

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

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from _____ to _____
Commission file number: 001-31326

ELOXX PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware
(State or Other Jurisdiction of
Incorporation or Organization)

84-1368850
(I.R.S. Employer
Identification No.)

480 Arsenal Way
Watertown, Massachusetts 02472
(Address of Principal Executive Offices and Zip Code)
(781) 577-5300
(Registrant's Telephone Number, Including Area Code)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, \$0.01 par value	ELOX	NASDAQ Capital Market

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

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

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

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

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

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

Large accelerated filer ☐
Non-accelerated filer ☒

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 Act). Yes ☐ No ☒

The aggregate market value of the voting stock held by non-affiliates of the registrant on June 30, 2022, the last business day of the registrant's most recently completed second quarter, was \$16,650,960, based on the closing price for such stock as reported on the NASDAQ Capital Market on that date.

As of March 28, 2023, there were 2,166,356 shares of the Registrant's common stock, par value \$0.01 per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Certain information required by Part III, Items 10-14 of this Form 10-K is incorporated by reference to the Registrant's definitive Proxy Statement for the 2022 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Form 10-K, provided that if such Proxy Statement is not filed within such period, such information will be included in an amendment to this Form 10-K to be filed within such 120-day period.

ELOXX PHARMACEUTICALS INC.
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Special Note Regarding Forward-Looking Statements

Eloxx Pharmaceuticals, Inc., together with its subsidiaries, is collectively referred to herein as “we,” “our,” “us,” “Eloxx” or the “Company”. *Hyperlinks and web addresses are provided as a convenience and for informational purposes only. Eloxx bears no responsibility for the security or content of external websites.*

This Annual Report on Form 10-K (the “Annual Report”) and the other documents we have filed with the U.S. Securities and Exchange Commission (the “SEC”) that are incorporated herein by reference, contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended (the “Securities Act”) and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”). All statements other than statements of present and historical facts contained in this Annual Report, including without limitation, statements regarding expected timing of trials and results from our clinical program, strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. Without limiting the foregoing, in some cases, you can identify forward-looking statements by terms such as “aim,” “may,” “will,” “would,” “should,” “expect,” “explore,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential,” “seeks,” or “continue” or the negative of these terms or other similar expressions, although not all forward-looking statements contain these words. No forward-looking statement is a guarantee of future results, performance, or achievements, and one should avoid placing undue reliance on such statements.

Forward-looking statements are based on our management’s beliefs and assumptions and on information currently available to us. Such beliefs and assumptions may or may not prove to be correct. Additionally, such forward-looking statements are subject to a number of known and unknown risks, uncertainties and assumptions, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various factors, including, but not limited to, those identified in Part I, Item 1A. “Risk Factors” and Part II, Item 7. “Management’s Discussion and Analysis of Financial Condition and Results of Operations.” These risks and uncertainties include, but are not limited to:

- risks related to our ability to obtain the capital necessary to fund our operations and continue as a going concern;
- risks related to our dependence on our lead product candidate, ELX-02 and our ability to progress any product candidates in preclinical or clinical trials;
- risks related to our ability to obtain adequate financing in the future through product licensing, public or private equity or debt financing or otherwise;
- the length and expense of preclinical and clinical trial development, the uncertainty of clinical trial results and the fact that positive results from preclinical studies are not always indicative of positive clinical results;
- risks related to the scope, rate and progress of our preclinical studies and clinical trials and other research and development activities;
- risks related to the competition for patient enrollment from drug candidates in development;
- the impact of the global COVID-19 pandemic on our clinical trials, operations, vendors, suppliers and employees;
- risks related to regulatory approvals and other requirements applicable to our product candidates;
- risks relating to the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- general business conditions, regulatory environment, competition and market for our products;
- business abilities and judgment of personnel, and the availability of qualified personnel; and
- those identified in Part I, Item 1A. “Risk Factors” and Part II, Item 7. “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in this Annual Report.

Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risks and uncertainties.

