat the disease in the trial;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of subjects for clinical trials would result in significant delays and could require us or them to abandon one or more clinical trials altogether. Enrollment delays in these clinical trials may result in increased development costs for our drug candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. Furthermore, we rely on and expect to continue to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials and we will have limited influence over their performance. Any delays in completing clinical trials would delay or prevent our ability to pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates.

Our clinical trials may fail to demonstrate the safety and efficacy of our drug candidates, or serious adverse or unacceptable side effects may be identified during the development of our drug candidates, which could increase our costs or necessitate the abandonment or limitation of the development of our drug candidates or prevent or delay our ability to pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates.

If our drug candidates are associated with side effects in clinical trials or have characteristics that are unexpected, our costs could increase or we may need to abandon their development or limit development to more narrow uses in which the side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. The FDA or an IRB may also require that we suspend, discontinue, or limit our clinical trials based on safety information. Such findings could further result in regulatory authorities failing to provide marketing authorization for our drug candidates. Many drug candidates that initially showed promise in early stage testing have later been found to cause side effects that prevented further development of the drug candidate.

Before any potential third-party partners can obtain marketing approvals for the commercial sale of our drug candidates, we must demonstrate through lengthy, complex and expensive preclinical testing and clinical trials that our drug candidates are both safe and effective for use in each target indication, and failures can occur at any stage of testing. Clinical trials often fail to demonstrate safety and efficacy of the drug candidate studied for the target indication.

Additionally, if we or others identify undesirable side effects caused by our drugs, a number of potentially significant negative consequences could result, including:

- we may need to abandon the development or limit the further development of our drug candidates, including in various populations and for certain indications;
- regulatory authorities may withdraw approval to market such product;
- regulatory authorities may require additional warnings on the labels;

- a medication guide outlining the risks of such side effects for distribution to patients may be required;
- we could be sued and held liable for harm caused to patients;
- our reputation and physician or patient acceptance of our drug candidates, if approved, may suffer; and
- our ability to pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates would be harmed.

Any of these events could prevent us from pursuing strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize the particular drug candidate and could significantly harm our business, results of operations and prospects.

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

From time to time, we may publicly disclose interim, topline or preliminary data from our clinical trials, which are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a full analysis of all data related to the particular trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. In addition, we may report preliminary analyses of only certain endpoints rather than all endpoints. As a result, the interim, topline or preliminary results that we report may differ from future results of the same trials, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim, topline and preliminary data should be viewed with caution until the final data are available. We may also disclose interim data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as subject enrollment continues and more subject data become available. Adverse differences between interim, topline or preliminary data and final data could significantly harm our reputation and business prospects. Further, disclosure of interim, topline or preliminary data by us or by our competitors could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the potential of the particular program, the likelihood of marketing approval or commercialization of the particular drug candidate, any approved product, and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is derived from information that is typically extensive, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular program, drug candidate or our business.

If the interim, topline or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

Changes in methods of drug candidate manufacturing or formulation may result in additional costs or delay.

As drug candidates are developed through preclinical studies to late-stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives, and may also require additional testing, FDA notification or FDA approval. Any of these changes could cause our drug candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our drug candidates and jeopardize our ability to pursue strategic alternatives, including identifying

and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates.

We currently conduct and may in the future conduct clinical trials for our drug candidates outside the United States. The FDA, EMA or comparable foreign regulatory authorities may not accept data from such trials.

We currently conduct and may in the future conduct clinical trials for our drug candidates outside the United States. The acceptance of trial data from clinical trials conducted outside the United States or another jurisdiction by the FDA or comparable foreign regulatory authorities may be subject to certain conditions or may not be accepted at all. Such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, EMA or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA, EMA or any comparable regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our drug candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

In addition, any escalation of political tensions, economic instability, military activity or civil hostilities outside the United States could disrupt our ability to conduct trials outside of the United States, or delay or adversely affect the timeliness of such trials. This could result in the need for alternative trial sites, which could be costly and time-consuming and delay the clinical development of our drug candidates.

We may not be successful in our efforts to increase our pipeline of drug candidates, including by in-licensing or acquiring additional drug candidates.

A key element of our strategy is to build and expand our pipeline of drug candidates. To build our pipeline, we may seek to in-license or acquire additional drug candidates, in addition to our in-house capabilities. We may not be able to identify or develop drug candidates that are safe, tolerable and effective. Even if we are successful in continuing to build our pipeline, the potential drug candidates that we develop, in-license or acquire may not be suitable for clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval and achieve market acceptance.

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

Because we have limited financial and management resources, we focus on development programs and drug candidates that we identify for specific indications. As such, we are currently primarily focused on the development of zunsemetinib as a potential treatment for moderate to severe rheumatoid arthritis, moderate to severe hidradenitis suppurativa and moderate to severe psoriatic arthritis, ATI-1777 as a potential treatment for moderate to severe atopic dermatitis, ATI-2138 as a potential treatment for T cell-mediated autoimmune diseases and ATI-2231 as a potential treatment for pancreatic cancer and metastatic breast cancer as well as in preventing bone loss in patients with metastatic breast cancer. As a result, we may forego or delay pursuit of opportunities with other drug candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spending on current and future development programs and drug candidates for specific indications may not yield any commercially viable drugs. If we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug candidate through partnerships, licensing or other arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such drug candidate.

For any of our drug candidates that receive marketing approval, our potential third-party partners 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.

For any of our drug candidates that receive marketing approval, our potential third-party partners may fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If such third-party partners fail to obtain an adequate level of acceptance for our drug candidates, we may not earn significant revenue

and we may not become profitable. The degree of market acceptance of any drug candidate, if approved, will depend on a number of factors, including:

- the efficacy, safety and potential advantages compared to alternative treatments;
- our potential third-party partners' ability to offer the products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new treatments and of physicians to prescribe these treatments;
- the ability of our potential third-party partners to retain a sales force;
- the strength of our potential third-party partners' marketing and distribution support;
- the availability of third-party payor coverage and adequate reimbursement or the willingness of patients to pay for these products;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our products together with other medications.

We face substantial competition, which may result in others discovering, developing or commercializing drugs before or more successfully than we do.

The development and commercialization of new drugs is highly competitive. We will face competition with respect to any drug candidates that we may seek to develop or through our potential third-party partners, commercialize, in the future, from many different sources, including major pharmaceutical, biotechnology and specialty pharmaceutical companies, academic institutions and governmental agencies and public and private research institutions.

With respect to zunsemetinib as a potential treatment for immuno-inflammatory diseases such as rheumatoid arthritis, hidradenitis suppurativa and psoriatic arthritis, there are several different types of therapies in the market. Medications for the treatment of rheumatoid arthritis and psoriatic arthritis currently fall into two categories: drugs that ease symptoms such as nonsteroidal anti-inflammatory drugs and drugs that slow disease activity. Drugs that slow disease activity include corticosteroids and DMARDs. DMARDs include (i) conventional synthetic DMARDs, such as methotrexate, sulfasalazine, leflunomide and hydroxychloroquine, (ii) biologic DMARDs (monoclonal antibodies which inhibit targets such as TNFα, IL1β, IL6, IL17 and costimulatory signaling mechanisms), and (iii) targeted synthetic DMARDs such as JAK inhibitors. Hidradenitis suppurativa is currently treated with antibiotics, corticosteroids and surgery, as well as anti-TNF therapy. Drugs for the treatment of immuno-inflammatory diseases such as rheumatoid arthritis, hidradenitis suppurativa and psoriatic arthritis are produced and sold, or are approved for marketing, by large pharmaceutical companies, including AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Johnson & Johnson, Pfizer, Novartis, UCB, Regeneron Pharmaceuticals, and Roche. In addition, we are aware of a number of companies developing and conducting clinical trials for investigational drug candidates, including biosimilars, that, if approved, could compete with zunsemetinib, if approved, for the treatment of immuno-inflammatory diseases.

With respect to ATI-1777 as a potential treatment for moderate to severe atopic dermatitis, there are several different types of therapies in the atopic dermatitis market, such as biologics, oral and topical corticosteroids, injectable and oral methotrexate products, oral and topical calcineurin inhibitors, oral mycophenolate products, other JAK inhibitors, other oral antibiotics and antihistamines and phototherapy. There are also several prescription, non-prescription and OTC topical products, including PDE4 inhibitors, utilized to treat atopic dermatitis. These types of drugs are produced and sold, or are approved for marketing, by large pharmaceutical companies, including AbbVie, Incyte, LEO Pharma A/S, Pfizer, and Sanofi and Regeneron Pharmaceuticals. In addition, we are aware of a number of companies including large pharmaceutical companies, such as Eli Lilly, Novartis, LEO Pharma A/S, Pfizer, and Dermavant Sciences developing and conducting clinical trials for investigational drug candidates, that, if approved, could compete with ATI-1777, if approved, for the treatment of atopic dermatitis.

The commercial opportunity for our drug candidates, if approved, could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than a drug that we may develop. Our competitors also may obtain FDA or other regulatory approval for their drugs more rapidly than our potential third-party partners' may obtain approval for our drug candidates, which could result in our competitors establishing a strong market position before our drug candidates are able to enter the market.

Many of the companies against which we are competing, or against which we may compete in the future, have significantly greater financial resources and expertise in research and development, manufacturing, and preclinical and clinical development than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or that may be necessary for, our development programs.

The success of our drug candidates, if approved, will depend significantly on coverage and adequate reimbursement or the willingness of patients to pay for these products.

We believe the success of our drug candidates, if approved, will depend on obtaining and maintaining coverage and adequate reimbursement as a prescription treatment or in the absence of coverage and adequate reimbursement, on the extent to which patients will be willing to pay out of pocket for these prescription drug products.

Third-party payors determine which prescription drug products they will cover and establish reimbursement levels. Reimbursement by a third-party payor may depend upon a number of factors, including: the third-party payor's determination that a product is safe, effective, and medically necessary; appropriate for the specific patient; cost-effective; supported by peer-reviewed medical journals or current clinical practice guidelines; and whether there are competitive products, either branded or generic, and the pricing of those products. Many private third-party payors, such as managed care plans, manage access to drug products' coverage partly to control costs for their plans, and may use drug formularies and medical policies to limit their exposure. Obtaining and maintaining favorable reimbursement can be a time-consuming and expensive process, and our potential third-party partners may not be able to negotiate or continue to negotiate reimbursement or pricing terms for our products with third-party payors at levels that are profitable to us, or at all. Further, 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 which receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In addition to uncertainties surrounding coverage policies, there are periodic changes to reimbursement. Third-party payors regularly update reimbursement amounts and also from time to time revise the methodologies used to determine reimbursement amounts. Accordingly, these updates could impact the demand for our drug candidates, if approved. Our drug candidates, if approved, may not be considered cost effective, and government and third-party private health insurance coverage and reimbursement may not be available to patients or sufficient to allow our potential third-party partners to sell our drug candidates, if approved, on a competitive and profitable basis. Our results of operations could be adversely affected by the Affordable Care Act and by other health care legislative reforms that may be enacted or adopted in the future. In addition, increasing emphasis on managed care in the United States will continue to put pressure on the pricing of pharmaceutical products. Cost control initiatives could decrease the price that our potential third-party partners could receive for any of our drug candidates, if approved, and could adversely affect our profitability. We cannot predict how pending and future health care legislation will impact our business, and any changes in coverage and reimbursement that further restricts coverage of our drug candidates could harm our business.

Foreign governments also have their own healthcare reimbursement systems, which vary significantly by country and region, and we cannot be sure that coverage and adequate reimbursement will be made available with respect to our drug candidates, if approved, under any foreign reimbursement system. In some foreign countries, including major markets in the European Union and Japan, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take up to 12 months or longer after the receipt of regulatory marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a pharmacoeconomic study that compares the cost-effectiveness of our drug candidate to other available therapies. Such pharmacoeconomic studies can be costly and the results uncertain. Our business could be harmed if reimbursement of our drug candidates, if approved, is unavailable or limited in scope or amount or if pricing is set at unsatisfactory levels.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any of our drug candidates that we may develop and are commercialized by our potential third-party partners or impact any commercial products that we have previously sold or are being sold by third-party partners.

We face an inherent risk of product liability exposure related to the testing of our drug candidates in human clinical trials and an even greater risk relating to any of our commercial products that we have previously sold or are being sold by third-party partners. If we cannot successfully defend ourselves against claims that our commercial products that we have previously sold or are being sold by third-party partners, or drug candidates, caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, product liability claims may result in:

- decreased demand for any drug candidates that we may develop and, if approved, are commercialized by our potential third-party partners;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards paid to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- our inability to pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates.

We currently hold $10 million in product liability insurance coverage in the aggregate, with a per incident limit of $10 million, which may not be adequate to cover all liabilities that we may incur. Insurance coverage is increasingly expensive. We may need to increase our insurance coverage and we may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct clinical trials for our drug candidates, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We engage CROs to conduct clinical trials of our drug candidates. We expect to continue to rely on third parties, such as clinical data management organizations, medical institutions and clinical investigators, to conduct those clinical trials. If any of our relationships with these third parties terminate, we may not be able to timely enter into arrangements with alternative third parties or to do so on commercially reasonable terms, if at all. In addition, any third parties conducting our clinical trials will not be our employees, and except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our clinical programs. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to identify and consummate transactions with third-party partners to further develop, obtain marketing approval for and/or commercialize our drug candidates. Consequently, our results of operations and the commercial prospects for our drug candidates would be harmed, our costs could increase substantially and our ability to earn revenue from those partnerships could be delayed significantly.

Switching or adding CROs involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

We rely on these parties for execution of our preclinical studies and clinical trials, and generally do not control their activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as good clinical practices, or GCPs, for

conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. If we or any of our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving 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 complies with GCP regulations. In addition, our clinical trials must be conducted with drug product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the marketing approval process for our potential third-party partners.

We also rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our drug candidates or commercialization of our drug candidates, if approved, producing additional losses and depriving us of potential revenue.

We contract with third parties for the manufacture and supply of our drug candidates for preclinical and clinical testing. This reliance on third parties increases the risk that we will not have sufficient quantities of our drug candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development efforts.

We do not have any manufacturing facilities. We currently rely, and expect to continue to rely, on third parties for the manufacture and supply of our drug candidates for preclinical and clinical testing. This reliance on third parties increases the risk that we will not have sufficient quantities of our drug candidates at an acceptable cost and/or quality, which could delay, prevent or impair our ability to timely conduct our clinical trials or our other development efforts.

The facilities used by our contract manufacturers to manufacture our drug candidates must be approved by the FDA or comparable foreign regulatory authorities pursuant to inspections that will be conducted after the NDA or comparable marketing application is submitted to the FDA or other regulatory authority. We do not have control over a supplier's or manufacturer's compliance with laws, regulations and applicable cGMP standards and other laws and regulations, such as those related to environmental health and safety matters. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our drug candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which could significantly impact our ability to develop, and identify and consummate transactions with third-party partners to further develop, obtain marketing approval for and/or commercialize, our drug candidates.

We may be unable to establish any agreements with future third-party manufacturers or do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how;
- the possible increase in costs by our third-party suppliers for the active pharmaceutical ingredients for our drug candidates; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our drug candidates.

Our drug candidates may compete with other products and drug candidates for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval of our drug candidates.

If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. We may incur added costs and delays in identifying and qualifying any such replacement. We do not currently have arrangements in place for redundant supply or a second source for the active pharmaceutical ingredients and/or drug product for our drug candidates.

We expect to continue to depend on third-party contract manufacturers for the foreseeable future. Our current and anticipated future dependence upon others for the manufacture of our drug candidates may adversely affect our future profit margins and our ability to pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates on a timely and competitive basis.

We intend to pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates. If those arrangements are not successful, we may not be able to capitalize on the market potential of these drug candidates.

We intend to pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates. Our likely partners for any such arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. If we do enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our partners dedicate to the development or commercialization of our drug candidates. Our ability to earn revenue from these arrangements will depend on our partners' abilities to successfully perform the functions assigned to them in these arrangements.

Partnerships involving our drug candidates would pose the following risks to us:

- partners have significant discretion in determining the efforts and resources that they will apply to these arrangements;
- partners may not perform their obligations as expected;
- partners may not pursue development, marketing approval or commercialization of any drug candidates that achieve marketing approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the partners' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- partners may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a drug candidate, repeat or conduct new clinical trials or require a new formulation of a drug candidate for clinical testing;
- partners could independently develop, or develop with third parties, products that compete directly or indirectly with our drug candidates if the partners believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- drug candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own products or drug candidates, which may cause our partners to cease to devote resources to the development and/or commercialization of our drug candidates, if approved;
- a partner with marketing and distribution rights to one or more of our drug candidates that achieve marketing approval may not commit sufficient resources to the marketing and distribution of such drug candidates;
- disagreements with partners, including disagreements over proprietary rights, contract interpretation or the preferred course of development or commercialization, might cause delays or termination of the research, development or commercialization of drug candidates, might lead to additional responsibilities for us with respect to drug candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;

- partners may not properly maintain or defend our or their intellectual property rights or may use our or their proprietary information in such a way as to invite litigation that could jeopardize or invalidate such intellectual property or proprietary information or expose us to potential litigation;
- partners may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- partnerships may be terminated for the convenience of the partner and, if terminated, we could be required to raise additional capital to pursue further development and/or commercialization of the applicable drug candidates.

Partnership agreements may not lead to development, marketing approval or commercialization of drug candidates in the most efficient manner or at all. If a present or future partner of ours were to be involved in a business combination, the continued pursuit and emphasis on our drug development or commercialization program could be delayed, diminished or terminated.

If we are not able to establish partnerships, we may have to alter our development and commercialization plans.

Our drug development programs for our drug candidates will require substantial additional capital. We intend to partner with pharmaceutical and biotechnology companies for the further development and/or commercialization of our drug candidates.

We face significant competition in seeking appropriate partners. Whether we reach a definitive agreement for a partnership will depend, among other things, upon our assessment of the partner's resources and expertise, the terms and conditions of the proposed arrangement and the proposed partner's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject drug candidate, the costs and complexities of manufacturing and delivering such drug candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The partner may also consider alternative drug candidates or technologies for similar indications that may be available to partner on and whether such a partnership could be more attractive than the one with us for our drug candidate. Partnerships are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future partners.

We may not be able to negotiate partnerships on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of such drug candidate, or reduce or delay its development program or one or more of our other development programs, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our drug candidates or bring them to market and generate revenue.

We may not have access to all information regarding our drug candidates that are subject to partnership agreements. Consequently, our ability to inform our stockholders about the status of our drug candidates that are subject to these agreements, and our ability to make business and operational decisions, may be limited.

We may not have access to all information regarding our drug candidates that may become subject to agreements with partners, including potentially material information about clinical trial design, execution and timing, safety and efficacy, clinical trial results, regulatory affairs, manufacturing, marketing, sales and other areas known by our potential partners. In addition, we may have confidentiality obligations under our agreements with such partners. Therefore, our ability to keep our stockholders informed about the status of our drug candidates will be limited by the degree to which our partners keep us informed and by the degree to which our partners allow us to disclose information to the public or provide such information to the public themselves. If our partners do not timely inform us about the status of our drug candidates that are the subject of the partnership, we may make operational and investment decisions that we would not have made had we been fully informed, which may have an adverse impact on our business, prospects, financial condition and results of operations.

Our sublease could terminate if the master lease is terminated for any reason, thus terminating our rights to our corporate headquarters.

We sublease space for our corporate headquarters. While the term of the sublease extends until October 2023, if for any reason the master lease is terminated or expires prior to October 2023, our sublease will also automatically terminate. In such an event, we would need to obtain a new direct lease with the master landlord or negotiate and enter into a new lease for office space at a different location, which we may not be able to do on commercially reasonable terms, if at all.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for our drug candidates, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and drugs similar or identical to ours, and ability to successfully identify a potential third-party partner to commercialize our technology and drug candidates may be impaired.

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 drug candidates. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our drug candidates.

The patent prosecution process is expensive and time-consuming, however, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our development output before it is too late to obtain patent protection. We may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the rights to patents licensed to third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States or vice versa. For example, European patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. 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 know with certainty whether we or our licensors were the first to make the inventions claimed in our patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our technology or drug candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies and drug candidates. 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.

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

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 our potential third-party partners or otherwise provide us or our potential third-party partners with any competitive advantage. Competitors may be able to circumvent our patents by developing similar or alternative technologies or drugs in a non-infringing manner.

In addition, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit the ability to stop others from using or commercializing similar or identical technology and drug candidates, or limit the duration of the patent protection of our technology and drug candidates. Our issued U.S. patents covering zunsemetinib expire in 2034. We currently do not have any patents issued directed to ATI-2231, but any claims that may issue would expire in 2040. Our issued U.S. patent covering ATI-1777 expires in 2038. Our issued U.S. patent directed to ATI-2138 expires in 2039. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us or our potential third-party partners with sufficient rights to exclude others from commercializing drugs similar or identical to ours.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time-consuming and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged in court.

Competitors may infringe our issued patents or other intellectual property. Our pending applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents or that our patents are invalid or unenforceable. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement or insufficient written description, or similar requirements outside of the United States. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before the USPTO, in post-grant proceedings such as *ex parte* reexaminations, *inter partes* review, or post-grant review, or oppositions or similar administrative proceedings outside the United States, in parallel with litigation or, even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our drug candidates. Such a loss of patent protection would harm our business.

In such a proceeding, a court or administrative board may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology. An adverse result in any such proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. We may find it impractical or undesirable to enforce our intellectual property against some third parties.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

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

Filing, prosecuting and defending patents on our drug candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. For example, zunsemetinib is currently covered by patents and applications in the United States, European Union and other foreign markets. While we have issued U.S. patents directed to ATI-1777 and ATI-2138, we do not currently have any patents for such drug candidates in the European Union or other foreign markets; rather, we have pending applications in the European Union and other foreign markets directed to each of ATI-

1777 and ATI-2138. Currently, we do not have any issued patents directed to ATI-2231, but we have a pending PCT application.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of some countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful.

Many countries, including European Union countries, India, Japan and China, have compulsory licensing laws under which a patent owner may be compelled under specified circumstances to grant licenses to third parties. In those countries, we may have limited remedies if patents are infringed or if we are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our ability to pursue strategic alternatives, including identifying and consummating transactions with potential third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates, and consequently our potential revenue opportunities. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

We may need to license intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property, including patent rights, that are important or necessary to the development and/or commercialization of our drug candidates. It may be necessary for us or our potential third-party partners to use the patented or proprietary technology of third parties to further develop and/or commercialize our drug candidates. If we or our potential third-party partners are not able to obtain a license from these third parties on commercially reasonable terms, our business could be harmed, possibly materially, and even if we or they are able to, it may result in the reduction of revenue we earn from such partner as a result of payment obligations to the licensor.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our success depends upon our ability to pursue strategic alternatives, including identifying and consummating transactions with potential third-party partners, to develop, obtain marketing approval for and/or commercialize our drug candidates and earn revenue from those partnerships, and for our proprietary technologies to be used without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our drug candidates and technologies, including interference or derivation proceedings before the USPTO. Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist in the fields in which we are developing our drug candidates. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future.