Although we believe the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, level of activity, performance or achievements. You should not rely upon forward-looking statements as predictions of future events. All forward-looking statements speak only as of the date of this Annual Report. Unless required by law, we will not undertake and we specifically disclaim any obligation to release publicly the result of any revisions which may be made to any forward-looking statements to reflect events or circumstances after the date of such statements or to reflect the occurrence of events, whether or not anticipated. In that respect, we wish to caution readers not to place undue reliance on any such forward-looking statements, which speak only as of the date they are made.

Market and Industry Data

This Annual Report and the other documents incorporated herein by reference include statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe these industry publications and third-party research, surveys and studies are reliable, we have not independently verified such data and disclaim responsibility for its content. Furthermore, management's estimates are derived from publicly available information, their knowledge of our industry and their assumptions based on such information and knowledge, which we believe to be reasonable. This data involves a number of assumptions and limitations which are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in this Annual Report under "Forward Looking Statements" and Part I, Item 1A "Risk Factors." These and other factors could cause our future performance to differ materially from our assumptions and estimates.

Risk Factor Summary

The following is a summary of the principal risks of an investment in our common stock. This summary does not list all the risks that we face. Additional discussion of the risks summarized below are included in Part I, Item 1A, "Risk Factors" and should be carefully considered, together with other information in this Annual Report and our other filings with the SEC before making an investment decision regarding our common stock.

- We are heavily dependent on the success of our lead product candidate, ELX-02. If ELX-02 does not achieve positive results during development or suffers any material development delays, it may adversely impact the commercial viability of ELX-02 and our business.
- We will need substantial additional funding by September 2023. If we are unable to raise capital when needed, we would be forced to delay, reduce, or eliminate our product development programs or commercialization efforts.
- Preclinical and clinical drug development is a lengthy and expensive process, with an uncertain outcome. Our preclinical and clinical programs may experience delays or may never advance, which would adversely affect ability to further advance clinical development, obtain regulatory approvals or commercialize our product candidates on a timely basis or at all, which could have an adverse effect on our business.
- We and our collaborating partners may be subject, directly or indirectly, to federal and state healthcare fraud and abuse and false claims laws and regulations. If we or our collaborating partners are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.
- Our product candidates, including ELX-02 and ZKN-13, may cause adverse events or have other properties that could delay or prevent their regulatory approval or limit the scope of any approved label or market acceptance.
- Even though we have received orphan drug designation from the FDA for ELX-02 for the treatment of cystic fibrosis, cystinosis, MPS I, and Rett syndrome, we may not be able to maintain the benefits of orphan drug designation or obtain orphan drug marketing exclusivity for ELX-02 or any of our other product candidates for Alport syndrome or other indications.
- A Fast Track Designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.
- We may find it difficult to recruit and enroll patients in our clinical trials, which could cause significant delays in the completion of such trials or may cause us to abandon one or more clinical trials.
- If we are unable to develop and commercialize our product candidates, our business will be adversely affected.
- We have incurred significant operating losses since our inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future. We may never achieve or maintain profitability.
- Our recurring losses from operations raise substantial doubt regarding our ability to continue as a going concern.
- If we fail to adequately protect or enforce our intellectual property rights or secure rights to third party patents, the value of our intellectual property rights would diminish, and our business, competitive position and results of operations would suffer.
- If we infringe the rights of third parties, we could be prevented from selling products, forced to pay damages and required to defend against litigation which could result in substantial costs and may have a material adverse effect on our business, results of operations and financial condition.
- Maintaining and improving our financial controls and the requirements of being a public company may strain our resources, divert management's attention and affect our ability to attract and retain qualified board members.
- Our ability to use our net operating losses to offset future taxable income may be subject to certain limitations.
- Our stock price may be volatile, and purchasers of our common stock could incur substantial losses.

PART I

ITEM 1. BUSINESS

Company Overview

We are a clinical-stage biopharmaceutical company engaged in the science of ribosome modulation, leveraging both our innovative TURBO-ZM™ chemistry technology platform and our library of novel aminoglycosides to develop novel oral small molecule Ribosome Modulating Agents (“RMAs”) and Eukaryotic Ribosome Selective Glycosides (“ERSGs”), for the treatment of rare and ultra-rare genetic diseases where patients have point nonsense genetic mutations that result in premature stop codons and less than full length proteins. Nonsense mutations result in premature stop codons in the impacted messenger RNA (“mRNA”) which in turn disrupt protein synthesis from that mRNA leading to less than full length proteins. Patients with these mutations have significantly worse outcomes than with missense mutations.

We have multiple programs in our pipeline including a clinical program for the treatment of Alport syndrome with ELX-02 (subcutaneous delivery), preclinical programs in investigational new drug (“IND”) enabling stages in Recessive Dystrophic (“RDEB”) and Junctional Epidermolysis Bullosa (“JEB”) and Familial Adenomatous Polyposis (“FAP”) with ZKN-013, and IND enabling stage program with inhaled delivery of ELX-02 in Class 1 cystic fibrosis (“CF”). We also have various earlier discovery stage programs in CF and oncology. As our programs advance, we plan to actively look to expand our pipeline by seeking new indications in other rare diseases for compounds designed with our platforms. The U.S. Food and Drug Administration (“FDA”) has granted Fast Track designation for ELX-02 for the treatment of CF patients with nonsense mutations. In addition, the FDA granted ELX-02 Orphan Drug Designation for the treatment of CF in July 2020 and, based on the European Medicines Agency’ s (“EMA”) positive opinion, the European Commission granted ELX-02 orphan medicinal product designation in September 2018.

In March 2022, we announced our decision to advance ELX-02 delivered subcutaneously for the restoration of collagen IV protein for the treatment of Alport syndrome. Alport syndrome with nonsense mutations is a genetic kidney disorder that occurs in 1 in 50,000 newborns in the United States. It is caused by the loss of one of three collagen IV subtypes. This disease is characterized by blood (hematuria) and protein (proteinuria) in the patient’s urine and results in progressive kidney disease, hearing loss, and eye abnormalities. In November 2022, we began a Phase 2 monotherapy clinical trial for ELX-02 for the treatment of Alport syndrome and in February 2023, we announced that the first patients had been enrolled. ELX-02 treatment has demonstrated restoration of full-length protein in multiple preclinical models, including collagen IV and collagen VII in cells, and also clinical activity in our Phase 2 cystic fibrosis trial. In February 2023 we announced that the first patients had been dosed in this Phase 2 trial. We believe our results, previously conducted *in vivo* studies showing improvement of kidney function with collagen IV restoration and the ability to achieve high kidney drug levels at tolerable doses support the clinical development of ELX-02 in Alport syndrome. This Phase 2 trial is targeting dosing of up to eight Alport syndrome patients with nonsense mutations in the collagen IV (COL4) gene. Patients will be dosed for two months with a three month follow-up. In addition to the primary endpoint of safety, the key secondary efficacy endpoint of proteinuria will be measured every two weeks. For eligible patients, induction of the COL IV protein will also be measured at the end of two months. Topline results are expected in the first half of 2023.

We are also advancing ZKN-013 as an oral agent for the treatment of RDEB/JEB and FAP patients with nonsense mutations. RDEB and JEB are rare skin diseases characterized by mutations in Collagen VII (RDEB) and LAMB3(JEB) proteins. We estimate that there are approximately 4,000 patients with nonsense mutations in these diseases in the major markets of the United States, Japan, and western Europe. Patients suffer from severe skin bruising, wounds and internal lesions resulting in increased risk of skin cancer and severe malnourishment. FAP patients have mutations in the APC gene that result in a proliferation of polyps in the colon that if untreated can lead to colon and other related cancers. There are currently no approved disease modifying therapies for these diseases. ZKN-013 has demonstrated robust collagen VII restoration in patient cells comparable to 5-10% of protein restoration across a range of mutations. We have also seen in two separate studies, that treatment of APC_{Min} mice, a validated model for evaluating potential treatment effects in FAP patients, with ZKN-013 for eight weeks reduced polyp number, polyp size and meaningfully improved survival. On March 24, 2023, we submitted an IND for ZKN-013 for the treatment of RDEB.