If we or our potential third-party partners are found to infringe a third party's intellectual property rights, we or such partners could be required to obtain a license from such third party to continue developing or commercializing our drug candidates and technology. However, we or our potential third-party partners may not be able to obtain any required license on commercially reasonable terms or at all. Even if we or our potential third-party partner were able to obtain a license, it could be non-exclusive, thereby giving competitors access to the same technologies licensed to us or our partner. Consequently, we or our potential third-party partner could be forced, including by court order, to cease developing or commercializing the infringing technology or drug candidate. In addition, we or our potential third-party partner could be found liable for monetary damages, including treble damages and attorneys' fees if we or such partner are found to have willfully infringed a patent. A finding of infringement could prevent our potential third-party partners from commercializing our drug candidates, if approved, or force such partners to cease some of their business operations. In the event of a successful claim of infringement against us or our potential third-party partners, we or our potential third-party partners may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing drug candidate or obtain one or more licenses from third parties, which may be impossible

or require substantial time and monetary expenditure. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

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

Many of our employees and our licensors' employees were previously employed at other biotechnology or pharmaceutical companies. Although we and our licensors try to ensure that our employees and our licensors' employees do not use the proprietary information or know-how of others in their work for us, we or our licensors may be subject to claims that these employees, our licensors or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require our employees 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. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we or our licensors fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we and our licensors are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Some of our competitors are larger than we are and have substantially greater resources. They are, therefore, likely to be able to sustain the costs of complex patent litigation longer than we could. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating our intellectual property. Litigation could result in substantial costs and diversion of management resources, which could harm our business. In addition, the uncertainties associated with litigation could compromise our ability to compete in the marketplace, including compromising our ability to raise the funds necessary to continue our clinical trials, continue our internal research programs, or pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates.

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

In addition to seeking and maintaining patents for our drug candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect our trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. 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 inside and outside the United States 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, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

The validity, scope and enforceability of any of our patents that cover any of our drug candidates can be challenged by competitors.

If any of our drug candidates advance through development or are approved by the FDA or foreign regulatory authority, one or more third parties may challenge the current patents, or patents that may issue in the future, within our portfolio covering these drug candidates. The challenge may come in the form of a patent office proceeding, such as an *inter partes* review challenging the validity of the patents, or a district court proceeding such as a paragraph IV litigation arising out of the filing of an ANDA. Litigation or other proceedings to enforce or defend intellectual property rights are often very complex in nature, may be expensive and time-consuming, may divert our management's attention from our core business, and may result in unfavorable results that could limit our ability to prevent third parties from competing with our drug candidates, if approved. Any such challenge could result in the invalidation of, or render unenforceable, some or all of the relevant patent claims or a finding of non-infringement, which would harm our ability to pursue strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates, and earn revenue from such arrangements. In addition, any such challenge on any divested product could harm our ability to earn revenue from the arrangements for such product.

If we do not obtain protection under the Hatch-Waxman Act by extending the patent term and obtaining data exclusivity for our drug candidates, our business may be materially harmed.

Our success will largely depend on our ability to obtain and maintain patent and other intellectual property in the United States and other countries with respect to our proprietary technology, drug candidates and our target indications. Our issued U.S. patents covering zunsemetinib expire in 2034. We currently do not have any patents issued directed to ATI-2231, but any claims that may issue would expire in 2040. Our issued U.S. patent covering ATI-1777 expires in 2038. Our issued U.S. patent directed to ATI-2138 expires in 2039. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting our drug candidates might expire before or shortly after such candidates begin to be commercialized. We expect to seek extensions of patent terms in the United States and, if available, in other countries where we are prosecuting patents.

Depending upon the timing, duration and specifics of FDA marketing approval of our drug candidates, one or more of our U.S. patents may be eligible for limited patent term extension under The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, for a drug candidate. The Hatch-Waxman Act permits a patent extension term of up to five years beyond the normal expiration of the patent as compensation for patent term lost during development and the FDA regulatory review process, which is limited to the approved indication (or any additional indications approved during the period of extension). However, the total patent term including the period of extension cannot exceed 14 years from the product's approval date. Furthermore, this extension is limited to only one patent per regulatory review period that covers the approved product. 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. We may not be granted 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. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. Similar provisions are available in certain foreign countries, such as the European Union and Japan.

If we are unable to extend the expiration date of our existing patents or obtain new patents with longer expiry dates, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data to obtain approval of competing products following our patent expiration and launch their product earlier than might otherwise be the case.

Any trademarks we have obtained or may obtain may be infringed or successfully challenged, resulting in harm to our business.

We expect to rely on trademarks as one means to distinguish our products, services or technologies from those of our competitors. Once we select new trademarks and apply to register them, our trademark applications may not be

approved. Third parties may oppose or attempt to cancel our trademark applications or trademarks, or otherwise challenge our use of the trademarks. In such an event, we may need to negotiate a settlement agreement with such third party over the use of our trademarks, which we may not be able to do on commercially reasonable terms, if at all. In the event that our trademarks are successfully challenged, our products, services or technologies may need to be rebranded, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe our trademarks and we may not have adequate resources to enforce our trademarks.

Outside of the United States we cannot be certain that any country's patent or trademark office will not implement new rules that could seriously affect how we draft, file, prosecute and maintain patents, trademarks and patent and trademark applications.

We cannot be certain that the patent or trademark offices of countries outside the United States will not implement new rules that increase costs for drafting, filing, prosecuting and maintaining patents, trademarks and patent and trademark applications or that any such new rules will not restrict our ability to file for patent or trademark protection. For example, we may elect not to seek patent protection in some jurisdictions or for some drug candidates in order to save costs. We may be forced to abandon or return the rights to specific patents due to a lack of financial resources.

For example, following the result of a referendum in 2016, the United Kingdom left the European Union on January 31, 2020, commonly referred to as Brexit. The impact of the withdrawal of the United Kingdom from the European Union will not be known for some time, which could lead to a period of uncertainty relating to our ability to obtain and maintain patents and trademarks in the United Kingdom. In 2012, the European Patent Package, or EU Patent Package, regulations were passed with the goal of providing for a single pan-European Unitary Patent, and a new European Unified Patent Court, or UPC, for litigation of European patents. It is possible that implementation of the EU Patent Package will occur in the first half of 2023. If the EU Patent Package is ratified and in effect, all European patents, including those issued prior to ratification, would by default automatically fall under the jurisdiction of the UPC and allow for the possibility of obtaining pan-European injunctions. Under the EU Patent Package as currently proposed, once the UPC is established, patent holders are permitted to "opt out" of the UPC on a patent-by-patent basis during an initial seven year period after the EU Patent Package is ratified. Owners of traditional European patent applications who receive notice of grant after the EU Patent Package is ratified could either accept a Unitary Patent or validate the patent nationally and file an opt-out demand. The EU Patent Package may increase the uncertainties and costs surrounding the enforcement or defense of our issued European patents and pending applications. The full impact on future European patent filing strategy and the enforcement or defense of our issued European patents in member states and/or the UPC is not known.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- we, our licensors or any potential third-party partners might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own;
- we, our licensors or any potential third-party partners might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or exclusively license may not provide us with any competitive advantages, or may be held invalid or unenforceable as a result of legal challenges;
- our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights, and then use the information learned from such activities to develop competitive products for sale in major commercial markets; and
- we may develop additional proprietary technologies that are not patentable.

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

If our potential third-party partners are not able to obtain, or if there are delays in obtaining, required regulatory approvals, our drug candidates will not be able to be commercialized, and our ability to earn revenue from arrangements with such third-party partners will be materially impaired.

Our drug candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA, other regulatory agencies in the United States and similar regulatory authorities outside the United States. Failure to obtain marketing approval for a drug candidate will prevent our potential third-party partners from commercializing the drug candidate. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the drug candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Our drug candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our potential third-party partners from obtaining marketing approval or prevent or limit commercial use. If any of our drug candidates receive marketing approval, the accompanying label may limit the approved use of our product in this way, which could limit sales of the product.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive and may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the drug candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted drug application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a drug candidate. Any marketing approval our potential third-party partners ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved drug not commercially viable.

If our potential third-party partners experience delays in obtaining approval or if they fail to obtain approval of our drug candidates, the commercial prospects for our drug candidates may be harmed and our ability to earn revenue from arrangements with such third-party partners will be materially impaired.

Failure to obtain marketing approval in international jurisdictions would prevent our drug candidates from being marketed abroad.

In order to market and sell our drugs in the European Union and any other jurisdictions outside the United States, our potential third-party partners must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the drug be approved for reimbursement before the drug can be approved for sale in that country. Our potential third-party partners may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, failure to obtain approval in one jurisdiction may impact our potential third-party partners' ability to obtain approval elsewhere. Our potential third-party partners may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our drug candidates in any market.

A variety of risks associated with marketing our drug candidates by our potential third-party partners internationally could harm our business.

If our drug candidates, if approved, are marketed internationally by our potential third-party partners, our potential third-party partners would be subject to additional risks related to operating in foreign countries, including:

- differing regulatory requirements in foreign countries;
- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market (with low or lower prices) rather than buying them locally;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- foreign reimbursement, pricing and insurance regimes;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, or comparable foreign regulations;
- challenges enforcing contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- logistical challenges resulting from distributing our drug candidates to foreign countries; and
- business interruptions resulting from geo-political actions, including war and terrorism.

These and other risks associated with international operations may compromise our ability to earn revenue from arrangements with potential third-party partners for our drug candidates.

Any drug candidate for which our potential third-party partners obtain marketing approval could be subject to post-marketing restrictions or recall or withdrawal from the market, and our potential third-party partners may be subject to penalties if they fail to comply with regulatory requirements or if they experience unanticipated problems with our drug candidates, when and if any of them are approved.

Any drug candidate for which our potential third-party partners obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such drug candidate, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a drug candidate is granted, the approval may be subject to limitations on the indicated uses for which the drug candidate may be marketed or to the conditions of approval, including the requirement to implement a risk evaluation and mitigation strategy. If any of our drug candidates receives marketing approval, the accompanying label may limit the approved use of our drug, which could limit sales of the drug by our potential third-party partners.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the drug. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if our potential third-party partners do not market our drugs for their approved indications, they may be subject to enforcement action for off-label marketing. Physicians, on the other hand, may prescribe products for off-label uses. Although the FDA and other regulatory agencies do not regulate a physician's choice of drug treatment made in the physician's independent medical judgment, they do restrict promotional communications from companies or their sales force with respect to off-

label uses of products for which marketing clearance has not been issued. However, companies may share truthful and not misleading information that is otherwise consistent with the product's FDA approved labeling. Violations of the FDCA relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our drugs, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may have negative consequences, including:

- restrictions on such drugs, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a drug;
- restrictions on drug distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters;
- recall or withdrawal of the drugs from the market;
- refusal to approve pending applications or supplements to approved applications;
- clinical holds;
- fines, restitution or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our drugs;
- drug seizure; or
- injunctions or the imposition of civil or criminal penalties.

Non-compliance with the European Union's requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of drugs for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can also lead to significant penalties and sanctions. These and other risks associated with the failure by our potential third-party partners to comply with regulatory requirements may compromise our ability to earn revenue from arrangements with such third-party partners for our drug candidates.

Our potential third-party partners' relationships with third-party payors, health care professionals and customers in the United States and elsewhere may be subject, directly or indirectly, to applicable anti-kickback, fraud and abuse, false claims, physician payment transparency, health information privacy and security and other health care laws and regulations, and any failure to comply with such laws and regulations could have a material adverse effect on our ability to earn revenue from arrangements with such third-party partners for our drug candidates.

Health care providers, physicians and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any of our drug candidates for which marketing approval is obtained. Our potential third-party partners' arrangements with third-party payors, health care professionals and customers may expose them to broadly applicable fraud and abuse and other health care laws and regulations, including, without limitation, the federal Anti-Kickback Statute and the federal civil False Claims Act, that may constrain the business or financial arrangements and relationships through which they sell, market and distribute any drug candidates for which marketing approval is obtained. In addition, we and our potential third-party partners may be subject to transparency laws and patient privacy regulation by the federal government and by the U.S. states and foreign jurisdictions in which we or they conduct business. The applicable federal, state and foreign health care laws and regulations that may affect our or our potential third-party partners' ability to operate include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state health care programs such as Medicare and Medicaid. Further, several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal health care covered business, the Anti-Kickback Statute has been violated. The intent standard was further amended by the Affordable Care Act, to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a

violation. Moreover, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;

- federal civil and criminal false claims laws, including, without limitation, the federal civil False Claims Act (that can be enforced through civil whistleblower or qui tam actions), and the civil monetary penalties law, which impose criminal and civil penalties, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, executing a scheme to defraud any health care benefit program or making false statements relating to health care matters. 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 to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, which impose obligations on covered health care providers, health plans, and health care clearinghouses, as well as their business associates that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity and their subcontractors that use, disclose, access, or otherwise process protected health information, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Open Payments program, created under Section 6002 of the Affordable Care Act (commonly known as the Physician Payments Sunshine Act) and its implementing regulations, which requires specified manufacturers of drugs, devices, biologics or medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to "payments or other transfers of value" made to physicians, which is defined to include doctors, dentists, optometrists, podiatrists and chiropractors, other health care professionals (such as physician assistants and nurse practitioners), and teaching hospitals, and for applicable manufacturers to report annually to CMS information regarding ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving health care items or services reimbursed by non-governmental third-party payors, including private insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to health care providers; state, local and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other health care providers or marketing expenditures; state laws that require drug manufacturers to report pricing information regarding certain drugs; and/or that require registration of certain employees engaged in marketing activities in the location; and state and foreign 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.

Efforts to ensure that our or our potential third-party partners' business arrangements with third parties will comply with applicable health care laws and regulations may involve substantial costs. It is possible that governmental authorities will conclude that our or our potential third-party partners' business practices, including relationships with physicians and other health care providers, some of whom may recommend, purchase and/or prescribe our drug candidates, if approved, may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other health care laws and regulations. By way of example, some of our consulting arrangements with physicians may not meet all of the criteria of the personal services safe harbor under the federal Anti-Kickback Statute. Accordingly, they may not qualify for safe harbor protection from government prosecution. A business arrangement that does not substantially comply with a safe harbor, however, is not necessarily illegal under the Anti-Kickback Statute, but may be subject to additional scrutiny by the government.

If our or our potential third-party partners' operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us or them, we or our potential third-party partners may be subject to significant civil, criminal and administrative penalties, including, without limitation, damages, fines, disgorgement, imprisonment, exclusion from participation in government health care programs, such as Medicare and Medicaid,

additional reporting requirements and oversight if we or they become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our or their operations, which could have a material adverse effect on our ability to earn revenue from arrangements with such third-party partners for our drug candidates. If any physician or other health care provider or entity with whom we or our potential third-party partners expect to do business is found not to be in compliance with applicable laws, it may be subject to significant criminal, civil or administrative sanctions, including exclusions from participation in government health care programs, which could also materially affect our ability to earn revenue from arrangements with such third-party partners for our drug candidates.

Recently enacted and future legislation may increase the difficulty and cost for our potential third-party partners to obtain marketing approval of our drug candidates and commercialize our drug candidates, if approved, and affect the prices our potential third-party partners may obtain.

In the United States, and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the health care system that could prevent or delay marketing approval of our drug candidates, restrict or regulate post-approval activities and affect our potential third-party partners' ability to profitably sell any of our drug candidates for which our potential third-party partners obtain marketing approval, and consequently affect our ability to earn revenue from arrangements with such third-party partners for our drug candidates.

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in health care systems with the stated goals of containing health care costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. The Affordable Care Act, which was signed into law in 2010, is a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of health care spending, enhance remedies against fraud and abuse, add new transparency requirements for the health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

Among the provisions of the Affordable Care Act of importance to commercial products are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government health care programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- expansion of health care fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, which include, among other things, new government investigative powers and enhanced penalties for non-compliance;
- a Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- requirements under the federal Open Payments program and its implementing regulations;
- a requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- the Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

There have been executive branch, judicial and Congressional challenges to certain aspects of the Affordable Care Act. While Congress has not passed comprehensive repeal legislation, several bills affecting the implementation of certain taxes under the Affordable Care Act have been signed into law. On June 17, 2021 the U.S. Supreme Court dismissed

a challenge on procedural grounds that argued the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace. 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 Affordable Care Act. Further, on August 16, 2022, President Biden signed the IRA into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in Affordable Care Act marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and through a newly established manufacturer discount program. It is possible that the Affordable Care Act will be subject to judicial or Congressional challenges in the future. It is unclear how such challenges and any additional health care reform measures of the Biden administration will impact the Affordable Care Act and our business.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. These changes included aggregate reductions to Medicare payments to providers of 2% per fiscal year that became effective on April 1, 2013 and, due to subsequent legislative amendments to the statute, including the BBA and the Infrastructure Investment and Jobs Act, will stay in effect through 2031 unless additional Congressional action is taken. Under current legislation the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. The American Taxpayer Relief Act of 2012, which was signed into law in January 2013, among other things, further reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Any similar new laws may result in additional reductions in Medicare and other health care funding, which could have a material adverse effect on our ability to earn revenue from arrangements with our potential third-party partners for our drug candidates.

We expect that the Affordable Care Act, as well as other health care reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that our potential third-party partners receive for any approved drug candidate. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other health care reforms may prevent our potential third-party partners from being able to generate revenue, attain profitability, or commercialize our drug candidates, if approved, which in turn may impact our ability to earn revenue from arrangements with such third-party partners for our drug candidates. Further, it is also possible that additional governmental action is taken in response to the COVID-19 pandemic.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for drugs. In addition, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. In July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, U.S. Department of Health and Human Services, or HHS, released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. In addition, the IRA, among other things, (1) directs HHS to negotiate the price of certain single-source drugs and biologics covered under Medicare and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be implemented but is likely to have a significant impact on the pharmaceutical industry. Further, the Biden administration released an additional executive order on October 14, 2022, directing HHS to submit a report on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. It is unclear whether this executive order or similar policy initiatives will be implemented in the future. It is unclear whether these or similar policy initiatives will be implemented in the future. The effect of reducing prices and reimbursement for certain of our drug candidates, if approved, could significantly impact our business and consolidated results of operations. In addition, the IRA may meaningfully influence our and pharmaceutical industry business strategies. In particular, it may reduce the attractiveness of investment in small molecule and biologic

innovation. At the state level, legislatures have become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain drug access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on obtaining marketing approvals for our drug candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject our potential third-party partners to more stringent drug labeling and post-marketing testing and other requirements. These risks may compromise our ability to earn revenue from arrangements with such third-party partners for our drug candidates.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenue.

In some countries, particularly the countries of the European Union, 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, our potential third-party partners may be required to conduct a clinical trial that compares the cost-effectiveness of our drug candidate to other available procedures. If reimbursement of our drug candidates is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our potential third-party partners may not able to generate revenue, which in turn may adversely affect our ability to earn revenue from arrangements with such third-party partners for our drug candidates.

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 harm 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 for failure to comply with such laws and regulations.

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.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our development or manufacturing efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

We are subject to governmental economic sanctions and export and import controls that could impair our potential third-party partners' ability to compete in international markets or subject us or our potential third-party partners to liability if we or they are not in compliance with applicable laws.

As a U.S. company, we are subject to U.S. import and export controls and economic sanctions laws and regulations, and we are required to import and export our drug candidates, technology and services in compliance with those laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, the International Traffic in Arms Regulations, and economic embargo and trade sanction programs administered by the U.S. Treasury Department's Office of Foreign Assets Control.

U.S. economic sanctions and export control laws and regulations prohibit the shipment of certain products and services to countries, governments and persons targeted by U.S. sanctions. While we are currently taking precautions to

prevent doing any business, directly or indirectly, with countries, governments and persons targeted by U.S. sanctions and to ensure that our drug candidates are not exported or used by countries, governments and persons targeted by U.S. sanctions, such measures may be circumvented.

Furthermore, if we or our potential third-party partners export our drug candidates, the exports may require authorizations, including a license, a license exception or other appropriate government authorization. Complying with export control and sanctions regulations may be time-consuming and may result in the delay or loss of sales opportunities. Failure to comply with export control and sanctions regulations may expose us or our potential third-party partners to government investigations and penalties.

If we are found to be in violation of U.S. sanctions or import or export control laws, it could result in civil and criminal, monetary and non-monetary penalties, including possible incarceration for those individuals responsible for the violations, the loss of export or import privileges and reputational harm.

We and our potential third-party partners are subject to anti-corruption and anti-money laundering laws with respect to our and their operations and non-compliance with such laws can subject us to criminal and/or civil liability and harm our business.

We and our potential third-party partners are subject to 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 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 and third-party intermediaries from authorizing, offering or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. We or our potential third-party partners may engage third-party intermediaries in connection with the development or commercialization of our drug candidates, if approved, and to obtain necessary permits, licenses and other regulatory approvals. We, our potential third-party partners or the third-party intermediaries may have direct or indirect interactions with officials and employees of government agencies or state-owned or affiliated entities. 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 such activities.

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. Responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense costs and other professional fees.

Risks Related to Employee Matters and Managing Our Growth

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

We are highly dependent on the management, development, clinical, financial, and business development expertise of Dr. Douglas Manion, our Chief Executive Officer and President, Kevin Balthaser, our Chief Financial Officer, Dr. Joseph Monahan, our Chief Scientific Officer, Dr. Gail Cawkwell, our Chief Medical Officer, and James Loerop, our Chief Business Officer, as well as the other members of our scientific and clinical teams. Although we have entered into employment agreements with our executive officers, each of them may currently terminate their employment with us or resign at any time. We do not maintain "key person" insurance for any of our key executives other than for Dr. Manion.

Recruiting and retaining qualified scientific, manufacturing and clinical personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our development objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop and partner drug candidates. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific

and clinical advisors, to assist us in formulating our development strategy. Our consultants and advisors may have commitments under employment, consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

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

We are exposed to the risk that our employees, independent contractors, consultants, third-party partners, principal investigators, CROs and vendors 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 violates FDA regulations, including those laws requiring the reporting of true, complete and accurate information to the FDA, manufacturing standards, federal and state health care laws and regulations, and laws that require the true, complete and accurate reporting of financial information or data. In particular, sales, marketing and business arrangements by our potential third-party partners in the health care industry are subject to extensive laws and regulations intended to prevent fraud, 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. Misconduct by these parties could also involve the improper use of individually identifiable information, including, without limitation, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent 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 be in compliance with such laws or regulations. 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 significant civil, criminal and administrative penalties, including, without limitation, damages, fines, disgorgement, imprisonment, exclusion from participation in government health care programs, such as Medicare and Medicaid, additional reporting obligations and oversight if we are subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations.

In addition, we have a hybrid work model of remote and in-person operations for our employees that enables us to continue to develop our drug candidates and provide contract research services to our clients. The effects of our hybrid work model may negatively impact productivity, disrupt our business and delay our preclinical drug development and clinical trials and timelines. These and similar, and perhaps more severe, disruptions in our operations could negatively impact our business, operating results and financial condition.

Risks Related to Ownership of Our Common Stock

The trading price of the shares of our common stock has been and is likely to continue to be volatile.

Our stock price has been and is likely to continue to be volatile. The stock market in general and the market for biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their common stock at or above the price paid for the shares. The market price for our common stock may be influenced by many factors, including:

- the commencement, enrollment and/or results of any preclinical studies and clinical trials we may conduct, or changes in the development status of our drug candidates;
- any delay in our regulatory filings for any of our drug candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information;
- adverse results from, delays in or termination of clinical trials;
- adverse regulatory decisions, including failure of any of our drug candidates to receive marketing approval;
- unanticipated serious safety concerns related to the use of any drug candidate or previously sold commercial product;
- changes in financial estimates by us or by any securities analysts who might cover our stock;

- conditions or trends in our industry;
- changes in the structure of health care payment systems;
- changes in the market valuations of similar companies;
- stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the biotechnology industry;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- announcements by us or our competitors of significant acquisitions, strategic partnerships or divestitures;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- investors' general perception of our company and our business;
- recruitment or departure of key personnel;
- overall performance of the equity markets;
- trading volume of our common stock;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- general political and economic conditions;
- the evolution of the COVID-19 pandemic and success of mass vaccination efforts; and
- other events or factors, many of which are beyond our control.

In the past, stockholders have initiated class action lawsuits against us and other pharmaceutical companies following periods of volatility in the market prices of these companies' stock. We have entered into indemnification agreements with our executive officers and directors which provide, among other things, that we will indemnify such officer or director, under the circumstances and to the extent provided for therein, for expenses, damages, judgments, fines and settlements he or she may be required to pay in actions or proceedings which he or she is or may be made a party by reason of his or her position as our director, officer or other agent, and otherwise to the fullest extent permitted under Delaware law and our bylaws. Such additional litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources from our business.

Sales of a substantial number of shares of our common stock into the market could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. If our stockholders sell, or the market perceives that our stockholders intend to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline significantly.

In addition, we have filed registration statements on Form S-8 under the Securities Act registering the issuance of shares of common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. Shares registered under these registration statements are available for sale in the public market subject to vesting arrangements and exercise of options, and the restrictions of Rule 144 under the Securities Act in the case of our affiliates.

Provisions in our corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management and hinder efforts to acquire a controlling interest in us, and the market price of our common stock may be lower as a result.

There are provisions in our certificate of incorporation and bylaws that may make it difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change of control was considered favorable by some or all of our stockholders. For example, our board of directors has the authority to issue up to 10,000,000 shares of preferred stock. The board of directors can fix the price, rights, preferences, privileges, and restrictions of the preferred stock without any further vote or action by our stockholders. The issuance of shares of preferred stock may delay or prevent a change of control transaction. As a result, the market price of our common stock and the voting and other rights of our stockholders may be adversely affected. An issuance of shares of preferred stock may result in the loss of voting control to other stockholders.

Our charter documents also contain other provisions that could have an anti-takeover effect, including:

- only one of our three classes of directors is elected each year;
- stockholders are not entitled to remove directors other than by a 66 2/3% vote and only for cause;
- stockholders are not permitted to take actions by written consent;
- stockholders cannot call a special meeting of stockholders; and
- stockholders must give advance notice to nominate directors or submit proposals for consideration at stockholder meetings.

In addition, we are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, which regulates corporate acquisitions by prohibiting Delaware corporations from engaging in specified business combinations with particular stockholders of those companies. These provisions could discourage potential acquisition proposals and could delay or prevent a change of control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act and the rules and regulations of the stock market on which our common stock is listed. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting, and perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting. This requires that we incur substantial additional professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts.

We may identify weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our consolidated financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements, and we may conclude that our internal control over financial reporting is not effective. If that were to happen, the market price of our stock could decline, and we could be subject to sanctions or investigations by the stock exchange on which our common stock is listed, the SEC, or other regulatory authorities.

We might not be able to utilize a significant portion of our net operating loss carryforwards and research and development tax credit carryforwards.

As of December 31, 2022, we had federal and state net operating loss carryforwards, or NOLs, of $446.7 million and $477.9 million, respectively, which will begin to expire in 2032. Under federal law, federal NOL carryforwards generated in tax years beginning after December 31, 2017 may be carried forward indefinitely but may only be used to offset 80% of our taxable income annually. It is uncertain if and to what extent various states will conform to the federal tax law. As of December 31, 2022, we also had federal research and development tax credit carryforwards of 15.1 million which will begin to expire in 2032, and state research and development tax credit carryforwards of $0.1 million which will begin to expire in 2022. We also have $0.2 million of loss carryforwards in the United Kingdom which can be carried forward indefinitely. These NOL and tax credit carryforwards could expire unused or due to limitation on use be unavailable to offset future income tax liabilities. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. We have completed an analysis under Section 382 for NOLs generated from July 13, 2012 through December 31, 2021. Although we have experienced Section 382 ownership changes since 2012, we have concluded that we should have sufficient ability to utilize NOLs accumulated during the periods tested. We have not yet determined if a Section 382 ownership change has occurred after December 31, 2021. In addition, we may experience ownership changes

in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. If we determine that an ownership change has occurred and our ability to use our historical NOL and tax credit carryforwards is materially limited, it might harm our future operating results by effectively increasing our future tax obligations.

We do not anticipate paying any cash dividends on our common stock in the foreseeable future and our stock may not appreciate in value.

We have not declared or paid cash dividends on our common stock to date. We currently intend to retain our future earnings, if any, to fund the development and growth of our business. There is no guarantee that shares of our common stock will appreciate in value or that the price at which our stockholders have purchased their shares will be able to be maintained.

Exclusive forum provisions in our amended and restated certificate of incorporation and amended and restated bylaws could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or other employees.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim for breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws or (iv) any action asserting a claim governed by the internal affairs doctrine. This provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated bylaws provide the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation and our amended and restated bylaws. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

Our amended and restated certificate of incorporation and amended and restated bylaws further provide any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the foregoing provisions. These exclusive forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers and other employees. If a court were to find either exclusive-forum provision to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving the dispute in other jurisdictions, all of which could seriously harm our business.

General Risk Factors

Our business and operations would suffer in the event of computer system failures, cyber-attacks or a 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, malware, supply chain attacks, ransomware attacks, natural disasters, terrorism, war, telecommunication and 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. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in obtaining

marketing approval for our drug candidates and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach was to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur material legal claims and liability, damage to our reputation, and the further development or commercialization of our drug candidates by a potential third-party partner could be delayed.

An active trading market for our common stock may not be sustained.

Although our common stock is listed on The Nasdaq Global Select Market, we cannot assure you that an active trading market for our shares will be sustained. If an active market for our common stock is not sustained, it may be difficult for investors in our common stock to sell shares without depressing the market price for the shares or to sell the shares at all.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock is influenced by the research and reports that equity research analysts publish about us or our business, our market and our competitors. Equity research analysts may elect not to initiate or continue to provide research coverage of our common stock, and such lack of research coverage may adversely affect the market price of our common stock. Even if we have equity research analyst coverage, we will not have any control over the analysts or the content and opinions included in their reports. The price of our stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which in turn could cause our stock price or trading volume to decline.

Environmental, social and governance matters may impact our business and reputation.

Increasingly, in addition to the importance of their financial performance, companies are being judged by their performance on a variety of environmental, social and governance, or ESG, matters, which are considered to contribute to the long-term sustainability of companies' performance.

A variety of organizations measure the performance of companies on such ESG topics, and the results of these assessments are widely publicized. In addition, investment in funds that specialize in companies that perform well in such assessments are increasingly popular, and major institutional investors have publicly emphasized the importance of such ESG measures to their investment decisions. Topics taken into account in such assessments include, among others, the company's efforts and impacts on climate change and human rights, ethics and compliance with law, and the role of the company's board of directors in supervising various sustainability issues. In addition to the topics typically considered in such assessments, in the healthcare industry, issues of the public's ability to access medicines are of particular importance.

In light of investors' increased focus on ESG matters, there can be no certainty that we will manage such issues successfully. Any failure or perceived failure by us in this regard could have a material adverse effect on our reputation and on our business, stock price, financial condition, or results of operations, including the sustainability of our business over time.

Unfavorable conditions, including inflationary pressure, in the global economy could limit our ability to grow our business and negatively affect our operating results.

General worldwide economic conditions have experienced significant instability in recent years including the recent global economic uncertainty and financial market conditions. For example, inflation rates, particularly in the United States and United Kingdom, have increased recently to levels not seen in years, and increased inflation may result in increases in our operating costs (including our labor costs), reduced liquidity and limits on our ability to access credit or otherwise raise capital. In addition, the Federal Reserve has raised, and may again raise, interest rates in response to concerns about inflation, which coupled with reduced government spending and volatility in financial markets may have the effect of further increasing economic uncertainty and heightening these risks. Additionally, financial markets around the world experienced volatility following the invasion of Ukraine by Russia in February 2022. These conditions make it extremely difficult for us to accurately forecast and plan future business activities.

The issuance of additional stock in connection with financings, acquisitions, investments, our equity incentive plan or otherwise will dilute all other stockholders.

Our certificate of incorporation authorizes us to issue up to 100,000,000 shares of common stock and up to 10,000,000 shares of preferred stock with such rights and preferences as may be determined by our board of directors. Subject to compliance with applicable rules and regulations, we may issue our shares of common stock or securities convertible into our common stock from time to time in connection with a financing, acquisition, investment, our equity incentive plan or otherwise. Any such issuance could result in substantial dilution to our existing stockholders and cause the trading price of our common stock to decline.

Changes in tax laws or regulations that are applied adversely to us may have a material adverse effect on our business, cash flow, financial condition or results of operations.

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business operations and financial performance. For example, the United States recently passed the Inflation Reduction Act, which provides for a minimum tax equal to 15% of the adjusted financial statement income of certain large corporations, as well as a 1% excise tax on certain share buybacks by public corporations that would be imposed on such corporations. In addition, it is uncertain if and to what extent various states will conform to newly enacted federal tax legislation. Changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, the taxation of foreign earnings, and the deductibility of expenses could have a material impact on the value of our deferred tax assets, could result in significant one-time charges, and could increase our future U.S. tax expense.

We incur significant costs and demands upon management as a result of being a public company.

As a public company listed in the United States, we incur, and will continue to incur, particularly now that we no longer qualify as a "smaller reporting company," significant legal, accounting and other costs. These costs could negatively affect our financial results. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure, including regulations implemented by the SEC and The Nasdaq Stock Market, may increase legal and financial compliance costs and make some activities more time-consuming. These laws, regulations and standards are subject to varying interpretations and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities. If notwithstanding our efforts to comply with new laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

Failure to comply with these rules might also make it more difficult for us to obtain some types of insurance, including director and officer liability insurance, and we might be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, on committees of our board of directors or as members of senior management.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We sublease 33,019 square feet of space for our headquarters in Wayne, Pennsylvania, which we use for our therapeutics business. The sublease has a term through October 2023. If for any reason the master lease is terminated or expires prior to October 2023, our sublease will automatically terminate.

We also sublease 26,694 square feet of office and laboratory space in St. Louis, Missouri, which we use for our therapeutics and contract research businesses. The sublease has an initial term through June 2029. We have the option to extend the initial term for two additional five-year periods.

We believe that our facilities are suitable and adequate to meet our current needs.

Item 3. Legal Proceedings

From time to time we are subject to litigation and claims arising in the ordinary course of business including intellectual property and product liability litigation. We are not currently a party to any material legal proceedings and we are not aware of any other pending or threatened legal proceeding against us that we believe could have a material adverse effect on our business, operating results, cash flows 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 for Common Stock

Our common stock is listed on the Nasdaq Global Select Market under the symbol "ACRS."

Dividend Policy

We have never declared or paid any dividends on our common stock. We anticipate that we will retain all of our future earnings, if any, for use in the operation and expansion of our business and do not anticipate paying cash dividends in the foreseeable future.

Stockholders

As of January 31, 2023, we had 66,692,964 shares of common stock outstanding held by 48 holders of record. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Recent Sales of Unregistered Securities

None.

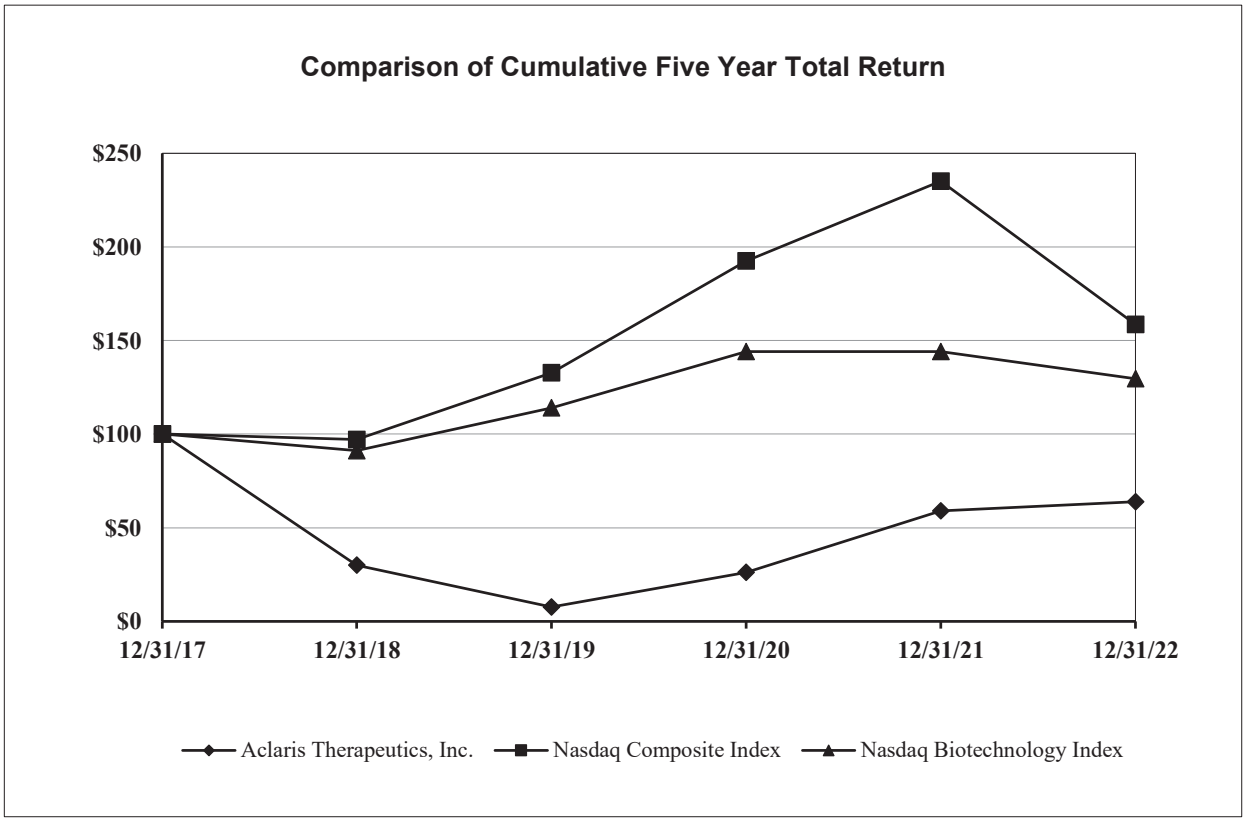
Purchases of Equity Securities by the Issuer and Affiliated Parties

None.

Stock Performance Graph

The graph below compares the cumulative total stockholder return for the period December 31, 2017 through December 31, 2022 for (i) our common stock, (ii) the Nasdaq Biotechnology Index and (iii) the Nasdaq Composite Index. The graph assumes an investment of $100 on December 31, 2017 in each of our common stock, the Nasdaq Biotechnology Index and the Nasdaq Composite Index and the reinvestment of dividends, if any, although we have never declared or paid any dividends on our common stock. The stock price performance shown on the graph below is based on historical data and is not indicative of future stock price performance.

The graph and table below shall not be deemed "soliciting material" or to be "filed" with the SEC for purposes of Section 18 of the Exchange Act or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act or the Exchange Act.



	12/31/17	12/31/18	12/31/19	12/31/20	12/31/21	12/31/22
Aclaris Therapeutics, Inc.	$ 100.00	$ 29.97	$ 7.66	$ 26.24	$ 58.96	$ 63.87
Nasdaq Composite Index	$ 100.00	$ 97.16	$ 132.81	$ 192.47	$ 235.15	$ 158.65
Nasdaq Biotechnology Index	$ 100.00	$ 91.14	$ 114.02	$ 144.15	$ 144.18	$ 129.59

Item 6. [Reserved]

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

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with the consolidated financial statements and the related notes to those statements included later in this Annual Report. In addition to historical financial information, the following discussion contains forward-looking statements that reflect our plans, estimates, beliefs and expectations that involve risks and uncertainties. Our actual results and the timing of events could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to these differences include those discussed below and elsewhere in this Annual Report, particularly in Part I, Item 1A. "Risk Factors," and "Special Note Regarding Forward-Looking Statements."

Overview

We are a clinical-stage biopharmaceutical company focused on developing novel drug candidates for immuno-inflammatory diseases. In addition to developing our novel drug candidates, we are pursuing strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our novel drug candidates.

Clinical Programs

Zunsemetinib, an Investigational Oral MK2 Inhibitor

We are developing zunsemetinib, an investigational oral, novel, small molecule selective MK2 inhibitor, as a potential for the treatment for rheumatoid arthritis, hidradenitis suppurativa and psoriatic arthritis. MK2 is a key regulator of pro-inflammatory mediators including TNFα, IL1β, IL6, IL8, IL17 and other essential pathogenic signals in chronic immuno-inflammatory diseases, as well as in oncology. As an oral drug candidate, we are developing zunsemetinib as a potential alternative to injectable anti-TNF/IL1/IL6/IL17 biologics and JAK inhibitors for treating certain immuno-inflammatory diseases. Zunsemetinib has been adopted as the nonproprietary name for ATI-450.

Moderate to Severe Rheumatoid Arthritis

In December 2021, we initiated a Phase 2b randomized, multicenter, double-blind, parallel group, placebo-controlled, dose-ranging trial to investigate the efficacy, safety, tolerability, pharmacokinetics and pharmacodynamics of multiple doses (20 mg and 50 mg twice daily) of zunsemetinib in combination with methotrexate in subjects with moderate to severe rheumatoid arthritis (ATI-450-RA-202). This trial consists of a 12-week treatment period and a 30-day follow-up period, and seeks to enroll approximately 240 subjects in the United States and in multiple countries in Europe. The primary endpoint is the proportion of subjects achieving ACR20 at week 12. We expect topline data in the second half of 2023.

Moderate to Severe Hidradenitis Suppurativa

In December 2021, we initiated a Phase 2a, randomized, multicenter, double-blind, placebo-controlled trial to investigate the efficacy, safety, tolerability, pharmacokinetics and pharmacodynamics of zunsemetinib (50 mg twice daily) in subjects with moderate to severe hidradenitis suppurativa (ATI-450-HS-201). This trial consists of a 12-week treatment period and a 30-day follow-up period. The primary endpoint is the change in inflammatory nodule and abscess count at week 12. The trial has completed enrollment with 95 subjects randomized in the United States. We expect topline data in March of 2023.

Moderate to Severe Psoriatic Arthritis

In June 2022, we initiated a Phase 2a, randomized, multicenter, double-blind, placebo-controlled trial to investigate the efficacy, safety, tolerability, pharmacokinetics and pharmacodynamics of zunsemetinib (50 mg twice daily) in subjects with moderate to severe psoriatic arthritis (ATI-450-PsA-201). This trial consists of a 12-week treatment period and a 30-day follow-up period, and seeks to enroll approximately 70 subjects in the United States and in Poland. The primary endpoint is the proportion of subjects achieving ACR20 at week 12. We expect topline data by the end of 2023.

ATI-1777, an Investigational Topical "Soft" JAK 1/3 Inhibitor

We are developing ATI-1777, an investigational topical "soft" JAK 1/3 inhibitor, as a potential treatment for moderate to severe atopic dermatitis. "Soft" JAK inhibitors are designed to be topically applied and active in the skin, but rapidly metabolized and inactivated when they enter the bloodstream, which may result in low systemic exposure.

In May 2022, we initiated a Phase 2b, multicenter, randomized, double-blind, vehicle-controlled, parallel-group trial to determine the efficacy, safety, tolerability and pharmacokinetics of ATI-1777 in subjects with moderate to severe atopic dermatitis (ATI-1777-AD-202). In this trial, we are exploring multiple concentrations of twice daily treatment with ATI-1777 and a single concentration of once daily treatment with ATI-1777, in patients 12 years and older. This trial consists of a 4-week treatment period and a 2-week follow-up period, and seeks to enroll approximately 240 subjects in the United States. The primary endpoint is the percentage change from baseline in EASI score at week 4. We expect topline data mid-2023.

ATI-2138, an Investigational Oral Covalent ITK/JAK3 Inhibitor

We are developing ATI-2138, an investigational oral covalent ITK/JAK3 inhibitor, as a potential treatment for T cell-mediated autoimmune diseases. The ITK/JAK3 compound interrupts T cell signaling through the combined inhibition of ITK/JAK3 pathways in lymphocytes. We have selected ulcerative colitis as the intended first clinical development target for ATI-2138. We are also exploring additional indications that are relevant to the mechanism of action.

In October 2022, we submitted a new IND for ATI-2138 for the treatment of ulcerative colitis, which was allowed by the FDA in November 2022. In December 2022, we initiated a Phase 1 placebo-controlled, randomized, multiple ascending dose (MAD) trial to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of ATI-2138 in healthy volunteers (ATI-2138-PKPD-102). This trial seeks to enroll approximately 60 healthy volunteers in the United States. We expect topline data in the second half of 2023.

Preclinical Programs

ATI-2231, an Investigational Oral MK2 Inhibitor

We are exploring the use of ATI-2231, an investigational oral MK2 inhibitor designed to have a long half-life, as a potential treatment for pancreatic cancer and metastatic breast cancer as well as in preventing bone loss in patients with metastatic breast cancer. We expect clinical development activities to be initiated in 2023, which we expect to advance as a collaboration with an academic third party.

Discovery Programs

We are developing oral gut-biased JAK inhibitors with limited systemic exposure as potential treatments for inflammatory bowel disease. In addition, we are engaged in research to identify brain penetrant kinase inhibitor candidates as potential treatments for neurodegenerative diseases.