In September 2022, in consultation with the Cystic Fibrosis Foundation (“CFF”), we terminated the development of ELX-02 delivered subcutaneously, for the treatment of CF patients with at least one nonsense (“Class 1 CF”) mutation. This decision was made after our Phase 2 trial of ELX-02 in combination with ivacaftor, an approved drug currently marketed for the treatment of certain CF patients under the trade name “Kalydeco” , did

not meet the secondary efficacy endpoint of reduction from baseline in sweat chloride concentration (SCC) or improvement from baseline in percent forced expiratory volume (FEV1). Encouragingly, we continued to see strong evidence of biological activity similar to that in our previously completed Phase 2 study that reported in November 2021 a reduction in sweat chloride concentration from baseline after one week of treatment with ELX-02. We believe that the lack of statistically significant clinical benefit in Class 1 CF patients was due to drug concentration in the lung tissue being significantly below that required for effect consistent with our preclinical studies. ELX-02 was well tolerated in the Phase 2 trial with no drug related adverse events even at the clinical dose of 1.5mg/kg. Going forward, we plan to only develop ELX-02 as an inhaled therapy for Class 1 CF patients because the achievable drug concentrations are more than one-hundred times higher in the lung tissue than when given subcutaneously. We have completed the IND enabling studies for inhaled ELX-02 in Class 1 CF but further clinical development is contingent upon funding from the CFF.

Acquisition of Zikani Therapeutics, Inc.

On April 1, 2021, the Company acquired Zikani Therapeutics, Inc. (“Zikani” and such acquisition, the “Zikani Merger”), a company in preclinical development and engaged in the science of ribosome modulation, leveraging its innovative TURBO-ZM™ chemistry technology platform to develop novel RMAs as potential therapeutics for diseases with limited treatment options. The TURBO-ZM™ platform is designed to enable rapid synthesis of novel compounds that can be optimized to modulate the ribosome in a disease specific manner. The TURBO-ZM™ synthetic chemistry platform can design oral novel macrolide-based small molecules that are potent oral modulators with favorable therapeutic indices. Macrolides are antibiotics that inhibit protein synthesis in bacteria.

Our Technology

We are working to unlock the potential of the ribosome to transform genetic diseases. Ribosomes form the translation machinery that generates functional proteins from genetic sequences; modulating the ribosome subunits provides a therapeutic approach to addressing a number of diseases. We are focused on modulating the ribosome to address two specific defects: (1) nonsense mutations implicated in many rare diseases and (2) ribosomal mutations driving cancer.

We are using our TURBO-ZM™ chemistry technology platform and our library of novel aminoglycosides to develop novel small molecule RMAs and ERSGs, that are uniquely positioned to correct both nonsense mutations and ribosomal mutations. Clinical and preclinical results for the ability of macrolide and aminoglycoside antibiotics to restore proteins in nonsense mutations have been shown in more than 36 rare diseases. These molecules have also shown an ability to selectively stop protein translation. However, significant safety, tolerability and delivery limitations have prevented further development for human diseases. Our RMA and ERSG molecules are designed to be safer, more potent, and easier to deliver than traditional macrolide and aminoglycoside antibiotics and thus fulfill their clinical promise.

Nonsense mutations

Nonsense mutations, also known as premature termination or stop codons, are single point mutations within the DNA sequence which are either inherited or acquired that result in the premature termination of the translational process leading to truncated or absent proteins. The ribosome manufactures protein one amino acid at a time designated by a series of three nucleotides, called a codon. A nonsense mutation changes the codon for an amino acid into the codon for a “STOP” signal leading to the formation of a truncated protein with loss of function.

We believe that the segment of patients with diagnosed nonsense mutations on one or both alleles represents a high unmet medical need as there are currently no approved therapeutics targeting the impairment caused by these mutations. Nonsense mutations are involved in a large number of genetic diseases such as cystic fibrosis, Alport, Polycystic Kidney disease, RDEB, JEB, and FAP. According to the Human Gene Mutation Database, nonsense mutations account for approximately 12% of patients with a given genetic disease. The disease phenotypes caused by nonsense mutations are frequently more severe than those caused by other kinds of mutations because these mutations often lead to a complete loss of protein production or function. In general, these diseases do not have specific therapies beyond symptomatic and palliative interventions.

Read-through of nonsense mutations is a naturally occurring process that can be attributed to the redundancy in the three-nucleotide codon structure. During read-through, either the typical healthy or a near-cognate substitute amino acid occurs resulting in the continuation of translation. Our RMAs and ERSGs (like ELX-02) are designed to

enhance the likelihood of readthrough by modulating the ribosome. Multiple compounds within our RMA and ERSG library are designed to demonstrate the readthrough of the premature stop codon.

Drivers of ribosomal mutations in cancer

Loss or gain of ribosomal proteins and ribosome modifying factors in cancer can lead to cancer progression through translation of oncogenic proteins. These altered ribosomes are structurally distinct and can be selectively targeted by rationally designed macrolides designed with the TURBO-ZM™ platform. Active screening of compounds has identified several leads and hits which have shown promising results in colon cancer and small cell lung cancer patient organoids characterized by over expression of cMYC.

Current Data Supporting the Potential Mechanism of Action of ELX-02

ELX-02 is a novel investigational ERSG designed based on aminoglycoside antibiotics, such as gentamicin, with increased selectivity for the eukaryotic ribosome. The early observations of eukaryotic read-through activity were made in patients treated with aminoglycosides due to bacterial infections. However, despite the promising clinical observations of read-through activity, the use of aminoglycoside antibiotics as a read-through therapy is restricted since aminoglycosides may cause damage to the kidney and ear after prolonged administration. The effect of aminoglycoside antibiotics on the hair cells of the ear and the proximal tubular cells of the kidney may be attributed, in part, to the inhibition of mitochondrial protein production in these cells. Due to the markedly decreased affinity for the prokaryotic and mitochondrial ribosomes, ERSG compounds have little of the antibiotic activity associated with aminoglycosides. When compared in laboratory tests to gentamicin (a classic aminoglycoside antibiotic), ELX-02 showed a 100-fold lower antibacterial activity and nine-fold higher read-through activity for nonsense mutations. We believe this result was attributable to higher selectivity towards the eukaryotic cytoplasmic ribosome. Because ERSGs are selective for the eukaryotic cytoplasmic ribosome and have markedly decreased affinity for the mitochondrial ribosome, we believe ERSGs have the potential to show an acceptable safety and tolerability profile for chronic use. We believe that our library of ERSG compounds has the potential to show improved read-through activity with a reduced potential for impairment of the mitochondrial ribosome and may have an improved safety profile.

We evaluated a subset of our compounds in the cell by quantitative polymerase chain reaction ("qPCR"), western blot protein analysis and for proper localization of the restored protein by immunofluorescence. Consistent with our overall hypothesis, we have found that molecules in our library significantly increase both the mRNA (dose-dependent increases of 30-fold over vehicle control) and protein of interest (increased normalized full-length protein 4.7-fold over vehicle control) as well as the protein's proper sub-cellular localization. In addition to supporting our overall mechanism of action hypothesis, these studies have enabled us to develop a robust (z' factor = 0.88), high-throughput assay within this system to further evaluate compound-mediated read-through across our library.

Scope of Activities

We are currently focused on the following program areas.

Alport Syndrome with Nonsense Mutations

Alport syndrome is a major inherited kidney diseases that affects an estimated 155,000 to 215,000 patients worldwide and results from mutations in the COL4 gene which cause truncated or missense COLIV proteins. It is estimated that 85% of patients are X-linked and 15% have recessive mutations

Approximately 6% of Alport patients carry a nonsense mutation on the COL4 gene and have truncated COLIV proteins. More than 70 nonsense mutations have been described. Alport is a progressive disease caused by a fragile (or none) base membrane of the glomeruli due to deficiency in COLIV protein. Alport patients have high levels of blood (Hematuria) and proteins (Proteinuria) in the urine. This in turn causes fibrosis, loss of kidney function (eGFR) and ultimately kidney failure. There are no approved treatments for Alport and 50% of patients with nonsense mutations lose their kidney function by the time they are 18 years old.

We are evaluating the treatment effect of ELX-02 delivered subcutaneously in a Phase 2 trial in Alport Patients. This Phase 2 trial is targeting dosing of up to eight Alport syndrome patients with nonsense mutations in the COL4 gene. Patients will be dosed for two months with a three-month follow-up. In addition to the primary endpoint of safety, the key secondary efficacy endpoint of proteinuria will be measured every two weeks. For eligible patients, induction of COL IV will also be measured at the end of two months. Topline results are expected in the first half of 2023.