Financial Overview

Since our inception, we have incurred significant net losses. Our net loss was $86.9 million for the year ended December 31, 2022 and $90.9 million for the year ended December 31, 2021. As of December 31, 2022, we had an accumulated deficit of $682.3 million. We expect to incur significant expenses and operating losses for the foreseeable future as we advance our drug candidates from discovery through preclinical and clinical development. In addition, our drug candidates, even if they are approved by regulatory agencies for marketing, may not achieve commercial success. We may also not be successful in pursuing strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize our drug candidates. Furthermore, we have incurred and expect to continue to incur significant costs associated with operating as a public company, including legal, accounting, investor relations and other expenses. We also expect to add additional personnel to support our operational plans and strategic direction. As a result, we will need substantial additional funding to support our continuing operations.

We have historically financed our operations primarily with sales of equity securities and incurring indebtedness in the form of loans from commercial lenders. In the near term, we expect to finance our operations through these and other capital sources, including potential partnerships with other companies or other strategic transactions. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on commercially acceptable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back or discontinue the development of one or more of our drug candidates.

Impact of Macroeconomic Conditions on Our Business

Unfavorable conditions in the economy both in the United States and abroad may negatively affect the growth of our business and our results of operations. For example, macroeconomic events, including the COVID-19 pandemic, rising inflation, the U.S. Federal Reserve raising interest rates and the Russia-Ukraine war, have led to economic uncertainty globally. The effect of macroeconomic conditions may not be fully reflected in our results of operations until future periods. If, however, economic uncertainty increases or the global economy worsens, our business, financial condition and results of operations may be harmed. For further discussion of the potential impacts of macroeconomic events on our business, financial condition, and operating results, see the section titled "Risk Factors."

Acquisition and License Agreements

Agreement and Plan of Merger with Confluence

In 2017, we entered into an Agreement and Plan of Merger, or the Confluence Agreement, with Confluence Life Sciences, Inc. (now known as Aclaris Life Sciences, Inc.), or Confluence, Aclaris Life Sciences, Inc., our wholly-owned subsidiary, or Merger Sub, and Fortis Advisors LLC, as representative of the equity holders of Confluence. Pursuant to the terms of the Confluence Agreement, Merger Sub merged with and into Confluence, with Confluence surviving as our wholly-owned subsidiary.

Under the Confluence Agreement, we have agreed to pay the former Confluence equity holders aggregate remaining contingent consideration of up to $75.0 million based upon the achievement of specified regulatory and commercial milestones set forth in the Confluence Agreement. In addition, we have agreed to pay the former Confluence equity holders future royalty payments calculated as a low single-digit percentage of annual net sales, subject to specified reductions, limitations and other adjustments, until the date that all of the patent rights for that product have expired, as determined on a country-by-country and product-by-product basis or, in specified circumstances, ten years from the first commercial sale of such product. In addition to the payments described above, if we sell, license or transfer any of the intellectual property acquired from Confluence pursuant to the Confluence Agreement to a third party, we will be obligated to pay the former Confluence equity holders a portion of any consideration received from such sale, license or transfer in specified circumstances.

Asset Purchase Agreement with EPI Health

In 2019, we entered into an asset purchase agreement with EPI Health, LLC, or EPI Health, pursuant to which we sold the worldwide rights to RHOFADE (oxymetazoline hydrochloride) cream, 1%, or RHOFADE, which included the assignment of certain licenses for related intellectual property assets, or the Disposition.

Pursuant to the asset purchase agreement, EPI Health paid us closing consideration of $35.2 million. In addition, EPI Health has agreed to pay us (i) potential sales milestone payments of up to $20.0 million in the aggregate upon the achievement of specified levels of net sales of products covered by the agreement, (ii) a specified high single-digit royalty calculated as a percentage of net sales, on a product-by-product and country-by-country basis, until the date that the patent rights related to a particular product, such as RHOFADE, have expired, provided, that with respect to sales of RHOFADE in any territory outside of the United States, such royalty shall be paid on a country-by-country basis until the date that the RHOFADE patent rights in the particular country have expired or, if later, 10 years from the date of the first commercial sale of RHOFADE in such country and (iii) 25% of any upfront, license, milestone, maintenance or fixed payment received by EPI Health in connection with any license or sublicense of the assets transferred in the Disposition in any territory outside of the United States, subject to specified exceptions. In addition, EPI Health has agreed to assume our obligation to pay specified royalties and milestone payments under certain agreements with third parties.

License Agreement with Eli Lilly and Company

In August 2022, we entered into a non-exclusive patent license agreement with Eli Lilly and Company, or Lilly. Under the license agreement, we granted Lilly non-exclusive rights under certain patents and patent applications that we exclusively license from a third party. The patents and patent applications relate to the use of baricitinib, Lilly's JAK inhibitor, to treat alopecia areata. Under the license agreement, Lilly has agreed to pay us an upfront payment, regulatory and commercial milestone payments, anniversary payments, and a low single-digit royalty calculated as a percentage of Lilly's net sales of baricitinib for the treatment of alopecia areata. We have separate contractual obligations under which we have agreed to pay to third parties an amount equal to any regulatory and commercial milestone payments we receive under the Lilly license agreement, as well as a portion of the upfront consideration and a portion of the royalties we may receive under the license agreement.

Upon execution of the agreement, we received $17.6 million from Lilly, a portion of which represented payments for regulatory and commercial milestones that were deemed to have been achieved as of the execution of the license agreement. We remain eligible to receive future milestone payments, all of which will be paid by us to third parties following receipt as described above. We recorded amounts paid to third parties of $7.3 million during the year ended December 31, 2022.

During the year ended December 31, 2022, we received $0.2 million in royalties from Lilly, a portion of which was payable to third parties.

License Agreement with Pediatrix Therapeutics, Inc.

In November 2022, we entered into a license agreement with Pediatrix Therapeutics, Inc., or Pediatrix, under which we granted Pediatrix the exclusive rights to develop, manufacture and commercialize ATI-1777 in Greater China. Pediatrix has agreed to pay us an upfront payment, development, regulatory and commercial milestone payments, and a tiered royalty ranging from a low-to-high single digit percentage of net sales of ATI-1777 by Pediatrix in Greater China. A portion of consideration received from Pediatrix is payable to the former Confluence equity holders as described above.

Upon execution of the agreement, we received an upfront payment of $5.0 million from Pediatrix, a portion of which was payable to the former Confluence equity holders as described above.

Components of Our Results of Operations

Revenue

Contract Research

We earn revenue from the provision of laboratory services. Contract research revenue is generally evidenced by contracts with clients which are on an agreed upon fixed-price, fee-for-service basis and are generally billed on a monthly basis in arrears for services rendered.

Licensing

Licensing revenue primarily consists of upfront consideration, royalties and milestone payments earned pursuant to license and acquisition agreements with third parties, as described above.

Other

Other revenue consists of amounts earned from the sub-sublease of our office space, which was terminated during the year ended December 31, 2022.

Cost and Expenses

Cost of Revenue

Cost of revenue consists of the costs incurred in connection with the provision of contract research services. Cost of revenue primarily includes:

- employee-related expenses, which include salaries, benefits and stock-based compensation;
- outsourced professional scientific services;
- depreciation of laboratory equipment;
- facility-related costs; and
- laboratory materials and supplies used to support the services provided.

Research and Development

Research and development expenses consist of expenses incurred in connection with the discovery and development of our drug candidates. These expenses primarily include:

- expenses incurred under agreements with contract research organizations, or CROs, as well as clinical trial sites and consultants that conduct our clinical trials and preclinical studies, and investigator-initiated trials;
- manufacturing scale-up expenses and the cost of acquiring and manufacturing active pharmaceutical ingredients and preclinical and clinical trial materials, including domestic technology transfer expenses;
- quality assurance and quality control costs;
- outsourced professional scientific development services;
- medical affairs expenses related to our drug candidates;
- employee-related expenses, which include salaries, benefits and stock-based compensation;
- payments made under agreements with third parties under which we have acquired or licensed intellectual property;
- expenses relating to regulatory activities, including filing fees paid to regulatory agencies; and
- laboratory materials and supplies used to support our research activities.

Research and development activities are central to our business model. Drug candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect to continue to incur research and development expenses in the near term as we continue the clinical development of zunsemetinib as a potential treatment for moderate to severe rheumatoid arthritis, moderate to severe hidradenitis suppurativa and moderate to severe psoriatic arthritis, ATI-1777 as a potential treatment for moderate to severe atopic dermatitis, ATI-2138 as a potential treatment for T cell-mediated autoimmune diseases, ATI-2231 as a potential treatment for pancreatic cancer and metastatic breast cancer as well as in preventing bone loss in patients with metastatic breast cancer, and as we continue the development of our preclinical compounds and discover and develop additional drug candidates. We expense research and development costs as incurred. Our direct research and development expenses primarily consist of external costs including fees paid to CROs, consultants, clinical trial sites, regulatory agencies and third parties that manufacture our preclinical and clinical trial materials and are tracked on a program-by-program basis. We do not allocate personnel costs or other indirect expenses to specific research and development programs.

The successful development of our drug candidates is highly uncertain. We cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the remainder of the development of, or when, if ever, material net cash inflows may commence from any of our drug candidates. This uncertainty is due to the numerous risks and uncertainties associated with the duration and cost of clinical trials, which vary significantly over the life of a project as a result of many factors, including:

- the number of clinical sites included in the trials;
- the length of time required to enroll suitable subjects;
- the number of subjects that ultimately participate in the trials;
- the number of doses subjects receive;

- the impact on the recruitment, enrollment, conduct and timing of our clinical trials due to the COVID-19 pandemic;
- the duration of subject follow-up; and
- the results of our clinical trials.

Our expenditures are subject to additional uncertainties, including the preparation of regulatory filings for our drug candidates. We may obtain unexpected results from our clinical trials or other development activities. We may elect to discontinue, delay or modify the development, including clinical trials, of some drug candidates or focus on others. A change in the outcome of any of these variables with respect to the development of a drug candidate could mean a significant change in the costs and timing associated with the development of that drug candidate. For example, if the FDA or other regulatory authorities were to require us to conduct clinical trials beyond those that we currently anticipate, or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

General and Administrative

General and administrative expenses consist principally of salaries and related costs, including stock-based compensation, for personnel in executive, administrative, finance and legal functions. General and administrative expenses also include facility-related costs, patent filing and prosecution costs, professional fees for legal, auditing and tax services, investor relations costs, business development costs, insurance costs and travel expenses.

Licensing

Licensing expenses consist of third-party contractual obligations incurred under license and acquisition agreements with third parties, as described above.

Revaluation of Contingent Consideration

Revaluation of contingent consideration consists of changes in the fair value of our contingent consideration liability between reporting dates.

Other Income (Expense), Net

Other income (expense), net primarily consists of interest earned on our cash, cash equivalents and marketable securities and in prior periods included interest expense related to debt obligations.

Critical Accounting Estimates

This discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements which have been prepared in accordance with generally accepted accounting principles in the United States. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of expenses during the reported period. We base our estimates on historical experience, known trends and events and various other factors that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and judgments on an ongoing basis. Our actual results may differ 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 on Form 10-K, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Intangible Assets

Our intangible assets include both definite-lived and indefinite-lived assets. Our definite-lived intangible assets consist of a drug discovery platform acquired through the acquisition of Confluence. Definite-lived intangible assets are amortized over their estimated useful life based on the pattern over which the intangible assets are consumed or otherwise

used up. If that pattern cannot be reliably determined, the straight-line method of amortization is used. Our indefinite-lived intangible assets consist of an in-process research and development, or IPR&D, drug candidate also acquired through the acquisition of Confluence. IPR&D assets are considered indefinite-lived until the completion or abandonment of the associated research and development efforts. The cost of IPR&D assets is either amortized over their estimated useful life beginning when the underlying drug candidate is approved and launched commercially, or expensed immediately if development of the drug candidate is abandoned.

Definite-lived intangible assets are tested for impairment when events or changes in circumstances indicate that the carrying value of the asset may not be recoverable. Indefinite-lived intangible assets are tested for impairment at least annually, which we perform during the fourth quarter, or when indicators of an impairment are present. We recognize an impairment loss when and to the extent that the estimated fair value of an intangible asset is less than its carrying value. The fair value of an intangible asset is dependent on significant unobservable inputs including the estimated future cash flows of the asset.

There were no impairment losses recorded during the years ended December 31, 2022 and 2021.

Contingent Consideration

We initially recorded a contingent consideration liability at fair value on the date of acquisition related to future potential payments resulting from the acquisition of Confluence based upon significant unobservable inputs including the achievement of development, regulatory and commercial milestones, as well as estimated future sales levels and the discount rates applied to calculate the present value of the potential payments. Significant judgement was involved in determining the appropriateness of these assumptions. These assumptions are considered Level 3 inputs. Revaluation of our contingent consideration liability can result from changes to one or more of these assumptions. These assumptions are highly dependent on the outcome and timing of the development of our drug candidates. We evaluate the fair value estimate of our contingent consideration liability on a quarterly basis with changes, if any, recorded as income or expense in our consolidated statement of operations. Any such changes could have a material impact on our financial results.

The fair value of contingent consideration is estimated using a probability-weighted expected payment model for regulatory milestone payments and a Monte Carlo simulation model for commercial milestone and royalty payments and then applying a risk-adjusted discount rate to calculate the present value of the potential payments. Significant assumptions used in our estimates include the probability of achieving regulatory milestones and commencing commercialization, which are based on an asset's current stage of development and a review of existing clinical data. Probability of success assumptions ranged between 10% and 40% at December 31, 2022 and 2021. Additionally, estimated future sales levels and the risk-adjusted discount rate applied to the potential payments are also significant assumptions used in calculating the fair value. The discount rate ranged between 9.8% and 10.2% depending on the year of each potential payment.

During the year ended December 31, 2022, we updated future sales level assumptions for zunsemetinib. These changes, and the impact from the passage of time, resulted in a net charge of $4.7 million during the year ended December 31, 2022.

Stock-Based Compensation

We measure the compensation expense of stock-based awards granted to employees and directors using the grant date fair value of the award. We have issued stock options and restricted stock unit, or RSU, awards with service-based vesting conditions, as well as with performance-based vesting conditions. We have not issued awards that include market-based conditions. For service-based awards, we recognize stock-based compensation expense on a straight-line basis over the requisite service period. For performance-based awards, we recognize stock-based compensation expense on a straight-line basis over the requisite service period beginning in the period that it becomes probable the performance conditions will occur. At each balance sheet date, we evaluate whether any performance conditions related to a performance-based award have changed. The effect of any change in performance conditions would be recognized as a cumulative catch-up adjustment in the period such change occurs, and any remaining unrecognized compensation expense would be recognized on a straight-line basis over the remaining requisite service period. The impact of forfeitures is recognized in the period in which they occur.

We measure the compensation expense of stock-based awards granted to consultants using the grant date fair value of the award. We recognize compensation expense over the period during which services are rendered by the consultant.

We estimate the fair value of each stock option grant using the Black-Scholes option-pricing model. Historically, we estimated expected volatility based on historical volatility of a set of peer companies, which are publicly traded. Starting in 2022, we estimated expected volatility based on our stock price's historical volatility, as we determined that we had adequate historical data regarding the volatility of our own publicly-traded stock price. The expected term of our stock options has been determined using the "simplified" method for awards that qualify as "plain vanilla" options. The expected term of stock options we granted to non-employees is equal to the contractual term of the option award. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. We use an expected dividend yield of zero because we have not paid cash dividends to date, and have no intention of paying cash dividends in the future.

The fair value of each RSU is measured using the closing price of our common stock on the date of grant.

Income Taxes

Since our inception, we have not recorded U.S. federal or state income tax benefits for the net operating losses we have incurred in each year or for our earned research and development tax credits, due to our uncertainty of realizing a benefit from those items.

Results of Operations

For discussion on financial condition and results of operations pertaining to the year ended December 31, 2021 compared to the year ended December 31, 2020, see our Annual Report on Form 10-K for the year ended December 31, 2021, Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

Comparison of Years Ended December 31, 2022 and 2021

(In thousands)	Year Ended December 31, 2022	2021	Change
Revenues:			
Contract research	$ 4,395	$ 5,830	**$ (1,435)**
Licensing	25,100	809	**24,291**
Other	257	122	**135**
Total revenue	29,752	6,761	**22,991**
Costs and expenses:			
Cost of revenue	4,023	4,713	**(690)**
Research and development	77,813	43,813	**34,000**
General and administrative	25,133	23,619	**1,514**
Licensing	7,937	—	**7,937**
Revaluation of contingent consideration	4,700	24,339	**(19,639)**
Total costs and expenses	119,606	96,484	**23,122**
Loss from operations	(89,854)	(89,723)	**(131)**
Other income (expense), net	2,946	(1,142)	**4,088**
Net loss	$ (86,908)	$ (90,865)	**$ 3,957**

Revenue

Contract Research

Contract research revenue was $4.4 million and $5.8 million for the years ended December 31, 2022 and 2021, respectively, and was comprised of fees earned from the provision of laboratory services to our clients. The decrease was driven by lower overall hours billed, partially due to an increased focus on internal development programs, which was offset by a higher average billing rate.

Licensing

Licensing revenue was $25.1 million and $0.8 million for the years ended December 31, 2022 and 2021, respectively. The increase was primarily driven by $17.6 million of upfront and milestone payments received under the Lilly agreement and the $5.0 million upfront payment received under the Pediatrix agreement.

Cost and Expenses

Cost of Revenue

Cost of revenue was $4.0 million and $4.7 million for the years ended December 31, 2022 and 2021, respectively, and in each case related to providing laboratory services to our clients. Changes in cost of revenue generally correlate to changes in contract research revenue. Cost of revenue decreased during the year ended December 31, 2022 due to lower variable costs resulting from the decrease in hours billed, partially offset by an increase in fixed overhead costs, including personnel-related costs.

Research and Development

The following table summarizes our research and development expenses by drug candidate or, for unallocated expenses, by type:

	Year Ended December 31,		
(In thousands)	2022	2021	Change
Zunsemetinib	$ 28,133	$ 17,887	$ 10,246
ATI-1777	12,113	2,439	9,674
ATI-2138	7,704	4,114	3,590
ATI-2231	4,828	2,949	1,879
Discovery	4,564	3,192	1,372
Other research and development	1,564	1,568	(4)
Personnel	15,162	7,798	7,364
Stock-based compensation	3,745	3,866	(121)
Total research and development expenses	$ 77,813	$ 43,813	$ 34,000

Zunsemetinib

The increase in expenses for zunsemetinib during the year ended December 31, 2022 compared to the year ended December 31, 2021 was primarily due to costs associated with clinical development activities for a Phase 2b trial in subjects with rheumatoid arthritis, which initiated in December 2021, a Phase 2a trial in subjects with hidradenitis suppurativa, which initiated in December 2021, a Phase 2a trial in subjects with psoriatic arthritis, which initiated in June 2022, and several ancillary clinical trials.

ATI-1777

The increase in expenses for ATI-1777 during the year ended December 31, 2022 compared to the year ended December 31, 2021 was primarily due to higher costs associated with drug candidate manufacturing and other preclinical development activities as well as costs associated with a Phase 2b clinical trial in subjects with atopic dermatitis. Lower

costs associated with a Phase 2a clinical trial in subjects with atopic dermatitis, which commenced in 2020 and concluded in 2021, partially offset the overall increase in expenses.

ATI-2138

Expenses for ATI-2138 were higher during the year ended December 31, 2022 compared to the year ended December 31, 2021 primarily due higher costs associated with preclinical development activities as well as costs associated with a Phase 1 SAD trial, which initiated in December 2021, and a Phase 1 MAD trial, which initiated in December 2022.

ATI-2231

Expenses for ATI-2231 were higher during the year ended December 31, 2022 compared to the year ended December 31, 2021 primarily due to preclinical development activities and IND-enabling studies as we progressed the program toward IND submission.

Discovery

Expenses related to discovery increased during the year ended December 31, 2022 compared to the year ended December 31, 2021 due to continued investment in our discovery-stage programs as we progressed programs toward candidate selection.

Personnel and stock-based compensation

Personnel and stock-based compensation expenses increased in the aggregate during the year ended December 31, 2022 compared to the year ended December 31, 2021 primarily due to an increase in costs associated with higher average headcount, which was partially offset by a decrease in stock-based compensation expense mainly attributable to forfeiture credits recorded during the period.

General and Administrative

The following table summarizes our general and administrative expenses:

	Year Ended December 31,		
(In thousands)	**2022**	**2021**	**Change**
Personnel	$ 6,028	$ 4,887	$ 1,141
Professional and legal fees	4,319	5,249	(930)
Facility and support services	2,302	1,984	318
Other general and administrative	2,341	2,286	55
Stock-based compensation	10,143	9,213	930
Total general and administrative expenses	$ 25,133	$ 23,619	$ 1,514

Personnel and stock-based compensation

Personnel and stock-based compensation expenses increased during the year ended December 31, 2022 compared to December 31, 2021 primarily due to higher average headcount and an increase in stock-based compensation expense associated with new equity awards granted in 2022, partially offset by lower costs associated with the separation of executive officers.

Professional and legal fees

Professional and legal fees, including accounting, investor relations and corporate communication costs, were lower during the year ended December 31, 2022 compared to the year ended December 31, 2021 primarily as a result of lower accounting and other professional expenses due to a reduction in temporary staffing costs.

Facility and support services

Facility and support services, including general office expenses, information technology costs and other expenses, increased during the year ended December 31, 2022 compared to the year ended December 31, 2021 primarily due to an increase in overhead expenses, including increases in tax and license fees and information technology support costs.

Licensing

We incurred licensing expense during the year ended December 31, 2022 due to amounts payable to third parties under third-party license and acquisition agreements. We did not incur licensing expense during the year ended December 31, 2021.

Revaluation of Contingent Consideration

The fair value of our contingent consideration liability increased during the year ended December 31, 2022 mainly due to an increase in future sales level assumptions for zunsemetinib and the passage of time.

The fair value of our contingent consideration liability increased during the year ended December 31, 2021 primarily from updates to the probability of success and estimated future sales level assumptions as a result of the completion of a Phase 2a clinical trial of zunsemetinib in subjects with rheumatoid arthritis, as well as the completion of a Phase 2a clinical trial of ATI-1777 in subjects with atopic dermatitis. Additionally, the inclusion of estimated future sales of zunsemetinib as a potential treatment for hidradenitis suppurativa and psoriatic arthritis, which are additional planned indications for zunsemetinib, also contributed to the increase during the year ended December 31, 2021.

Other Income (Expense), net

Other income (expense), net increased during the year ended December 31, 2022 compared to the year ended December 31, 2021 primarily due to there being no interest expense associated with the Loan and Security Agreement with Silicon Valley Bank, or SVB, which was repaid in July 2021, and higher interest income on investment portfolio balances.

Liquidity and Capital Resources

Overview

Since our inception, we have incurred net losses and negative cash flows from our operations. Prior to our acquisition of Confluence in August 2017, we did not generate any revenue. We have financed our operations over the last several years primarily through sales of our equity securities and incurring indebtedness in the form of loans from commercial lenders. We may engage in additional debt and equity financing transactions in order to raise funds. We may receive royalties and milestone payments from third-party licensing and acquisition agreements. In addition, to the extent we are able to consummate transactions with potential third-party partners to further develop, obtain marketing approval for and/or commercialize our drug candidates, we may receive upfront payments, milestone payments or royalties from such arrangements that would increase our liquidity.