Recessive Dystrophic Epidermolysis Bullosa (“RDEB”) and Junctional Epidermolysis Bullosa (“JEB”)

Epidermolysis bullosa (“EB”) is a group of rare inherited skin disorders that cause the skin to become very fragile. Any trauma or friction to the skin can cause painful blisters. RDEB and JEB are the two main types of EB.

RDEB is caused by mutations in the COL7A1 gene that codes for COL7A1 protein. The COL7A1 gene is involved in coding for the collagen that helps attach the epidermis to underlying layers of skin. We are targeting nonsense mutations in COL7A1. These represent approximately 30–40% of all mutations in COL7A1.

JEB is most commonly caused by mutations in the LAMA3, LAMB3 and LAMC2 genes. The LAMA3, LAMB3, and LAMC2 genes are involved in coding for a protein that plays an important role in strengthening and stabilizing the skin. We are targeting nonsense mutations in LAMB3 genes that represent approximately 70% of all mutations.

Infants are typically born with widespread blistering and areas of missing skin, often caused by trauma during birth. Most RDEB patients develop skin cancer by age 35 and the average mortality of patients with JEB is 18 months. RDEB affects approximately 4,000 patients worldwide with nonsense mutations and there are no approved treatments; management is palliative.

ZKN-013 is our lead TURBO-ZM™ based molecule in our program to address nonsense mutations in RDEB/JEB.

Familial Adenomatous Polyposis (“FAP”)

FAP is caused by a mutation in the APC gene coding for APC protein, which acts as a tumor suppressor and keeps cells from growing too fast or in an uncontrolled way. It is characterized by polyps developing in subjects as young as in their teens. These polyps have a high propensity for progression to cancer. Hence patients undergo prophylactic colectomy in adolescence or early adulthood to prevent colorectal cancer development.

Our program to address FAP includes TURBO-ZM™ based RMAs including ZKN-013 and additional undisclosed compounds.

Research and Development Programs

Our pipeline of programs is summarized in the following table:

Indication	Protein restored	Discovery	Lead optimization	IND-enabling	Phase 1 – first-in-human	Phase 2	Key Milestones
Alport Syndrome (nonsense)	Collagen IV	ELX-02 (SC)					PoC trial start (2H22)
RDEB/JEB (nonsense)	Collagen VII/LAMB3	ZKN013 (oral)					IND submission (2H22)
FAP (nonsense)	APC	ZKN013 (oral)					IND preparation
Class 1 CF	CFTR	RMAs (oral)	CYSTIC FIBROSIS FOUNDATION				
Targeted oncology	Undisclosed	RMAs (oral)					
Class 1 CF (inhaled)	CFTR	ELX-02 (inhaled)					TBD

Development Program for ELX-02 for the Treatment of Alport Syndrome

In March 2022, we announced our decision to advance ELX-02 delivered subcutaneously for the restoration of the COL IV protein for the treatment of Alport syndrome, a rare kidney disease, with nonsense mutations, a rare kidney disease. In November 2022, we began a Phase 2 monotherapy clinical trial for ELX-02 for the treatment of Alport syndrome and in January 2023, we announced that the first patients had been enrolled and in February 2023 we announced that the first patients had been dosed. Alport syndrome with nonsense mutations is a genetic kidney disorder that occurs in 1 in 50,000 newborns in the United States. It is caused by the loss of one of three collagen IV subtypes. This disease is characterized by blood (hematuria) and protein (proteinuria) in the patient’s urine, and results in progressive kidney disease, hearing loss, and eye abnormalities. ELX-02 treatment has demonstrated restoration of full-length protein in multiple preclinical models, including collagen IV and collagen VII in cells, and also clinical activity in our Phase 2 cystic fibrosis trial. We believe our results, previously conducted *in vivo* studies

showing improvement of kidney function with collagen IV restoration and the ability to achieve high kidney drug levels at tolerable doses support the clinical development of ELX-02 in Alport syndrome. In preclinical studies, significant improvement in kidney function and survival has been seen in Alport mice that lack full length Collagen IV proteins at very low protein levels when treated with protein restoration therapies. ELX-02 has demonstrated 6 to 15% collagen IV restoration in cellular systems. ELX-02 treatment in mice with another rare kidney disease, cystinosis, also resulted in a reduction of cystine levels, a marker for disease improvement. ELX-02 drug levels in the kidney are approximately 50-fold higher than in the plasma. As a result, at our targeted dose of 0.75mg/kg, which is half of the dose previously given to patients in our Phase 2 CF trial with ELX-02 and ivacaftor, we believe that ELX-02 levels in the kidney could result in protein restoration levels that may be sufficient to reduce proteinuria in Alport patients, a key endpoint for kidney function improvement. This Phase 2 trial is targeting dosing of up to eight Alport syndrome patients with nonsense mutations in the COL4 gene. Patients will be dosed for two months with a three month follow-up. In addition to the primary endpoint of safety, the key secondary efficacy endpoint of proteinuria will be measured every two weeks. For eligible patients, induction of COL IV will also be measured at the end of two months. Topline results are expected in the first half of 2023 and we plan to advance to a pivotal clinical trial if we observe a significant improvement in our efficacy endpoint of proteinuria reduction in the kidney.

ZKN-013 - RDEB and JEB

ZKN-013 is our lead TURBO-ZM™ based molecule in our program to address nonsense mutations in RDEB/JEB. Existing third-party data has paved the way for our development program, including third-party clinical studies evaluating gentamicin. Patients receiving gentamicin in these studies had an approximate 70% increase in wound closure and an approximate 70% decrease in blistering events.

Preclinical results support the potential for RMAs to restore functional collagen protein at levels comparable to high-dose gentamicin. IND-enabling pre-clinical studies have been completed and on March 24, 2023 we filed an IND for ZKN-013 for the treatment of RDEB.

FAP

ZKN-013 has also shown promising in vivo and in vitro preclinical activity in FAP. Existing third-party data has paved the way for our development program, including results from third-party clinical studies evaluating erythromycin, a macrolide antibiotic and Celecoxib. Patients receiving erythromycin in these studies had an approximate 50% reduction in polyp number and polyp burden (area of polyps) after at 12 months after 6 months 400mg/day once daily Celecoxib showed an approximate 30% reduction (vs. those treated with placebo) in polyp number and size after 6 months of treatment.

In a pre-clinical study, evaluating the activity of ZKN-013 in mice models known as APC^{min}, that are considered to be representative of FAP patients, ZKN-013 showed a 40% reduction in polyp number (vs. untreated mice), an approximately 50% reduction in polyp burden (vs. untreated mice) and 50% survival benefit (vs. untreated mice). We believe that these results support the further development of ZKN-013 for the treatment of FAP patients. We continue to evaluate ZKN-013 and other RMAs for their potential to treat FAP patients with nonsense mutations.

ELX-02 – Class 1 CF Program

In September 2022, in consultation with the Cystic Fibrosis Foundation (“CFF”), we terminated the development of ELX-02 delivered subcutaneously, for the treatment CF patients with at least one nonsense (“Class 1 CF”) mutations. This decision was made after our Phase 2 trial of ELX-02 in combination with ivacaftor, an approved drug currently marketed for the treatment of certain CF patients under the trade name “Kalydeco”, did not meet the secondary efficacy endpoint of reduction from baseline in sweat chloride concentration (SCC) or improvement from baseline in percent forced expiratory volume (FEV1). Encouragingly, we continued to see strong evidence of biological activity similar to that in our previously completed Phase 2 study that reported in November 2021 a reduction in sweat chloride concentration from baseline after one week of treatment with ELX-02. We believe that the lack of statistically significant clinical benefit in Class 1 CF patients was due to drug concentration in the lung tissue being significantly below that required for effect consistent with our preclinical studies. ELX-02 was well tolerated in the Phase 2 trial with no drug related adverse events even at the clinical dose of 1.5mg/kg.

Going forward, we plan to only develop ELX-02 as an inhaled therapy for Class 1 CF patients because the achievable drug concentrations are more than one-hundred times higher in the lung tissue than when given subcutaneously. We have completed the IND enabling studies for inhaled ELX-02 in Class 1 CF but further clinical development is contingent upon funding from the CFF.