As of December 31, 2022, we had cash, cash equivalents and marketable securities of $229.8 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view towards liquidity and capital preservation.

We currently have no ongoing material financing commitments, such as lines of credit or guarantees, that are expected to affect our liquidity, other than our contingent obligations under the Confluence Agreement, which is summarized above under “Overview—Acquisition and License Agreements,” and our lease obligations.

Equity Financing

Sale of Common Stock under At-the-Market Facility

In April 2022, we sold 4,838,709 shares of our common stock at a weighted average price per share of $15.50, for aggregate gross proceeds of $75.0 million, pursuant to a sales agreement with SVB Securities LLC and Cantor Fitzgerald & Co., as sales agents, dated May 20, 2021. We paid selling commissions and other fees of $2.2 million in connection with the sale.

June 2021 Public Offering

In June 2021, we closed a public offering in which we sold 8,098,592 shares of common stock at a price to the public of $17.75 per share, for aggregate gross proceeds of $143.8 million. We paid underwriting discounts and commissions of $8.6 million, and also incurred expenses of $0.3 million in connection with the offering. As a result, the net offering proceeds received by us, after deducting underwriting discounts, commissions and offering expenses, were $134.9 million.

January 2021 Public Offering

In January 2021, we closed a public offering in which we sold 6,306,271 shares of common stock at a price to the public of $17.50 per share, for aggregate gross proceeds of $110.4 million. We paid underwriting discounts and commissions of $6.6 million, and also incurred expenses of $0.4 million in connection with the offering. As a result, the net offering proceeds received by us, after deducting underwriting discounts, commissions and offering expenses, were $103.3 million.

Equity Purchase Agreement with Lincoln Park Capital Fund, LLC

In August 2020, we entered into a purchase agreement, or the Purchase Agreement, with Lincoln Park Capital Fund, LLC, or Lincoln Park, which provided that, upon the terms and subject to the conditions and limitations set forth therein, we could sell to Lincoln Park, at our discretion, up to $15.0 million of shares of our common stock over the 36-month term of the Purchase Agreement. Upon execution of the Purchase Agreement, we issued 121,584 shares of our common stock to Lincoln Park as commitment shares in accordance with the closing conditions contained within the Purchase Agreement. The commitment shares were valued using the closing price of our common stock on the effective date of the Purchase Agreement resulting in an aggregate fair value of $0.3 million. Through December 31, 2020, we sold 2,111,170 shares of our common stock to Lincoln Park under the Purchase Agreement for net proceeds of $7.7 million. We terminated the Purchase Agreement in January 2021 in connection with the public offering of common stock described above. We did not sell any additional shares prior to terminating the Purchase Agreement.

Debt Financing

Loan and Security Agreement with Silicon Valley Bank

In March 2020, we entered into a Loan and Security Agreement with SVB. The Loan and Security Agreement provided for $11.0 million in term loans, of which we borrowed the entire amount on March 30, 2020. In July 2021, we repaid in full the $11.0 million that was outstanding under the Loan and Security Agreement, together with all accrued and unpaid interest and fees as of the payoff date, for a total payment of $11.7 million.

Cash Flows

Cash and cash equivalents were $45.3 million as of December 31, 2022 compared to $27.3 million as of December 31, 2021. We also had $184.5 million in short- and long-term marketable securities as of December 31, 2022 compared to $198.3 million as of December 31, 2021.

The sources and uses of cash that contributed to the change in cash and cash equivalents were:

(In thousands)	Year Ended December 31, 2022	2021
Cash and cash equivalents beginning balance	$ 27,349	$ 22,063
Net cash used in operating activities	(67,567)	(52,134)
Net cash provided by (used in) investing activities	12,628	(167,632)
Net cash provided by financing activities	72,867	225,052
Cash and cash equivalents ending balance	$ 45,277	$ 27,349

Operating Activities

Cash flow related to operating activities was the result of:

(In thousands)	Year Ended December 31, 2022	2021
Net loss	$ (86,908)	$ (90,865)
Non-cash adjustments to reconcile net loss to net cash used in operating activities	20,536	40,074
Change in accounts payable and accrued expenses	960	4,125
Change in accounts receivable	139	149
Change in prepaid expenses and other assets	(2,294)	(5,617)
Net cash used in operating activities	$ (67,567)	$ (52,134)

Net cash used in operating activities increased for the year ended December 31, 2022 compared to the year ended December 31, 2021 primarily as a result of higher net losses after adjusting for revaluation of contingent consideration and other non-cash items and an increase in cash paid for prepaid expenses and other assets. This change was partially offset by a decrease in cash paid to settle outstanding accounts payable.

The decrease in non-cash adjustments to reconcile net loss to net cash used in operating activities was mainly the result of a decrease in revaluation of contingent consideration during the year ended December 31, 2022 compared to the year ended December 31, 2021. The decrease in revaluation of contingent consideration during the year ended December 31, 2022 compared to the year ended December 31, 2021 was primarily the result of higher charges during the year ended December 31, 2021 from updates to the probability of success and estimated future sales level assumptions as a result of the completion of a Phase 2a clinical trial of zunsemetinib in subjects with rheumatoid arthritis, as well as the completion of a Phase 2a clinical trial of ATI-1777 in subjects with atopic dermatitis. Additionally, the inclusion of estimated future sales of zunsemetinib as a potential treatment for hidradenitis suppurativa and psoriatic arthritis, which are additional planned indications for zunsemetinib, also contributed to the higher charges during the year ended December 31, 2021.

Investing Activities

Cash flow related to investing activities was the result of:

(In thousands)	Year Ended December 31, 2022	2021
Purchases of property and equipment	$ (605)	$ (308)
Purchases of marketable securities	(164,753)	(235,153)
Proceeds from sales and maturities of marketable securities	177,986	67,829
Net cash provided by (used in) investing activities	$ 12,628	$ (167,632)

The change in net cash provided by investing activities for the year ended December 31, 2022 compared to net cash used in investing activities for the year ended December 31, 2021 primarily resulted from higher sales and maturities of marketable securities during the year ended December 31, 2022, which were used to fund our operations, and a reduction of purchases of marketable securities, which were higher during the year ended December 31, 2021 following our January 2021 and June 2021 public offerings.

Financing Activities

Cash flow related to financing activities was the result of:

(In thousands)	Year Ended December 31, 2022	2021
Proceeds from issuance of common stock in connection with public offerings, net of issuance costs	$ —	$ 238,200
Proceeds from issuance of common stock under the at-the-market sales agreement, net of issuance costs	72,744	—
Repayment of debt	—	(11,483)
Payments of employee withholding taxes related to restricted stock unit award vesting	(34)	(3,124)
Proceeds from exercise of employee stock options and the issuance of stock	157	1,459
Net cash provided by financing activities	$ 72,867	$ 225,052

Cash provided by financing activities decreased for the year ended December 31, 2022 compared to December 31, 2021 primarily due to our January 2021 and June 2021 public offerings, partially offset by the proceeds from our April 2022 sale under the at-the-market sales agreement.

Funding Requirements

We anticipate we will incur net losses in the near term as we continue the clinical development of zunsemetinib as a potential treatment for moderate to severe rheumatoid arthritis, moderate to severe hidradenitis suppurativa and moderate to severe psoriatic arthritis, ATI-1777 as a potential treatment for moderate to severe atopic dermatitis, ATI-2138 as a potential treatment for T cell-mediated autoimmune diseases and ATI-2231 as a potential treatment for pancreatic cancer and metastatic breast cancer as well as in preventing bone loss in patients with metastatic breast cancer, continue the development of our preclinical compounds, and continue to discover and develop additional drug candidates. We may not be able to generate revenue from these programs if, among other things, our clinical trials are not successful, the FDA does not approve our drug candidates currently in clinical trials when we expect, or at all, or we are not able to identify and consummate transactions with third-party partners to further develop, obtain marketing approval for and/or commercialize our drug candidates.

Our primary uses of capital are, and we expect will continue to be, compensation and related expenses, clinical costs, external research and development services, laboratory and related supplies, legal and other regulatory expenses, and administrative and overhead costs. We expect to add additional personnel to support our operational plans and strategic direction. Our future funding requirements will be heavily determined by the resources needed to support the development of our drug candidates.

As a publicly traded company, we incur and will continue to incur significant legal, accounting and other similar expenses. In addition, the Sarbanes-Oxley Act of 2002, as well as rules adopted by the SEC and the Nasdaq Stock Market LLC, requires public companies to implement specified corporate governance practices that could increase our compliance costs.

We believe our existing cash, cash equivalents and marketable securities are sufficient to fund our operating and capital expenditure requirements for a period greater than 12 months from the date of issuance of our consolidated financial statements that appear in Item 8 of this Annual Report on Form 10-K based on our current operating assumptions. We will require additional capital to complete the clinical development of zunsemetinib, ATI-1777 and ATI-2138, to develop our preclinical compounds, and to support our discovery efforts. Additional funds may not be available on a timely basis, on commercially acceptable terms, or at all, and such funds, if raised, may not be sufficient to enable us to continue to implement our long-term business strategy. Our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions caused by a variety of factors including geopolitical tensions, rising interest rates, and inflationary pressures. If we are unable to raise sufficient additional capital or generate revenue from transactions with potential third-party partners for the development and/or commercialization of our drug candidates, we may need to substantially curtail our planned operations.

We may raise additional capital through the sale of equity or debt securities. In such an event, our stockholders' ownership will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of a holder of our common stock.

Because of the numerous risks and uncertainties associated with research and development of pharmaceutical drugs, we are unable to estimate the exact amount of our working capital requirements. Our funding requirements in the near term will depend on many factors, including:

- the number and development requirements of the drug candidates that we may pursue;
- the scope, progress, results and costs of preclinical development, laboratory testing and conducting preclinical and clinical trials for our drug candidates;
- the costs, timing and outcome of regulatory review of our drug candidates;
- the extent to which we in-license or acquire additional drug candidates and technologies;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the impact on the timing of our preclinical studies, the recruitment, enrollment, conduct and timing of our clinical trials and our business due to the COVID-19 pandemic;
- our ability to identify and consummate transactions with third-party partners to further develop, obtain marketing approval for and/or commercialize our drug candidates; and
- our ability to earn revenue as a result of licenses to, or partnerships or other arrangements with, third parties.

See "Risk Factors" for additional risks associated with our substantial capital requirements.

Leases

We occupy space for our headquarters in Wayne, Pennsylvania under a sublease agreement which has a term through October 2023. In December 2020, we entered into a sub-sublease agreement under which we sub-subleased 8,115 square feet. The sub-sublease was terminated in December 2022. We also occupy office and laboratory space in St. Louis, Missouri under a sublease agreement which has a term through June 2029.

Our aggregate remaining lease payment obligations for these two spaces was $2.9 million as of December 31, 2022. In February 2023, we added an additional 6,261 square feet of office and laboratory space in St. Louis.

Agreement and Plan of Merger – Confluence

Under the Confluence Agreement, we agreed to pay the former Confluence equity holders aggregate remaining contingent consideration of up to $75.0 million based upon the achievement of specified regulatory and commercial milestones set forth in the Confluence Agreement. In addition, we have agreed to pay the former Confluence equity holders future royalty payments calculated as a low single-digit percentage of annual net sales, subject to specified reductions, limitations and other adjustments, until the date that all of the patent rights for that product have expired, as determined on a country-by-country and product-by-product basis or, in specified circumstances, ten years from the first commercial sale of such product. In addition to the payments described above, if we sell, license or transfer any of the intellectual property acquired from Confluence pursuant to the Confluence Agreement to a third party, we will be obligated to pay the former Confluence equity holders a portion of any consideration received from such sale, license or transfer in specified circumstances.

R&D Obligations

We enter into contracts in the normal course of business with CROs, contract manufacturing organizations and other service providers for clinical trials, preclinical studies and testing, manufacturing and other services and products for operating purposes. These contracts generally provide for termination upon notice, and therefore we believe that our non-cancelable obligations under these agreements are not material.

Segment Information

We have two reportable segments, therapeutics and contract research. The therapeutics segment is focused on identifying and developing innovative therapies to address significant unmet needs for immuno-inflammatory diseases. The contract research segment earns revenue from the provision of laboratory services.

Recently Issued Accounting Pronouncements

In November 2018, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, 2018-18, Collaborative Arrangements (Topic 808): Clarifying the Interaction Between Topic 808 and Topic 606, which, among other things, provides guidance on how to assess whether certain collaborative arrangement transactions should be accounted for under Topic 606. We adopted this standard as of January 1, 2020, the impact of which on our consolidated financial statements was not significant.

In August 2018, the FASB issued ASU 2018-15, Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40). ASU 2018-15 requires a customer in a cloud computing arrangement that is a service contract to follow the internal-use software guidance in Accounting Standards Codification, or ASC, 350-40 to determine which implementation costs to capitalize as assets or expense as incurred. We adopted this standard as of January 1, 2020, the impact of which on our consolidated financial statements was not significant.

In August 2018, the FASB issued ASU 2018-13, Fair Value Measurement (Topic 820). The FASB developed the amendments to ASC 820 as part of its broader disclosure framework project, which aims to improve the effectiveness of disclosures in the notes to financial statements by focusing on requirements that clearly communicate the most important information to users of the financial statements. This update eliminates certain disclosure requirements for fair value measurements for all entities, requires public entities to disclose certain new information and modifies some of the existing disclosure requirements. We adopted this standard as of January 1, 2020, the impact of which on our consolidated financial statements was not significant.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Our cash equivalents and marketable securities consist of money market funds, asset-backed debt securities, commercial paper, corporate debt securities, U.S. government debt securities and U.S. government agency debt securities. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Our marketable securities are subject to interest rate risk and will fall in value if market interest rates increase. However, due to the short-term nature and low-risk profile of our investment portfolio, we do not expect that an immediate 10% change in market interest rates would have a material effect on the fair market value of our investment portfolio. We have the ability to hold our marketable securities until maturity, and therefore we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments.

Inflation Risk

Inflation generally affects us by increasing our cost of labor. Although inflation has increased generally in the United States in recent months, we do not believe that inflation has had a material effect on our business, financial condition or results of operations during the year ended December 31, 2022.

Item 8. Financial Statements and Supplementary Data

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Aclaris Therapeutics, Inc.

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of Aclaris Therapeutics, Inc. and its subsidiaries (the "Company") as of December 31, 2022 and 2021, and the related consolidated statements of operations and comprehensive loss, of stockholders' equity and of cash flows for each of the three years in the period ended December 31, 2022, including the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2022, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the COSO.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report on Internal Control over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on the Company's consolidated financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

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

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely

detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Critical Audit Matters

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

Fair Value of the Contingent Consideration Liability related to zunsemetinib

As described in Notes 2 and 3 to the consolidated financial statements, the Company's contingent consideration balance was $33.1 million as of December 31, 2022, of which a significant portion of the liability relates to zunsemetinib. Management initially recorded a contingent consideration liability at fair value on the date of acquisition related to future potential payments resulting from the acquisition of Confluence based upon significant unobservable inputs including the achievement of development, regulatory and commercial milestones, as well as estimated future projected sales levels and the discount rates applied to calculate the present value of the potential payments. Management evaluates fair value estimates of the contingent consideration liability on a quarterly basis using a probability-weighted expected payment model for regulatory milestone payments and a Monte Carlo simulation model for commercial milestone and royalty payments and then applying a risk-adjusted discount rate to calculate the present value of the potential payment. Changes in the fair value of the contingent consideration are recorded as income or expense in the Company's consolidated statement of operations and comprehensive loss. Significant assumptions used in management's estimates include the probability of achieving regulatory milestones and commencing commercialization, which are based upon an asset's current stage of development and review of existing clinical data.

The principal considerations for our determination that performing procedures relating to the fair value of the contingent consideration liability related to zunsemetinib is a critical audit matter are (i) the significant judgment by management, when developing the fair value estimate, which in turn led to (ii) a high degree of auditor judgment, subjectivity and effort in performing procedures and evaluating management's significant assumptions related to the probability of achieving regulatory milestones and commencing commercialization. In addition, the audit effort involved the use of professionals with specialized skill and knowledge.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included testing the effectiveness of controls relating to management's contingent consideration evaluation, including controls over the valuation of the Company's contingent consideration liability related to zunsemetinib. These procedures also included, among others, (i) testing management's process for developing the fair value of the contingent consideration liability, (ii) evaluating the appropriateness of the probability-weighted expected payment and Monte Carlo simulation valuation models, (iii) testing the completeness and accuracy of the underlying data used in the models, and (iv) evaluating the reasonableness of the significant assumptions used by management related to the probability of achieving regulatory milestones and commencing commercialization. Evaluating management's assumptions related to the probability of achieving regulatory milestones and commencing commercialization involved evaluating whether the assumptions were reasonable considering the agreements associated with the transaction as well as the consistency with industry information, the stage of product development and whether the assumptions were consistent with evidence obtained in other areas of the audit. Professionals with specialized skill and knowledge were used to assist in the evaluation of the Company's probability-weighted expected payment and Monte Carlo simulation valuation models.

/s/ PricewaterhouseCoopers LLP

Philadelphia, Pennsylvania
February 23, 2023

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

ACLARIS THERAPEUTICS, INC.
CONSOLIDATED BALANCE SHEETS

(In thousands, except share and per share data)

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 45,277	$ 27,349
Short-term marketable securities	172,294	164,065
Accounts receivable, net	484	623
Prepaid expenses and other current assets	13,495	12,995
Total current assets	231,550	205,032
Marketable securities	12,242	34,242
Property and equipment, net	1,099	1,335
Intangible assets	6,973	7,048
Other assets	2,732	3,554
Total assets	$ 254,596	$ 251,211
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 10,351	$ 9,985
Accrued expenses	8,701	10,051
Current portion of lease liabilities	684	693
Discontinued operations	2,202	2,202
Total current liabilities	21,938	22,931
Other liabilities	1,570	2,172
Contingent consideration	33,100	28,400
Deferred tax liability	367	367
Total liabilities	56,975	53,870
Commitments and contingencies (Note 17)		
Stockholders' Equity:		
Preferred stock, $0.00001 par value; 10,000,000 shares authorized and no shares issued or outstanding at December 31, 2022 and December 31, 2021	—	—
Common stock, $0.00001 par value; 100,000,000 shares authorized at December 31, 2022 and December 31, 2021; 66,688,647 and 61,228,446 shares issued and outstanding at December 31, 2022 and December 31, 2021, respectively	1	1
Additional paid-in capital	880,832	792,971
Accumulated other comprehensive loss	(897)	(224)
Accumulated deficit	(682,315)	(595,407)
Total stockholders' equity	197,621	197,341
Total liabilities and stockholders' equity	$ 254,596	$ 251,211

The accompanying notes are an integral part of these consolidated financial statements.

ACLARIS THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(In thousands, except share and per share data)

	Year Ended December 31,		
	2022	2021	2020
Revenues:			
Contract research	$ 4,395	$ 5,830	$ 5,786
Licensing	25,100	809	690
Other	257	122	6
Total revenue	29,752	6,761	6,482
Costs and expenses:			
Cost of revenue	4,023	4,713	5,133
Research and development	77,813	43,813	29,338
General and administrative	25,133	23,619	20,530
Licensing	7,937	—	—
Revaluation of contingent consideration	4,700	24,339	2,393
Total costs and expenses	119,606	96,484	57,394
Loss from operations	(89,854)	(89,723)	(50,912)
Other income (expense), net	2,946	(1,142)	(424)
Loss from continuing operations before income taxes	(86,908)	(90,865)	(51,336)
Income tax benefit	—	—	(182)
Loss from continuing operations	(86,908)	(90,865)	(51,154)
Income from discontinued operations, net of tax	—	—	139
Net loss	$ (86,908)	$ (90,865)	$ (51,015)
Net loss per share, basic and diluted	$ (1.33)	$ (1.60)	$ (1.20)
Weighted average common shares outstanding, basic and diluted	65,213,944	56,730,583	42,539,293
Other comprehensive (loss) income:			
Unrealized loss on marketable securities, net of tax of $0	$ (673)	$ (229)	$ (2)
Foreign currency translation adjustment	—	99	(26)
Total other comprehensive loss	(673)	(130)	(28)
Comprehensive loss	$ (87,581)	$ (90,995)	$ (51,043)

The accompanying notes are an integral part of these consolidated financial statements.

ACLARIS THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

(In thousands, except share data)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Par Value				
Balance at December 31, 2019	41,485,638	$	$ 523,505	$ (66)	$ (453,527)	$ 69,912
Issuance of common stock in connection with exercise of stock options and vesting of restricted stock units	1,390,922	—	(669)	—	—	(669)
Issuance of common stock in connection with an equity purchase agreement, net of offering costs of $168	2,232,754	—	7,865	—	—	7,865
Unrealized loss on marketable securities	—	—	378	(2)	—	376
Foreign currency translation adjustment	—	—	—	(26)	—	(26)
Stock-based compensation expense	—	—	11,207	—	—	11,207
Net loss	—	—	—	—	(51,015)	(51,015)
Balance at December 31, 2020	45,109,314	$ —	$ 542,286	$ (94)	$ (504,542)	$ 37,650
Issuance of common stock in connection with exercise of stock options and warrants and vesting of restricted stock units	1,714,269	—	(1,574)	—	—	(1,574)
Issuance of common stock in connection with public offerings, net of offering costs of $15,910	14,404,863	1	238,199	—	—	238,200
Unrealized loss on marketable securities	—	—	—	(229)	—	(229)
Foreign currency translation adjustment	—	—	—	99	—	99
Stock-based compensation expense	—	—	14,060	—	—	14,060
Net loss	—	—	—	—	(90,865)	(90,865)
Balance at December 31, 2021	61,228,446	$ 1	$ 792,971	$ (224)	$ (595,407)	$ 197,341
Issuance of common stock in connection with exercise of stock options and vesting of restricted stock units	621,492	—	163	—	—	163
Issuance of common stock under at-the-market sales agreement, net of offering costs of $2,341	4,838,709	—	72,659	—	—	72,659
Unrealized loss on marketable securities	—	—	—	(673)	—	(673)
Stock-based compensation expense	—	—	15,039	—	—	15,039
Net loss	—	—	—	—	(86,908)	(86,908)
Balance at December 31, 2022	66,688,647	$ 1	$ 880,832	$ (897)	$ (682,315)	$ 197,621

The accompanying notes are an integral part of these consolidated financial statements.

ACLARIS THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS

(In thousands)

	Year Ended December 31,		
	2022	**2021**	**2020**
Cash flows from operating activities:			
Net loss	$ (86,908)	$ (90,865)	$ (51,015)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	797	923	1,324
Stock-based compensation expense	15,039	14,060	11,207
Revaluation of contingent consideration	4,700	24,339	2,393
Loss on extinguishment of debt	—	752	—
Deferred taxes	—	—	(182)
Changes in operating assets and liabilities:			
Accounts receivable	139	149	4,898
Prepaid expenses and other assets	(2,294)	(5,617)	1,689
Accounts payable	368	3,655	(5,219)
Accrued expenses	592	470	(3,728)
Net cash used in operating activities	(67,567)	(52,134)	(38,633)
Cash flows from investing activities:			
Purchases of property and equipment	(605)	(308)	(453)
Purchases of marketable securities	(164,753)	(235,153)	(47,714)
Proceeds from sales and maturities of marketable securities	177,986	67,829	54,554
Net cash provided by (used in) investing activities	12,628	(167,632)	6,387
Cash flows from financing activities:			
Proceeds from issuance of common stock in connection with public offerings, net of issuance costs	—	238,200	—
Proceeds from issuance of common stock under the at-the-market sales agreement, net of issuance costs	72,744	—	—
Proceeds from issuance of common stock in connection with an equity purchase agreement, net of issuance costs	—	—	7,737
Proceeds from debt financing (including warrants), net of issuance costs	—	—	10,913
Repayment of debt	—	(11,483)	—
Payments of employee withholding taxes related to restricted stock unit award vesting	(34)	(3,124)	—
Finance lease payments	—	—	(137)
Deferred issuance costs	—	—	(211)
Proceeds from exercise of employee stock options and the issuance of stock	157	1,459	70
Net cash provided by financing activities	72,867	225,052	18,372
Net increase (decrease) in cash and cash equivalents	17,928	5,286	(13,874)
Cash and cash equivalents at beginning of period	27,349	22,063	35,937
Cash and cash equivalents at end of period	$ 45,277	$ 27,349	$ 22,063
Supplemental disclosure of non-cash investing and financing activities:			
Additions to property and equipment included in accounts payable	$ 24	$ 143	$ —
Fair value of warrants issued in connection with debt financing	$ —	$ —	$ 378
Fair value of common stock issued in connection with an equity purchase agreement	$ —	$ —	$ 263

The accompanying notes are an integral part of these consolidated financial statements.

1. Organization and Nature of Business

Overview

Aclaris Therapeutics, Inc. was incorporated under the laws of the State of Delaware in 2012. In August 2017, Confluence Life Sciences, Inc. (now known as Aclaris Life Sciences, Inc.) ("Confluence") was acquired by Aclaris Therapeutics, Inc. and became a wholly owned subsidiary thereof. Aclaris Therapeutics, Inc. and its wholly owned subsidiaries are referred to collectively as the "Company." The Company is a clinical-stage biopharmaceutical company focused on developing novel drug candidates for immuno-inflammatory diseases. In addition to developing its novel drug candidates, the Company is pursuing strategic alternatives, including identifying and consummating transactions with third-party partners, to further develop, obtain marketing approval for and/or commercialize its novel drug candidates.

Liquidity

The Company's consolidated financial statements have been prepared on the basis of continuity of operations, realization of assets and the satisfaction of liabilities in the ordinary course of business. As of December 31, 2022, the Company had cash, cash equivalents and marketable securities of $229.8 million and an accumulated deficit of $682.3 million. Since inception, the Company has incurred net losses and negative cash flows from its operations. Prior to the acquisition of Confluence in August 2017, the Company had never generated revenue. There can be no assurance that profitable operations will ever be achieved, and, if achieved, will be sustained on a continuing basis. In addition, development activities, including clinical and preclinical testing of the Company's drug candidates, will require significant additional financing. The future viability of the Company is dependent on its ability to successfully develop its drug candidates and to generate revenue from identifying and consummating transactions with third-party partners to further develop, obtain marketing approval for and/or commercialize its development assets or to raise additional capital to finance its operations. The Company will require additional capital to complete the clinical development of zunsemetinib (ATI-450), ATI-1777, ATI-2138 and ATI-2231, to develop its preclinical compounds, and to support its discovery efforts.

Additional funds may not be available on a timely basis, on commercially acceptable terms, or at all, and such funds, if raised, may not be sufficient to enable the Company to continue to implement its long-term business strategy. The Company's ability to raise additional capital may be adversely impacted by potential worsening global economic conditions caused by a variety of factors including geopolitical tensions, rising interest rates and inflationary pressures. If the Company is unable to raise sufficient additional capital or generate revenue from transactions with potential third-party partners for the development and/or commercialization of its drug candidates, it may need to substantially curtail planned operations. The Company's failure to raise capital as and when needed could have a negative impact on its financial condition and ability to pursue its business strategies.

In accordance with Accounting Standards Codification ("ASC") Subtopic 205-40, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern, the Company evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that its consolidated financial statements are issued. As of the report date, the Company does not believe that substantial doubt exists about its ability to continue as a going concern. The Company believes its existing cash, cash equivalents and marketable securities are sufficient to fund its operating and capital expenditure requirements for a period greater than 12 months from the date of issuance of these consolidated financial statements.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the United States ("GAAP"). The consolidated financial statements of the Company include the accounts of the operating parent company, Aclaris Therapeutics, Inc., and its wholly owned subsidiaries. All intercompany transactions have been eliminated. Based upon the Company's revenue, the Company believes that gross profit does not

provide a meaningful measure of profitability and, therefore, has not included a line item for gross profit on the consolidated statement of operations.

Reclassifications

Certain prior year amounts have been reclassified to conform to the current year financial statement presentation.

Discontinued Operations

In September 2019, the Company announced the completion of a strategic review and its decision to refocus its resources on its immuno-inflammatory development programs and to actively seek partners for its commercial products.

As of December 31, 2022 and 2021, the Company had $2.2 million in accrued expenses reported as discontinued operations in the Company's consolidated balance sheet. During the year ended December 31, 2020, the Company reported $0.1 million as income from discontinued operations in the Company's consolidated statements of operations and comprehensive loss.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting periods. Significant estimates and assumptions reflected in these financial statements include, but are not limited to, contingent consideration and the valuation of stock-based awards. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. As of the date of issuance of these financial statements, the Company is not aware of any specific event or circumstance that would require an update to its estimates, assumptions and judgments or revise the carrying value of its assets or liabilities. Actual results could differ from the Company's estimates.

Revenue Recognition

The Company accounts for revenue in accordance with ASC Topic 606, Revenue from Contracts with Customers. Under ASC Topic 606, revenue is recognized when a customer obtains control of promised goods or services in an amount that reflects the consideration to which the Company expects to be entitled in exchange for those goods or services.

To determine revenue recognition in accordance with ASC Topic 606, the Company performs the following five steps: (i) identify the contract(s) with a customer, (ii) identify the performance obligations in the contract, (iii) determine the transaction price, (iv) allocate the transaction price to the performance obligations in the contract, and (v) recognize revenue when (or as) performance obligations are satisfied. At contract inception, the Company assesses the goods or services promised within a contract with a customer to identify the performance obligations, and to determine if they are distinct. The Company recognizes the revenue that is allocated to each distinct performance obligation when (or as) that performance obligation is satisfied. The Company only recognizes revenue when collection of the consideration it is entitled to under a contract with a customer is probable.

Contract Research

The Company earns contract research revenue from the provision of laboratory services. Contract research revenue is generally evidenced by contracts with clients which are on an agreed upon fixed-price, fee-for-service basis and are generally billed on a monthly basis in arrears for services rendered. Revenue related to these contracts is generally recognized as the laboratory services are performed, based upon the rates specified in the contracts. Under ASC Topic 606, the Company elected to apply the "right to invoice" practical expedient when recognizing contract research revenue and as such, recognizes revenue in the amount which it has the right to invoice. ASC Topic 606 also provides an optional exemption, which the Company has elected to apply, from disclosing remaining performance obligations when revenue is recognized from the satisfaction of the performance obligation in accordance with the "right to invoice" practical expedient.

Licensing Revenue

Licenses of Intellectual Property – The Company recognizes revenue received from non-refundable, upfront fees related to the licensing of intellectual property when the intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the license has been transferred to the customer, and the customer is able to use and benefit from the license.

Milestone and Royalty Payments – The Company considers any future potential milestones and sales-based royalties to be variable consideration. The Company recognizes revenue from development, regulatory and anniversary milestone payments as they are achieved. The Company recognizes revenue from commercial milestones and royalty payments as the sales occur.

Cash Equivalents

The Company considers all short-term, highly liquid investments with original maturities of three months or less at acquisition date to be cash equivalents. Cash equivalents, which have consisted of money market accounts and commercial paper, are stated at fair value.

Marketable Securities

Marketable securities with original maturities of greater than three months and remaining maturities of less than one year from the balance sheet date are classified as short-term. Marketable securities with remaining maturities of greater than one year from the balance sheet date are classified as long-term.

The Company classifies all marketable securities as available-for-sale securities. The Company's marketable securities are measured and reported at fair value using either quoted prices in active markets for identical securities or quoted prices in markets that are not active for identical or similar securities. Unrealized gains and losses are reported as a separate component of stockholders' equity. The cost of securities sold is determined on a specific identification basis, and realized gains and losses, if any, are included in other expense, net within the consolidated statement of operations and comprehensive loss. If any adjustment to fair value reflects a decline in the value of the investment, the Company considers available evidence to evaluate the extent to which the decline is "other than temporary" and reduces the investment to fair value through a charge to the statement of operations and comprehensive loss.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation. Depreciation expense is recognized using the straight-line method over the useful life of the asset. Computer equipment is depreciated over three years. Laboratory equipment is depreciated over three to five years. Furniture and fixtures are depreciated over five years. Leasehold improvements are depreciated over the shorter of the lease term or their useful life. Expenditures for repairs and maintenance of assets are charged to expense as incurred. Upon retirement or sale, the cost and related accumulated depreciation of assets disposed of are removed from the accounts and any resulting gain or loss is included in loss from continuing operations.

Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset over its fair value, determined based on discounted cash flows.

Intangible Assets

Intangible assets include both definite-lived and indefinite-lived assets. Definite-lived intangible assets consist of a drug discovery platform the Company acquired through the acquisition of Confluence. Definite-lived intangible assets are amortized over their estimated useful life based on the pattern over which the intangible assets are consumed or otherwise used up. If that pattern cannot be reliably determined, the straight-line method of amortization is used. Indefinite-lived intangible assets consist of an in-process research and development ("IPR&D") drug candidate acquired through the acquisition of Confluence. IPR&D assets are considered indefinite-lived until the completion or abandonment of the associated research and development efforts. The cost of IPR&D is either amortized over its estimated useful life beginning when the underlying drug candidate is approved and launched commercially, or expensed immediately if development of the drug candidate is abandoned or otherwise impaired.

Definite-lived intangible assets are tested for impairment when events or changes in circumstances indicate that the carrying value of the asset may not be recoverable. Indefinite-lived intangible assets are tested for impairment at least annually, which the Company performs during the fourth quarter, or when indicators of an impairment are present. The Company recognizes impairment losses when and to the extent that the estimated fair value of an intangible asset is less than its carrying value.

During the years ended December 31, 2022, 2021 and 2020, the Company did not record an IPR&D impairment.

Leases

Leases represent a company's right to use an underlying asset and a corresponding obligation to make payments to a lessor for the right to use those assets. The Company evaluates leases at their inception to determine if they are an operating lease or a finance lease. A lease is accounted for as a finance lease if it meets one of the following five criteria: the lease has a purchase option that is reasonably certain of being exercised, the present value of the future cash flows are substantially all of the fair market value of the underlying asset, the lease term is for a significant portion of the remaining economic life of the underlying asset, the title to the underlying asset transfers at the end of the lease term, or if the underlying asset is of such a specialized nature that it is expected to have no alternative uses to the lessor at the end of the term. Leases that do not meet the finance lease criteria are accounted for as an operating lease.

The Company recognizes assets and liabilities for leases at their inception based upon the present value of all payments due under the lease. The Company uses an implicit interest rate to determine the present value of finance leases, and its incremental borrowing rate to determine the present value of operating leases. The Company determines incremental borrowing rates by referencing collateralized borrowing rates for debt instruments with terms similar to the respective lease. The Company recognizes expense for operating and finance leases on a straight-line basis over the term of each lease, and interest expense related to finance leases is recognized over the lease term based on the effective interest method. The Company includes estimates for any residual value guarantee obligations under its leases in lease liabilities recorded on its consolidated balance sheet.

Right-of-use assets are included in other assets and property and equipment, net on the Company's consolidated balance sheet for operating and finance leases, respectively. Obligations for lease payments are included in current portion of lease liabilities and other liabilities on the Company's consolidated balance sheet for both operating and finance leases.

Contingent Consideration

The Company initially recorded a contingent consideration liability at fair value on the date of acquisition related to future potential payments resulting from the acquisition of Confluence based upon significant unobservable inputs including the achievement of development, regulatory and commercial milestones, as well as estimated future sales levels and the discount rates applied to calculate the present value of the potential payments. Significant judgement was involved in determining the appropriateness of these assumptions. These assumptions are considered Level 3 inputs. Revaluation of the contingent consideration liability can result from changes to one or more of these assumptions. The Company evaluates the fair value estimate of the contingent consideration liability on a quarterly basis with changes, if any, recorded as income or expense in the consolidated statement of operations.

The fair value of contingent consideration is estimated using a probability-weighted expected payment model for regulatory milestone payments and a Monte Carlo simulation model for commercial milestone and royalty payments and

then applying a risk-adjusted discount rate to calculate the present value of the potential payments. Significant assumptions used in the Company's estimates include the probability of achieving regulatory milestones and commencing commercialization, which are based on an asset's current stage of development and a review of existing clinical data. Probability of success assumptions ranged between 10% and 40% at December 31, 2022. Additionally, estimated future sales levels and the risk-adjusted discount rate applied to the potential payments are also significant assumptions used in calculating the fair value. The discount rate ranged between 9.8% and 10.2% depending on the year of each potential payment.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expenses include salaries, stock-based compensation and benefits of employees, and other operational costs related to the Company's research and development activities, including depreciation expenses and the cost of research and development contracts which the Company has entered into with outside vendors to conduct both preclinical studies and clinical trials. Significant judgment and estimates are made in determining the amount of research and development costs recognized in each reporting period. The Company analyzes the progress of its preclinical studies and clinical trials, completion of milestone events, invoices received and contracted costs when estimating research and development costs. Actual results could differ from the Company's estimates. The Company's historical estimates for research and development costs have not been materially different from the actual costs.

Stock-Based Compensation

The Company measures the compensation expense of stock-based awards granted to employees and directors using the grant date fair value of the award. The Company has issued stock options and restricted stock unit ("RSU") awards with service-based vesting conditions, as well as with performance-based vesting conditions. The Company has not issued awards that include market-based conditions. For service-based awards the Company recognizes stock-based compensation expense on a straight-line basis over the requisite service period, which is typically four years. For performance-based awards the Company recognizes stock-based compensation expense on a straight-line basis over the requisite service period beginning in the period that it becomes probable the performance conditions will occur. At each balance sheet date, the Company evaluates whether any performance conditions related to a performance-based award have changed. The effect of any change in performance conditions would be recognized as a cumulative catch-up adjustment in the period such change occurs, and any remaining unrecognized compensation expense would be recognized on a straight-line basis over the remaining requisite service period. The impact of forfeitures is recognized in the period in which they occur.

The Company measures the compensation expense of stock-based awards granted to consultants using the grant date fair value of the award. The Company recognizes compensation expense over the period during which services are rendered by the consultant.

The Company classifies stock-based compensation expense in its statement of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipients' service payments are classified.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model. Historically, the Company estimated expected volatility based on historical volatility of a set of peer companies, which are publicly traded. Starting in 2022, the Company estimated expected volatility based on its stock price's historical volatility, as the Company determined that it had adequate historical data regarding the volatility of its own publicly-traded stock price. The expected term of the Company's stock options has been determined using the "simplified" method for awards that qualify as "plain vanilla" options. The expected term of stock options granted to non-employees is equal to the contractual term of the option award. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. The Company uses an expected dividend yield of zero based on the fact that the Company has never paid cash dividends and does not expect to pay cash dividends in the future.

The fair value of each RSU is measured using the closing price of the Company's common stock on the date of grant.

Patent Costs

All patent related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the financial statements or in the Company's tax returns. Deferred taxes are determined based on the difference between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect in the years in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

The Company accounts for uncertainty in income taxes recognized in the consolidated financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more likely than not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the consolidated financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity that result from transactions and economic events other than those with stockholders. Comprehensive loss is primarily comprised of net loss and unrealized gains (losses) on marketable securities.

Net Loss per Share

Basic net loss per share is computed using the weighted average number of common shares outstanding during the period. Diluted net loss per share is computed using the sum of the weighted average number of common shares outstanding during the period, plus the weighted average number of potential shares of common stock from the assumed exercise of stock options and warrants and the assumed vesting of RSUs, if dilutive. Since the Company was in a net loss position, basic and diluted net loss per share was the same for each of the periods presented.

Fair Value Measurements

Certain assets and liabilities are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1 — Quoted prices in active markets for identical assets or liabilities.

- Level 2 — Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.

- Level 3 — Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The Company's cash equivalents, marketable securities and contingent consideration are carried at fair value, determined according to the fair value hierarchy described above. The carrying value of the Company's accounts payable and accrued expenses approximate fair value due to the short-term nature of these liabilities.

Concentration of Credit Risk and of Significant Suppliers

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents and marketable securities. The Company holds all cash, cash equivalents and marketable securities balances at one accredited financial institution, in amounts that exceed federally insured limits. The Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company is dependent on third-party manufacturers to supply drug product, including all underlying components, for its research and development activities, including preclinical and clinical testing. These activities could be adversely affected by a significant interruption in the supply of active pharmaceutical ingredients or other components.

Segment Reporting

Operating segments are components of a company for which separate financial information is available and evaluated regularly by the chief operating decision maker in assessing performance and deciding how to allocate resources. The Company has two reportable segments, therapeutics and contract research. The therapeutics segment is focused on identifying and developing innovative therapies to address significant unmet needs for immuno-inflammatory diseases. The contract research segment earns revenue from the provision of laboratory services. Contract research revenue is generally evidenced by contracts with clients which are on an agreed upon fixed-price, fee-for-service basis. The Company does not report balance sheet information by segment since it is not reviewed by the chief operating decision maker, and all of the Company's tangible assets are held in the United States.

Recently Issued Accounting Pronouncements

In November 2018, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2018-18, Collaborative Arrangements (Topic 808): Clarifying the Interaction Between Topic 808 and Topic 606, which, among other things, provides guidance on how to assess whether certain collaborative arrangement transactions should be accounted for under Topic 606. The Company adopted this standard as of January 1, 2020, the impact of which on its consolidated financial statements was not significant.

In August 2018, the FASB issued ASU 2018-15, Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40). ASU 2018-15 requires a customer in a cloud computing arrangement that is a service contract to follow the internal-use software guidance in ASC 350-40 to determine which implementation costs to capitalize as assets or expense as incurred. The Company adopted this standard as of January 1, 2020, the impact of which on its consolidated financial statements was not significant.

In August 2018, the FASB issued ASU 2018-13, Fair Value Measurement (Topic 820). The FASB developed the amendments to ASC 820 as part of its broader disclosure framework project, which aims to improve the effectiveness of disclosures in the notes to financial statements by focusing on requirements that clearly communicate the most important information to users of the financial statements. This update eliminates certain disclosure requirements for fair value measurements for all entities, requires public entities to disclose certain new information and modifies some of the existing disclosure requirements. The Company adopted this standard as of January 1, 2020, the impact of which on its consolidated financial statements was not significant.

3. Fair Value of Financial Assets and Liabilities

The following tables present information about the fair value measurements of the Company's financial assets and liabilities which are measured at fair value on a recurring and non-recurring basis, and indicate the level of the fair value hierarchy utilized to determine such fair values:

	December 31, 2022			
(In thousands)	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents	$ 38,516	$ —	$ —	$ 38,516
Marketable securities	—	184,536	—	184,536
Total assets	$ 38,516	$ 184,536	$ —	$ 223,052
Liabilities:				
Contingent consideration	$ —	$ —	$ 33,100	$ 33,100
Total liabilities	$ —	$ —	$ 33,100	$ 33,100

	December 31, 2021			
(In thousands)	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents	$ 21,678	$ —	$ —	$ 21,678
Marketable securities	—	198,307	—	198,307
Total assets	$ 21,678	$ 198,307	$ —	$ 219,985
Liabilities:				
Contingent consideration	$ —	$ —	$ 28,400	$ 28,400
Total liabilities	$ —	$ —	$ 28,400	$ 28,400

As of December 31, 2022 and 2021, the Company's cash equivalents consisted of a money market fund, which was valued based upon Level 1 inputs. The Company's marketable securities as of December 31, 2022 and 2021 consisted of commercial paper, and corporate debt, asset-backed and U.S. government agency debt securities, which were valued based upon Level 2 inputs. The Company's marketable securities as of December 31, 2021 also included foreign government agency debt securities, which were valued based upon Level 2 inputs. The Company's marketable securities as of December 31, 2022 also included U.S. government debt securities, which were valued based upon Level 2 inputs.

In determining the fair value of its Level 2 investments, the Company relied on quoted prices for identical securities in markets that are not active. These quoted prices were obtained by the Company with the assistance of a third-party pricing service based on available trade, bid and other observable market data for identical securities. Quarterly, the Company compares the quoted prices obtained from the third-party pricing service to other available independent pricing information to validate the reasonableness of the quoted prices provided. The Company evaluates whether adjustments to third-party pricing are necessary and, historically, the Company has not made adjustments to quoted prices obtained from the third-party pricing service. During the years ended December 31, 2022 and 2021, there were no transfers into or out of Level 3.

The increase in contingent consideration of $4.7 million during the year ended December 31, 2022 primarily resulted from an increase in future sales level assumptions for zunsemetinib and the passage of time.

As of December 31, 2022 and 2021, the fair value of the Company's available-for-sale marketable securities by type of security was as follows:

	December 31, 2022			
(In thousands)	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Marketable securities:				
Corporate debt securities[1]	$ 40,626	$ —	$ (251)	$ 40,375
Commercial paper	79,598	—	—	79,598
Asset-backed debt securities[2]	14,641	4	(123)	14,522
U.S. government and government agency debt securities[3]	50,571	—	(530)	50,041
Total marketable securities	$ 185,436	$ 4	$ (904)	$ 184,536

[1] Included in Corporate debt securities is $4.8 million with maturity dates between one and five years.

[2] Included in Asset-backed debt securities is $2.4 million with maturity dates between one and five years.

[3] Included in US government and government agency debt securities is $5.0 million with maturity dates between one and five years.

	December 31, 2021			
(In thousands)	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Marketable securities:				
Corporate debt securities[1]	$ 40,993	$ 6	$ (50)	$ 40,949
Commercial paper	71,837	—	—	71,837
Asset-backed debt securities	36,166	—	(43)	36,123
Foreign government agency debt securities	4,073	—	(13)	4,060
U.S. government agency debt securities[2]	45,465	—	(127)	45,338
Total marketable securities	$ 198,534	$ 6	$ (233)	$ 198,307

[1] Included in Corporate debt securities is $9.2 million with maturity dates between one and five years.

[2] Included in U.S. government debt securities is $25.0 million with maturity dates between one and five years.

4. Property and Equipment, Net

Property and equipment, net consisted of the following:

(In thousands)	December 31, 2022	December 31, 2021
Computer equipment	$ 1,381	$ 1,380
Lab equipment	2,010	1,605
Furniture and fixtures	620	620
Leasehold improvements	1,123	1,123
Property and equipment, gross	5,134	4,728
Accumulated depreciation	(4,035)	(3,393)
Property and equipment, net	$ 1,099	$ 1,335

Depreciation expense was $0.7 million, $0.8 million and $1.1 million for the years ended December 31, 2022, 2021 and 2020, respectively.

5. Intangible Assets

Intangible assets consisted of the following:

(In thousands, except years)	Remaining Life (years)	Gross Cost December 31, 2022	Gross Cost December 31, 2021	Accumulated Amortization December 31, 2022	Accumulated Amortization December 31, 2021
Other intangible assets	4.6	$ 751	$ 751	$ 407	$ 332
In-process research and development	n/a	6,629	6,629	—	—
Total intangible assets		$ 7,380	$ 7,380	$ 407	$ 332

Amortization expense was $75 thousand for each of the years ended December 31, 2022, 2021 and 2020.

As of December 31, 2022, estimated future amortization expense was as follows:

(In thousands)	Year Ending December 31,
2023	$ 75
2024	75
2025	75
2026	75
2027	44
Total	$ 344

6. Accrued Expenses

Accrued expenses consisted of the following:

(In thousands)	December 31, 2022	December 31, 2021
Employee compensation expenses	$ 5,295	$ 4,389
Research and development expenses	2,689	1,278
Litigation settlements (see Note 17)	—	2,650
Other	717	1,734
Total accrued expenses	$ 8,701	$ 10,051

7. Debt

Loan and Security Agreement – Silicon Valley Bank

In March 2020, the Company entered into a Loan and Security Agreement with Silicon Valley Bank ("SVB"). The Loan and Security Agreement provided for $11.0 million in term loans, of which the Company borrowed the entire amount on March 30, 2020. In connection with the Loan and Security Agreement, the Company issued to SVB a warrant to purchase up to 460,251 shares of common stock (the "Warrant") (see Note 8). The proceeds of the Loan and Security Agreement were allocated to the term loan and Warrant using a relative fair value approach.

In July 2021, the Company repaid in full the $11.0 million that was outstanding under the Loan and Security Agreement, together with all accrued and unpaid interest and fees as of the payoff date, for a total payment of $11.7 million. Following this repayment, all of the Company's obligations under the Loan and Security Agreement are deemed to be terminated, except as set forth in the agreement.

8. Stockholders' Equity

Preferred Stock

As of December 31, 2022 and 2021, the Company's amended and restated certificate of incorporation authorized the Company to issue 10,000,000 shares of undesignated preferred stock. There were no shares of preferred stock outstanding as of December 31, 2022 and 2021.

Common Stock

As of December 31, 2022 and 2021, the Company's amended and restated certificate of incorporation authorized the Company to issue 100,000,000 shares of $0.00001 par value common stock. There were 66,688,647 and 61,228,446 shares of common stock issued and outstanding as of December 31, 2022 and 2021, respectively.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are entitled to receive dividends, as may be declared by the board of directors, if any, subject to any preferential dividend rights of any series of preferred stock that may be outstanding. No dividends have been declared through December 31, 2022.

Warrants

The Warrant issued to SVB in March 2020 had an initial exercise price of $0.956 per share, subject to adjustment as provided in the Warrant. The Warrant became immediately exercisable in full upon the funding of the term loan facility. The Company assigned a fair value of $0.4 million to the Warrant using a Black-Scholes valuation methodology, and also concluded that the Warrant was indexed to its own stock and therefore classified the Warrant as an equity instrument. In January 2021, SVB net exercised the Warrant in full, and the Company issued to SVB 388,119 shares of common stock.

Equity Purchase Agreement with Lincoln Park Capital Fund, LLC

In August 2020, the Company entered into an equity purchase agreement (the "Purchase Agreement") with Lincoln Park Capital Fund, LLC ("Lincoln Park") which provided that, upon the terms and subject to the conditions and limitations set forth therein, the Company could sell to Lincoln Park, at its discretion, up to $15.0 million of shares of its common stock over the 36-month term of the Purchase Agreement. Upon execution of the Purchase Agreement, the Company issued 121,584 shares of its common stock to Lincoln Park as commitment shares in accordance with the closing conditions contained within the Purchase Agreement. The commitment shares were valued using the closing price of the Company's common stock on the effective date of the Purchase Agreement resulting in an aggregate fair value of $0.3 million. Through December 31, 2020, the Company sold 2,111,170 shares of its common stock to Lincoln Park under the Purchase Agreement for net proceeds of $7.7 million. The Company terminated the Purchase Agreement in January 2021 in connection with the public offering of common stock described below. The Company did not sell any additional shares prior to terminating the Purchase Agreement.

January 2021 Public Offering

In January 2021, the Company closed a public offering in which it sold 6,306,271 shares of common stock at a price to the public of $17.50 per share, for aggregate gross proceeds of $110.4 million. The Company paid underwriting discounts and commissions of $6.6 million, and also incurred expenses of $0.4 million in connection with the offering. As a result, the net offering proceeds received by the Company, after deducting underwriting discounts, commissions and offering expenses, were $103.3 million.

June 2021 Public Offering

In June 2021, the Company closed a public offering in which it sold 8,098,592 shares of common stock at a price to the public of $17.75 per share, for aggregate gross proceeds of $143.8 million. The Company paid underwriting discounts and commissions of $8.6 million, and also incurred expenses of $0.3 million in connection with the offering. As a result, the net offering proceeds received by the Company, after deducting underwriting discounts, commissions and offering expenses, were $134.9 million.

Sales of Common Stock Pursuant to At-The-Market Facility

In April 2022, the Company sold 4,838,709 shares of its common stock at a weighted average price per share of $15.50, for aggregate gross proceeds of $75.0 million, pursuant to a sales agreement with SVB Securities LLC and Cantor Fitzgerald & Co., as sales agents, dated May 20, 2021. The Company paid selling commissions and other fees of $2.2 million in connection with the sale.

9. Stock-Based Awards

2015 Equity Incentive Plan

In September 2015, the Company's board of directors adopted the 2015 Equity Incentive Plan (the "2015 Plan"), and the Company's stockholders approved the 2015 Plan. The 2015 Plan became effective in connection with the Company's initial public offering in October 2015. Beginning at the time the 2015 Plan became effective, no further grants may be made under the Company's 2012 Equity Compensation Plan, as amended and restated (the "2012 Plan"). The 2015 Plan provides for the grant of incentive stock options, nonqualified stock options, stock appreciation rights, restricted stock awards, RSU awards, performance stock awards, cash-based awards and other stock-based awards. The number of shares initially reserved for issuance under the 2015 Plan was 1,643,872 shares of common stock. The number of shares of common stock that may be issued under the 2015 Plan will automatically increase on January 1 of each year ending on January 1, 2025, in an amount equal to the lesser of (i) 4.0% of the shares of the Company's common stock outstanding on December 31 of the preceding calendar year or (ii) an amount determined by the Company's board of directors. The shares of common stock underlying any awards that expire, are otherwise terminated, settled in cash or repurchased by the Company under the 2015 Plan and the 2012 Plan will be added back to the shares of common stock available for issuance under the 2015 Plan. As of December 31, 2022, 3,095,380 shares remained available for grant under the 2015 Plan. As of January 1, 2023, the number of shares of common stock that may be issued under the 2015 Plan was automatically increased by 2,667,545 shares. The Company had 4,322,587 stock options and 1,520,730 RSUs outstanding as of December 31, 2022 under the 2015 Plan.

2017 Inducement Plan

In July 2017, the Company's board of directors adopted the 2017 Inducement Plan (the "2017 Inducement Plan"). The 2017 Inducement Plan is a non-stockholder approved stock plan adopted pursuant to the "inducement exception" provided under Nasdaq listing rules. The Company had 370,600 stock options outstanding as of December 31, 2022 under the 2017 Inducement Plan. All shares of common stock that were eligible for issuance under the 2017 Inducement Plan after October 1, 2018, including any shares underlying any awards that expire or are otherwise terminated, reacquired to satisfy tax withholding obligations, settled in cash or repurchased by the Company in the future that would have been eligible for re-issuance under the 2017 Inducement Plan, were retired.

2012 Equity Compensation Plan

Upon the 2015 Plan becoming effective, no further grants can be made under the 2012 Plan. The Company granted stock options to purchase a total of 1,140,524 shares under the 2012 Plan, of which 473,977 were outstanding as of December 31, 2022. Stock options granted under the 2012 Plan expire after ten years.

Stock Option Valuation

The weighted average assumptions the Company used to estimate the fair value of stock options granted during the years ended December 31, 2022, 2021 and 2020 were as follows:

	Year Ended December 31,		
	2022	2021	2020
Risk-free interest rate	2.22 %	0.92 %	0.87 %
Expected term (in years)	6.2	6.2	6.1
Expected volatility	77.95 %	76.60 %	85.19 %
Expected dividend yield	0 %	0 %	0 %

The Company recognizes compensation expense for awards over their vesting period. Compensation expense for awards includes the impact of forfeitures in the period when they occur.

Stock Options

The following table summarizes stock option activity for the years ended December 31, 2022, 2021 and 2020:

(In thousands, except share and per share data and years)	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding as of December 31, 2019	3,102,221	$ 20.33	6.6	$ 148
Granted	734,800	1.30		
Exercised	(53,737)	1.30		145
Forfeited and cancelled	(911,786)	22.41		
Outstanding as of December 31, 2020	2,871,498	$ 15.16	6.8	$ 4,890
Granted	1,068,100	23.44		
Exercised	(115,548)	12.63		1,373
Forfeited and cancelled	(31,600)	23.26		
Outstanding as of December 31, 2021	3,792,450	$ 17.50	6.8	$ 13,710
Granted	2,548,750	14.40		
Exercised	(88,172)	1.78		1,120
Forfeited and cancelled	(1,085,864)	18.44		
Outstanding as of December 31, 2022	5,167,164	$ 16.04	7.2	$ 15,288
Options vested and expected to vest as of December 31, 2022	5,167,164	$ 16.04	7.2	$ 15,288
Options exercisable as of December 31, 2022	2,348,821	$ 17.30	5.0	$ 9,419

The weighted average grant date fair value of stock options granted during the years ended December 31, 2022, 2021 and 2020 was $9.95, $15.67, and $0.93 per share, respectively.

Restricted Stock Units

The following table summarizes RSU activity for the years ended December 31, 2022, 2021 and 2020.

(In thousands, except share and per share data)	Number of Shares	Weighted Average Grant Date Fair Value Per Share	Aggregate Intrinsic Value
Outstanding as of December 31, 2019	3,592,915	$ 4.62	
Granted	1,168,805	1.36	
Vested	(1,804,429)	3.33	$ 2,607
Forfeited and cancelled	(713,134)	4.77	
Outstanding as of December 31, 2020	2,244,157	$ 3.83	
Granted	664,948	23.33	
Vested	(1,340,042)	3.18	$ 31,492
Forfeited and cancelled	(72,117)	10.36	
Outstanding as of December 31, 2021	1,496,946	$ 12.75	
Granted	936,563	14.43	
Vested	(533,212)	11.61	$ 7,943
Forfeited and cancelled	(379,567)	13.40	
Outstanding as of December 31, 2022	1,520,730	$ 14.02	

Stock-Based Compensation

Stock-based compensation expense included in total costs and expenses on the consolidated statement of operations included the following:

	Year Ended December 31,		
(In thousands)	2022	2021	2020
Cost of revenue	$ 1,151	$ 981	$ 946
Research and development	3,745	3,866	2,919
General and administrative	10,143	9,213	7,342
Total stock-based compensation expense	$ 15,039	$ 14,060	$ 11,207

As of December 31, 2022, the Company had unrecognized stock-based compensation expense for stock options and RSUs of $23.6 million and $16 million, respectively, which is expected to be recognized over weighted average periods of 3.0 years and 2.8 years, respectively.

10. Net Loss per Share

Basic and diluted net loss per share is summarized in the following table:

(In thousands, except for share and per share data)	Year Ended December 31, 2022	2021	2020
Numerator:			
Net loss	$ (86,908)	$ (90,865)	$ (51,015)
Denominator:			
Weighted average shares of common stock outstanding, basic and diluted	65,213,944	56,730,583	42,539,293
Net loss per share, basic and diluted	$ (1.33)	$ (1.60)	$ (1.20)

The Company's potentially dilutive securities, which included stock options, RSUs and warrants, have been excluded from the computation of diluted net loss per share since the effect would be to reduce the net loss per share. Therefore, the weighted average number of shares of common stock outstanding used to calculate both basic and diluted net loss per share is the same. The following table presents potential shares of common stock excluded from the calculation of diluted net loss per share for the years ended December 31, 2022, 2021 and 2020. All share amounts presented in the table below represent the total number outstanding as of December 31 of each year.

	December 31, 2022	2021	2020
Options to purchase common stock	5,167,164	3,792,450	2,871,498
Restricted stock unit awards	1,520,730	1,496,946	2,244,157
Warrants	—	—	460,251
Total potential shares of common stock	6,687,894	5,289,396	5,575,906

11. Leases

The Company has operating leases for office space and laboratory facilities, and had finance leases for its laboratory equipment and vehicles. The components of lease expense were as follows:

(In thousands)	Year Ended December 31, 2022	2021	2020
Operating lease expense	$ 1,013	$ 1,013	$ 1,013
Finance Leases:			
Amortization of right-to-use assets	$ —	$ —	$ 113
Interest expense	—	—	5
Total finance lease expenses	$ —	$ —	$ 118

Rent expense was $1.0 million for each of the years ended December 31, 2022, 2021 and 2020, which was recognized on a straight-line basis over the term of the lease.

Operating Leases

Agreements for Office and Laboratory Space

The Company has a sublease agreement with Auxilium Pharmaceuticals, LLC (the "Sublandlord") pursuant to which it subleases 33,019 square feet of office space for its headquarters in Wayne, Pennsylvania. The sublease has a term that runs through October 2023. If for any reason the lease between Chesterbrook Partners, LP ("Landlord") and Sublandlord is terminated or expires prior to October 2023, the Company's sublease will automatically terminate. In December 2020, the Company entered into a sub-sublease agreement under which it sub-subleased 8,115 square feet to a third party. The sub-sublease was terminated in December 2022.

In February 2019, the Company entered into a sublease agreement with a third party for 20,433 square feet of office and laboratory space in St. Louis, Missouri. The lease commenced in June 2019 and has a term that runs through June 2029.

Supplemental balance sheet information related to operating leases is as follows:

(In thousands)	December 31, 2022	December 31, 2021
Operating Leases:		
Gross cost	$ 5,240	$ 5,240
Accumulated amortization	(2,560)	(1,803)
Other assets	$ 2,680	$ 3,437
Current portion of lease liabilities	$ 684	$ 693
Other liabilities	1,570	2,151
Total operating lease liabilities	$ 2,254	$ 2,844

Amortization expense related to operating lease right-of-use assets and accretion of operating lease liabilities totaled $1.0 million for each of the years ended December 31, 2022, 2021 and 2020.

Finance Leases

Laboratory Equipment

The Company leased laboratory equipment which it used in its laboratory space in St. Louis, Missouri under two finance lease financing arrangements which the Company entered into in August 2017 and October 2017, for which terms ended in October 2020 and December 2020, respectively.

Supplemental information related to operating and finance leases is as follows:

(In thousands, except for years and percentages)	Year Ended December 31,		
Supplemental Cash Flow Lease Information:	**2022**	**2021**	**2020**
Operating cash flows from operating leases	$ 846	$ 924	$ 907
Operating cash flows from finance leases	$ —	$ —	$ 5
Financing cash flows from finance leases	$ —	$ —	$ 137
Weighted-Average Remaining Lease Term (in years):			
Operating leases	5.2	5.4	6.0
Weighted-Average Discount Rate:			
Operating leases	10.1 %	10.1 %	10.1 %

Future minimum lease payments under operating lease agreements are as follows:

(In thousands) Year Ending December 31,	Operating Leases
2023	$ 919
2024	343
2025	352
2026	361
2027	370
Thereafter	571
Total undiscounted lease payments	2,916
Less: unrecognized interest	(662)
Total lease liability	$ 2,254

12. Income Taxes

During the years ended December 31, 2022, 2021 and 2020, the Company did not record an income tax benefit for net operating losses incurred in each year due to the uncertainty of realizing a benefit from those items.

Loss before income taxes is allocated as follows:

	Year Ended December 31,		
(In thousands)	2022	2021	2020
U.S. operations	$ (86,908)	$ (90,865)	$ (51,215)
Foreign operations	—	—	18
Loss before income taxes	$ (86,908)	$ (90,865)	$ (51,197)

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,		
	2022	2021	2020
Federal statutory income tax rate	(21.0)%	(21.0)%	(21.0)%
State taxes, net of federal benefit	(2.3)	(7.7)	(7.5)
Research and development tax credits	(4.3)	(3.0)	(2.6)
Excess equity compensation tax benefit net of officer limitation	0.2	(3.9)	1.4
Revaluation of contingent consideration	1.1	5.6	1.0
Permanent differences	—	—	0.2
Change in deferred tax asset valuation allowance	26.3	30.0	28.1
Effective income tax rate	— %	— %	(0.4)%

Deferred tax liabilities, net consisted of the following:

(In thousands)	December 31, 2022	December 31, 2021
Deferred tax assets:		
Net operating loss carryforwards	$ 120,554	$ 123,583
Capitalized start-up costs	5,506	6,334
Research and development tax credit carryforwards	15,233	11,502
Capitalized research and development expense	25,087	4,046
Stock-based compensation expense	19,432	17,728
Accrued compensation	1,146	825
Lease liabilities	558	721
Other	534	648
Total deferred tax assets	188,050	165,387
Deferred tax liabilities:		
Property and equipment	(137)	(171)
Intangible asset	(1,576)	(1,567)
Right-to-use assets	(651)	(852)
Other	(1,365)	(1,340)
Total deferred tax liabilities	(3,729)	(3,930)
Valuation allowance	(184,688)	(161,824)
Deferred tax liabilities, net	$ (367)	$ (367)

As of December 31, 2022, the Company had federal and state net operating loss ("NOL") carryforwards of $446.7 million and $477.9 million, respectively, which will begin to expire in 2032. As of December 31, 2022, the Company also had federal research and development tax credit carryforwards of $15.1 million which will begin to expire in 2032, and state research and development tax credit carryforwards of $0.1 million which will begin to expire in 2022. The Company also has $0.2 million of loss carryforwards in the United Kingdom which can be carried forward indefinitely. Utilization of the NOLs and research and development tax credit carryforwards in the United States may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 due to ownership changes that may have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain stockholders or public groups in the stock of a corporation by more than 50% over a three-year period. The Company has completed an analysis under Section 382 for NOLs generated from July 13, 2012 through December 31, 2021. Although the Company has experienced Section 382 ownership changes since 2012, the Company has concluded that it should have sufficient ability to utilize NOLs accumulated during the periods tested. The Company has not yet determined if a Section 382 ownership change has occurred after December 31, 2021. In addition, the Company may experience ownership changes in the future as a result of subsequent shifts in its stock ownership, some of which may be outside of the Company's control.

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets. The Company considered its history of cumulative net losses incurred since inception, its lack of substantial revenue generated to date, and its forecasted future operating losses and concluded that it is more likely than not that the Company will not realize the benefits of its deferred tax assets. Accordingly, a full valuation allowance has been established against the deferred tax assets as of December 31, 2022 and 2021. The Company evaluates positive and negative evidence of its ability to realize deferred tax assets at each reporting period.

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2022, 2021 and 2020 related primarily to the increases in NOLs, capitalized start-up costs, and research and development tax credit carryforwards and were as follows:

	Year Ended December 31,		
(In thousands)	2022	2021	2020
Valuation allowance at beginning of year	$ (161,824)	$ (134,559)	$ (120,966)
Decreases recorded as benefit to income tax provision	—	—	—
Decreases recorded to opening balance sheet	—	—	58
Increases recorded to income tax provision	(22,864)	(27,265)	(13,651)
Valuation allowance as of end of year	$ (184,688)	$ (161,824)	$ (134,559)

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. There are currently no pending income tax examinations. The Company's tax years are still open under statute from 2020 to the present. All open years may be examined to the extent that tax credit or NOLs are used in future periods. The Company's policy is to record interest and penalties related to income taxes as part of its income tax provision.

13. Related Party Transactions

Mallinckrodt plc

In April 2018, Bryan Reasons was appointed to the Company's board of directors. Subsequently, in March 2019, Mr. Reasons became the Chief Financial Officer of Mallinckrodt plc. Prior to Mr. Reasons joining Mallinckrodt plc, the Company entered into a master services agreement with a subsidiary of Mallinckrodt plc, pursuant to which Confluence provides laboratory services to a subsidiary ("Mallinckrodt") in the ordinary course of business. Mr. Reasons was not involved in the negotiation or execution of the agreement, but may be deemed to have an interest in the ongoing transactions based on his employment as an executive officer of Mallinckrodt plc. During the years ended December 31, 2022, 2021 and 2020, the Company invoiced Mallinckrodt for $0, $24 thousand and $0.3 million, respectively, under the master services agreement. Mr. Reasons had no financial interest in these transactions.

14. Agreements Related to Intellectual Property

License Agreement – Pediatrix Therapeutics, Inc.

In November 2022, the Company entered into a license agreement with Pediatrix Therapeutics, Inc. ("Pediatrix"), under which the Company granted Pediatrix the exclusive rights to develop, manufacture and commercialize ATI-1777 in Greater China. Pediatrix has agreed to pay the Company an upfront payment, development, regulatory and commercial milestone payments, and a tiered royalty ranging from a low-to-high single digit percentage of net sales of ATI-1777 by Pediatrix in Greater China. A portion of consideration received from Pediatrix is payable to the former Confluence equity holders as described below.

Upon execution of the agreement, the Company received an upfront payment of $5.0 million from Pediatrix, a portion of which was payable to the former Confluence equity holders as described below.

License Agreement – Eli Lilly and Company

In August 2022, the Company entered into a non-exclusive patent license agreement with Eli Lilly and Company ("Lilly"). Under the license agreement, the Company granted Lilly non-exclusive rights under certain patents and patent applications that the Company exclusively licenses from a third party. The patents and patent applications relate to the use of baricitinib, Lilly's JAK inhibitor, to treat alopecia areata. Under the license agreement, Lilly has agreed to pay the Company an upfront payment, regulatory and commercial milestone payments, anniversary payments, and a low single-digit royalty calculated as a percentage of Lilly's net sales of baricitinib for the treatment of alopecia areata. The Company has separate contractual obligations under which the Company has agreed to pay to third parties an amount equal to any regulatory and commercial milestone payments it receives under the Lilly license agreement, as well as a portion of the upfront consideration and a portion of the royalties it may receive under the license agreement.

During the year ended December 31, 2022, the Company received $17.8 million from Lilly, a portion of which represented payments for regulatory and commercial milestones that were deemed to have been achieved as of the execution of the license agreement. The Company recognized the payments received during the year ended December 31, 2022 as licensing revenue on its consolidated statements of operations and comprehensive loss. During the year ended December 31, 2022, the Company recorded amounts paid to third parties of $7.4 million as licensing expense on its consolidated statements of operations and comprehensive loss.

Asset Purchase Agreement – EPI Health, LLC

In October 2019, the Company sold RHOFADE (oxymetazoline hydrochloride) cream, 1% ("RHOFADE") to EPI Health, LLC ("EPI Health") pursuant to an asset purchase agreement. EPI Health agreed to pay the Company a high single-digit royalty calculated as a percentage of net sales on a country-by-country basis until the date that the patent rights related to RHOFADE have expired or, if later, ten years from the date of the first commercial sale of RHOFADE in such country. The Company recorded royalty income under the asset purchase agreement of $1.0 million, $0.8 million and $0.7 million during the years ended December 31, 2022, 2021 and 2020, respectively. Royalty income is included in licensing revenue on the consolidated statements of operations and comprehensive loss. EPI Health has also agreed to pay the Company potential sales milestone payments of up to $20.0 million in the aggregate upon the achievement of specified levels of net sales of products covered by the asset purchase agreement, and 25% of any upfront, license, milestone, maintenance or fixed payment received by EPI Health in connection with any license or sublicense of the assets transferred in the disposition in any territory outside of the United States, subject to specified exceptions.

Agreement and Plan of Merger – Confluence

In August 2017, the Company entered into an Agreement and Plan of Merger, pursuant to which it acquired Confluence (the "Confluence Agreement"). Under the Confluence Agreement, the Company agreed to pay the former Confluence equity holders aggregate remaining contingent consideration of up to $75.0 million based upon the achievement of specified regulatory and commercial milestones set forth in the Confluence Agreement. In addition, the Company agreed to pay the former Confluence equity holders future royalty payments calculated as a low single-digit percentage of annual net sales, subject to specified reductions, limitations and other adjustments, until the date that all of the patent rights for that product have expired, as determined on a country-by-country and product-by-product basis or, in specified circumstances, ten years from the first commercial sale of such product. In addition to the payments described above, if the Company sells, licenses or transfers any of the intellectual property acquired from Confluence pursuant to the Confluence Agreement to a third party, the Company will be obligated to pay the former Confluence equity holders a portion of any consideration received from such sale, license or transfer in specified circumstances.

As of December 31, 2022 and December 31, 2021, the balance of the Company's contingent consideration liability was $33.1 million and $28.4 million, respectively (see Note 3).

License and Collaboration Agreement – Rigel Pharmaceuticals, Inc.

In August 2015, the Company entered into an exclusive, worldwide license and collaboration agreement with Rigel Pharmaceuticals, Inc. ("Rigel") for the development and commercialization of products containing two specified JAK inhibitors. In connection with an amendment of the agreement with Rigel in October 2019, the Company paid Rigel an amendment fee of $1.5 million during the year ended December 31, 2020. The Company terminated the license and collaboration with Rigel effective as of April 2021.

15. Retirement Savings Plan

The Company has a defined contribution savings plan under Section 401(k) of the Internal Revenue Code. This plan covers substantially all employees who meet minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. Company contributions to the plan may be made at the discretion of the Company's board of directors. The Company has elected to match employee contributions to the 401(k) Plan up to 4% of the employee's earnings, subject to certain limitations. Company contributions under the 401(k) Plan were $0.5 million, $0.3 million and $0.4 million for the years ended December 31, 2022, 2021 and 2020, respectively.

16. Segment Information

The Company has two reportable segments, therapeutics and contract research. The therapeutics segment is focused on identifying and developing innovative therapies to address significant unmet needs for immuno-inflammatory diseases. The contract research segment earns revenue from the provision of laboratory services. Contract research revenue is generally evidenced by contracts with clients which are on an agreed upon fixed-price, fee-for-service basis. Corporate and other includes general and administrative expenses as well as eliminations of intercompany transactions. The Company does not report balance sheet information by segment since it is not reviewed by the chief operating decision maker, and all of the Company's tangible assets are held in the United States.

The Company's results of operations by segment for the years ended December 31, 2022, 2021 and 2020 are summarized in the tables below:

(In thousands) Year Ended December 31, 2022	Therapeutics	Contract Research	Corporate and Other	Total Company
Total revenue	$ 25,356	$ 17,005	$ (12,609)	$ 29,752
Cost of revenue	—	15,847	(11,824)	4,023
Research and development	78,599	—	(786)	77,813
General and administrative	—	3,505	21,628	25,133
Licensing	7,937	—	—	7,937
Revaluation of contingent consideration	4,700	—	—	4,700
Loss from operations	$ (65,880)	$ (2,347)	$ (21,627)	$ (89,854)

(In thousands) Year Ended December 31, 2021	Therapeutics	Contract Research	Corporate and Other	Total Company
Total revenue	$ 932	$ 13,447	$ (7,618)	$ 6,761
Cost of revenue	—	11,885	(7,172)	4,713
Research and development	44,259	—	(446)	43,813
General and administrative	—	3,047	20,572	23,619
Revaluation of contingent consideration	24,339	—	—	24,339
Loss from operations	$ (67,666)	$ (1,485)	$ (20,572)	$ (89,723)

(In thousands) Year Ended December 31, 2020	Therapeutics	Contract Research	Corporate and Other	Total Company
Total revenue	$ 696	$ 13,319	$ (7,533)	$ 6,482
Cost of revenue	—	12,228	(7,095)	5,133
Research and development	29,777	—	(439)	29,338
General and administrative	—	2,794	17,736	20,530
Revaluation of contingent consideration	2,393	—	—	2,393
Loss from operations	$ (31,474)	$ (1,703)	$ (17,735)	$ (50,912)
Income (loss) from discontinued operations	$ 140	$ —	$ (1)	$ 139

Intersegment Revenue

Revenue for the contract research segment included $12.6 million, $7.6 million and $7.5 million for services performed on behalf of the therapeutics segment for the years ended December 31, 2022, 2021 and 2020, respectively. All intersegment revenue has been eliminated in the Company's consolidated statement of operations.

17. Legal Proceedings

Securities Class Action

On July 30, 2019, plaintiff Linda Rosi ("Rosi") filed a putative class action complaint captioned *Rosi v. Aclaris Therapeutics, Inc., et al.* in the U.S. District Court for the Southern District of New York against the Company and certain of its executive officers. On September 5, 2019, an additional plaintiff, Robert Fulcher ("Fulcher"), filed a substantially identical putative class action complaint captioned *Fulcher v. Aclaris Therapeutics, Inc., et al.* in the same court against the same defendants. On November 6, 2019, the court consolidated the Rosi and Fulcher actions (together, the "Consolidated Securities Action") and appointed Fulcher "lead plaintiff" for the putative class. The parties signed and filed a settlement agreement in July 2021. The court granted final approval of the settlement on December 9, 2021. As of

December 31, 2021, the Company's financial obligation under the settlement was $2.7 million, which was within the limits of its insurance coverage. The settlement was paid in January 2022.

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

Under the supervision of and with the participation of our management, including our chief executive officer, who is our principal executive officer, and our chief financial officer, who is our principal financial officer, we conducted an evaluation of the effectiveness of our disclosure controls and procedures as of December 31, 2022, the end of the period covered by this Annual Report. The term "disclosure controls and procedures," as set forth in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to provide reasonable assurance that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the rules and forms promulgated by the SEC. Disclosure controls and procedures include, without limitation, controls and procedures designed to provide reasonable assurance that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2022, our chief executive officer and chief financial officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act. Management conducted an assessment of our internal control over financial reporting based on the framework established in 2013 by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control—Integrated Framework*. Based on the assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2022 to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with U.S. GAAP. Our independent registered public accounting firm, PricewaterhouseCoopers LLP, has issued an audit report with respect to our internal control over financial reporting, which appears in Part II, Item 8 of this Annual Report.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rules 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the quarter ended December 31, 2022 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Limitations on Effectiveness of Disclosure Controls and Procedures and Internal Control over Financial Reporting

In designing and evaluating the disclosure controls and procedures and internal control over financial reporting, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures and internal control over financial reporting must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Item 9B. Other Information

Not applicable.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

We will file a definitive Proxy Statement for our 2023 Annual Meeting of Stockholders, or the 2023 Proxy Statement, with the SEC, pursuant to Regulation 14A, not later than 120 days after the end of our fiscal year. Accordingly, certain information required by Part III has been omitted under General Instruction G(3) to Form 10-K. Only those sections of the 2023 Proxy Statement that specifically address the items set forth herein are incorporated by reference.

Item 10. Directors, Executive Officers and Corporate Governance

The information required by Item 10 is hereby incorporated by reference to the sections of the 2023 Proxy Statement under the captions "Information Regarding the Board of Directors and Corporate Governance," "Election of Directors" and "Information about our Executive Officers."

Item 11. Executive Compensation

The information required by Item 11 is hereby incorporated by reference to the sections of the 2023 Proxy Statement under the captions "Executive Compensation" and "Non-Employee Director Compensation."

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

The information required by Item 12 is hereby incorporated by reference to the sections of the 2023 Proxy Statement under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Securities Authorized for Issuance under Equity Compensation Plans."

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

The information required by Item 13 is hereby incorporated by reference to the sections of the 2023 Proxy Statement under the captions "Transactions with Related Persons" and "Independence of the Board of Directors."

Item 14. Principal Accountant Fees and Services

The information required by Item 14 is hereby incorporated by reference to the sections of the 2023 Proxy Statement under the caption "Ratification of Selection of Independent Registered Public Accounting Firm."

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) The following documents are filed as part of this report:

(1) Financial Statements

Our consolidated financial statements are listed in the "Index to Consolidated Financial Statements" under Part II. Item 8 of this Annual Report on Form 10-K.

(2) Financial Statement Schedules

Financial statement schedules have been omitted in this report because they are not applicable, not required under the instructions, or the information required is set forth in the consolidated financial statements or related notes thereto.

(3) *Exhibits*

See exhibits listed under part (b) below.

(b) Exhibits

Exhibit Number	Description of Document
2.1#	Agreement and Plan of Merger, dated as of August 3, 2017, by and among the Registrant, Aclaris Life Sciences, Inc., Confluence Life Sciences, Inc. and Fortis Advisors LLC (incorporated by reference to Exhibit 2.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37581), filed with the SEC on November 7, 2017).
2.2^&	Asset Purchase Agreement, by and between the Registrant and EPI Health, LLC, dated as of October 10, 2019 (incorporated by reference to Exhibit 2.1 to the Registrant's Current Report on Form 8-K (File No. 001-37581), filed with the SEC on October 11, 2019).
3.1	Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-37581), filed with the SEC on October 13, 2015).
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-37581), filed with the SEC on June 24, 2020).
4.1	Specimen stock certificate evidencing shares of Common Stock (incorporated by reference to Exhibit 4.1 to Amendment No. 2 to the Registrant's Registration Statement on Form S-1 (File No. 333-206437), filed with the SEC on September 25, 2015).
4.2	Description of Securities (incorporated by reference to Exhibit 4.2 to the Registrant's Annual Report on Form 10-K (File No. 001-37581), filed with the SEC on February 25, 2021).
10.1+	Amended and Restated 2012 Equity Compensation Plan (incorporated by reference to Exhibit 10.7 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-206437), filed with the SEC on September 4, 2015).
10.2+	Form of Stock Option Grant under Amended and Restated 2012 Equity Compensation Plan (incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1 (File No. 333-206437), filed with the SEC on August 17, 2015).
10.3+	2015 Equity Incentive Plan (incorporated by reference to Exhibit 4.6 to the Registrant's Registration Statement on Form S-8 (File No. 333-207434), filed with the SEC on October 15, 2015).
10.4+	Form of Stock Option Grant Notice and Stock Option Agreement under 2015 Equity Incentive Plan (incorporated by reference to Exhibit 10.10 to Amendment No. 2 to the Registrant's Registration Statement on Form S-1 (File No. 333-206437), filed with the SEC on September 25, 2015).
10.5+	Form of Restricted Stock Unit Grant Notice and Restricted Stock Unit Award Agreement under 2015 Equity Incentive Plan (incorporated by reference to Exhibit 10.11 to Amendment No. 2 to the Registrant's Registration Statement on Form S-1 (File No. 333-206437), filed with the SEC on September 25, 2015).

10.6+	Form of Performance Stock Option Grant Notice and Stock Option Agreement used in connection with the 2015 Equity Incentive Plan (incorporated by reference to Exhibit 10.11 to the Registrant's Annual Report on Form 10-K (File No. 001-37581), filed with the SEC on March 18, 2019).
10.7+	Form of Performance Restricted Stock Unit Grant Notice and Restricted Stock Unit Award Agreement used in connection with the 2015 Equity Incentive Plan (incorporated by reference to Exhibit 10.12 to the Registrant's Annual Report on Form 10-K (File No. 001-37581), filed with the SEC on March 18, 2019).
10.8+	Aclaris Therapeutics, Inc. Inducement Plan (incorporated herein by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-37581), filed with the SEC on August 1, 2017).
10.9+	Form of Stock Option Grant Notice and Stock Option Agreement used in connection with the Aclaris Therapeutics, Inc. Inducement Plan (incorporated herein by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K (File No. 001-37581), filed with the SEC on August 1, 2017).
10.10+	Sixth Amended and Restated Non-Employee Director Compensation Policy (incorporated herein by reference to Exhibit 10.12 to the Registrant's Annual Report on Form 10-K (File No. 001-37581), filed with the SEC on February 24, 2022).
10.11+	Seventh Amended and Restated Non-Employee Director Compensation Policy (incorporated herein by reference to Exhibit 10.23 to the Registrant's Annual Report on Form 10-K (File No. 001-37581), filed with the SEC on February 24, 2022).
10.12+*	Eighth Amended and Restated Non-Employee Director Compensation Policy.
10.13+	Form of Indemnification Agreement (incorporated by reference to Exhibit 10.12 to the Registrant's Registration Statement on Form S-1 (File No. 333-206437), filed with the SEC on August 17, 2015).
10.14+	Severance Agreement and General Release, dated as of November 1, 2021, by and between the Registrant and Kamil Ali-Jackson (incorporated herein by reference to Exhibit 10.17 to the Registrant's Annual Report on Form 10-K (File No. 001-37581), filed with the SEC on February 24, 2022).
10.15+	Amended and Restated Employment Agreement, dated as of January 12, 2022, by and between the Registrant and Neal Walker (incorporated herein by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-37581), filed with the SEC on January 14, 2022).
10.16+*	Letter Agreement, dated as of November 22, 2022, by and between the Registrant and Neal Walker.
10.17+	Amended and Restated Employment Agreement, dated as of January 12, 2022, by and between the Registrant and Frank Ruffo (incorporated herein by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-37581), filed with the SEC on January 14, 2022).
10.18+^ *	Separation Agreement and General Release, dated as of December 9, 2022, by and between the Registrant and Frank Ruffo.
10.19+*	Consulting Agreement, dated as of January 1, 2023, by and between the Registrant and Frank Ruffo.
10.20+	Employment Agreement, dated as of January 12, 2022, by and between the Registrant and Joseph Monahan (incorporated herein by reference to Exhibit 10.15 to the Registrant's Annual Report on Form 10-K (File No. 001-37581), filed with the SEC on February 24, 2022).
10.21+	Employment Agreement, dated as of January 31, 2022, by and between the Registrant and James Loerop (incorporated herein by reference to Exhibit 10.16 to the Registrant's Annual Report on Form 10-K (File No. 001-37581), filed with the SEC on February 24, 2022).
10.22+	Employment Agreement, dated as of August 1, 2022, by and between the Registrant and Douglas Manion (incorporated herein by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-37581), filed with the SEC on August 1, 2022).
10.23+*	Amended and Restated Employment Agreement, dated as of January 1, 2023, by and between the Registrant and Douglas Manion.
10.24+*	Employment Agreement, dated as of January 1, 2023, by and between the Registrant and Kevin Balthaser.
10.25+	Employment Agreement, dated as of June 27, 2022, by and between the Registrant and Gail Cawkwell (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37581), filed with the SEC on August 3, 2022).
10.26+	Severance Agreement and General Release, dated as of January 7, 2022, by and between the Registrant and David Gordon (incorporated herein by reference to Exhibit 10.18 to the Registrant's Annual Report on Form 10-K (File No. 001-37581), filed with the SEC on February 24, 2022).
10.27	Sublease, dated November 2, 2017, by and between the Registrant and Auxilium Pharmaceuticals, LLC (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-37581), filed with the SEC on November 2, 2017).
10.28	First Amendment to Sublease, dated as of December 13, 2017, by and between the Registrant and Auxilium Pharmaceuticals, LLC (incorporated by reference to Exhibit 10.27 to the Registrant's Annual Report on Form 10-K (File No. 001-37581), filed with the SEC on March 18, 2019).

10.29	Second Amendment to Sublease, dated as of April 29, 2020, by and between the Registrant and Auxilium Pharmaceuticals, LLC (incorporated by reference to Exhibit 10.5 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37581), filed with the SEC on May 7, 2020).
10.30	Sales Agreement, dated May 20, 2021, by and among the Registrant, SVB Leerink LLC and Cantor Fitzgerald & Co. (incorporated herein by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-37581), filed with the SEC on May 20, 2021).
21.1*	Subsidiaries of the Registrant.
23.1*	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm.
24.1*	Power of Attorney (contained on signature page hereto).
31.1*	Certification of Principal Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as 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 Rules 13a-14(b) and 15d-14(b) promulgated under the Securities Exchange Act of 1934 and 18 U.S.C. Section 1350, as adopted pursuant to section 906 of The Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document (the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document)
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

* Filed herewith.

† This certification is being furnished solely to accompany this Annual Report pursuant to 18 U.S.C. Section 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and is not to be incorporated by reference into any filing of the Registrant, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

+ Indicates management contract or compensatory plan.

Confidential treatment has been granted with respect to portions of this exhibit (indicated by asterisks) and those portions have been separately filed with the SEC.

^ Pursuant to Item 601(a)(5) of Regulation S-K promulgated by the SEC, certain exhibits and schedules to this agreement have been omitted. The Company hereby agrees to furnish supplementally to the SEC, upon its request, any or all of such omitted exhibits or schedules.

& Pursuant to Item 601(b)(2)(ii) of Regulation S-K promulgated by the SEC, certain portions of this exhibit have been redacted because such portions, indicated by asterisks, are both not material and would likely cause competitive harm to the Company if publicly disclosed. The Company hereby agrees to furnish supplementally to the SEC, upon its request, an unredacted copy of the exhibit.

Item 16. Form 10-K Summary

Not applicable.

SIGNATURES

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

ACLARIS THERAPEUTICS, INC.

By: /s/ Douglas Manion
Douglas Manion
President and Chief Executive Officer

Date: February 23, 2023

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Douglas Manion and Kevin Balthaser, jointly and severally, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign this Annual Report on Form 10-K of Aclaris Therapeutics, Inc., and any or all amendments thereto, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises hereby ratifying and confirming all that said attorneys-in-fact and agents, or his, her or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, 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/ Douglas Manion Douglas Manion	President, Chief Executive Officer and Director *(Principal Executive Officer)*	February 23, 2023
/s/ Kevin Balthaser Kevin Balthaser	Chief Financial Officer *(Principal Financial Officer and Principal Accounting Officer)*	February 23, 2023
/s/ Neal Walker Neal Walker	Chairman of the Board of Directors	February 23, 2023
/s/ Christopher Molineaux Christopher Molineaux	Lead Independent Director	February 23, 2023
/s/ Anand Mehra, M.D. Anand Mehra, M.D.	Director	February 23, 2023
/s/ William Humphries William Humphries	Director	February 23, 2023
/s/ Andrew Powell Andrew Powell	Director	February 23, 2023
/s/ Andrew Schiff Andrew Schiff	Director	February 23, 2023
/s/ Bryan Reasons Bryan Reasons	Director	February 23, 2023
/s/ Maxine Gowen Maxine Gowen	Director	February 23, 2023
/s/ Vincent Milano Vincent Milano	Director	February 23, 2023

DIRECTORS

Dr. Neal Walker
Chair

Christopher P. Molineaux[3]
Lead Independent Director

Maxine Gowen, Ph.D.[2,5,8]
Director

William Humphries[7]
Director

Douglas Manion, M.D., FRCP(C)
Director, President and Chief Executive Officer

Anand Mehra, M.D.[4,6]
Director

Vincent Milano[6]
Director

Andrew Powell[5,7]
Director

Bryan Reasons[1]
Director

Andrew Schiff, M.D.[6,8]
Director

[1] Chair of Audit Committee
[2] Chair of Compensation Committee
[3] Chair of Nominating and Corporate Governance Committee
[4] Chair of Research and Development Committee
[5] Member of Audit Committee
[6] Member of Compensation Committee
[7] Member of Nominating and Corporate Governance Committee
[8] Member of Research and Development Committee

OFFICERS

Douglas Manion, M.D., FRCP(C)
President and Chief Executive Officer

Kevin Balthaser
Chief Financial Officer

Joseph Monahan, Ph.D.
Chief Scientific Officer

James Loerop
Chief Business Officer

Gail Cawkwell, M.D., Ph.D.
Chief Medical Officer

SHAREHOLDER REFERENCE

Annual Meeting
The annual meeting of shareholders will be held virtually at www.virtualshareholdermeeting.com/ACRS2023, at 9:00 a.m. Eastern Time on Thursday, June 1, 2023.

Registrar and Transfer Agent
Broadridge Corporate Issuer Solutions
P.O. Box 1342
Brentwood, NY 11717
www.broadridge.com

Investor Information
Exchange: Nasdaq Global Select Market
Ticker Symbol: ACRS

Investor Relations
A copy of the Form 10-K for 2022 filed with the Securities and Exchange Commission accompanies this Annual Report. Copies of the announcements and quarterly earnings are available without charge to any shareholder, beneficial owner or interested investor upon request to:

640 Lee Road
Suite 200
Wayne, PA 19087
Tel: 484-639-7235
Email: rdoody@aclaristx.com
Attention: Robert A. Doody Jr.

Legal Counsel
Cooley LLP
One Freedom Square
Reston Town Center
11951 Freedom Drive
Reston, VA 20190

Independent Auditors
PricewaterhouseCoopers LLP
Two Commerce Square
2001 Market Street | Suite 1800
Philadelphia, PA 19103

Forward–Looking Statement
This annual report to shareholders contains forward-looking information about Aclaris' future operating and financial performance, business plans and prospects, and drug candidates that involve substantial risk and uncertainties. Please refer to the special note regarding forward-looking statements in the Form 10-K found in this annual report and on our website for additional risk factors affecting our forward-looking statements.

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