Ongoing earlier stage discovery programs with our library of RMAs and ESGs

We continue to explore the potential of our libraries of RMAs and ESGs, while expanding our RMA library using our TURBO-ZM™ platform, to expand into other rare diseases and cancers in our earlier stage discovery efforts. We have observed promising early in vitro and in vivo results in various cell line and animal cancer models that support our current efforts.

Intellectual Property

Patent Portfolio

Our licensed and owned patent portfolio includes patents and applications relating to our lead compound, ELX-02 (formerly known as NB124), and over 40 other read-through inducing compounds, as well as methods of making and using these compounds. Each of our patent families is described briefly below.

With regard to ELX-02, our primary composition of matter coverage derives from a first patent family that we exclusively license under the Research and License Agreement (the “Technion Agreement”) with Technion Institute for Research and Development Ltd. (“TRDF”) dated August 29, 2013. As of December 31, 2022, this family included issued patents in the United States, Europe, Canada, Hong Kong, India, Israel, and Japan, and a pending application in the United States and Israel. Issued patents in this family have claims directed to ELX-02 and other read-through inducing compounds, as well as claims directed to pharmaceutical compositions of the disclosed compounds and methods of using the compounds and compositions to treat genetic disorders associated with premature stop codon mutations including cystic fibrosis, nephropathic cystinosis, DMD, ataxia-telangiectasia, Hurler syndrome, hemophilia A and B, Usher Syndrome, and Tay-Sachs. Patents that have issued or which may issue in the future from this family are currently expected to expire in 2031, not including any extensions of term for which we may be eligible and that we may be granted. A second patent family licensed under the Research and License Agreement with TRDF includes one issued U.S. patent with claims directed to the use of ELX-02 and other read-through inducing compounds to treat Rett syndrome.

We own two patent families that may provide additional protection for specific methods of using or manufacturing ELX-02 beyond the anticipated expiration date of the primary composition of matter patents.

The first of these families is directed to methods for large-scale synthesis of ELX-02 and other read-through inducing compounds. As of December 31, 2022, this family included issued patents in the United States, Australia, Israel, India, and Japan and pending applications in the United States, Europe, Brazil, Canada, China Hong Kong, and India. Patents that have issued or which may issue in the future from this family are currently expected to expire in 2038, not including any extensions of term for which we may be eligible that we may be granted.

The second family is directed to methods of using ELX-02 and other read-through inducing compounds to treat various ocular conditions associated with nonsense mutations, including retinitis pigmentosa, Usher Syndrome, Stickler Syndrome, aniridia, Leber congenital amaurosis, and choroideremia. As of December 31, 2022, this family includes pending applications in the United States, Europe, Australia, Canada, China, Hong Kong, Israel, Japan, Mexico, Malaysia, New Zealand, Philippines, Singapore, South Africa, and South Korea. Any patents issuing from this family are currently expected to expire in 2039, not including any extensions of term for which we may be eligible and that we may be granted.

Three additional patent families licensed under the Research and License Agreement with TRDF are directed to additional read-through inducing compounds.

The first of these families includes claims directed to ELX-03 (formerly known as NB84) and other read-through inducing compounds, as well as claims directed to pharmaceutical compositions and methods of using the compounds and compositions to treat genetic disorders including cystic fibrosis, DMD, ataxia-telangiectasia, Hurler syndrome, hemophilia A, hemophilia B, Usher Syndrome, and Tay-Sachs. As of December 31, 2022, this family included issued patents in the U.S., Europe, Canada, India, Israel and Japan, and a pending application in the United States. Patents that have issued or which may issue in the future from this family are currently expected to expire in 2027 and 2028, not including any additional extensions of term for which we may be eligible and that we may be granted.

The second family includes claims directed to ELX-10 (formerly known as NB157) and other read-through inducing compounds and pharmaceutical compositions and uses thereof. As of December 31, 2022, this family included issued patents in the U.S., Australia, China, India, Israel and Japan, and pending applications in the U.S., Europe, Australia, Brazil, Canada, China, Hong Kong, Israel and Japan. Patents that have issued or which may issue in the future from this family are currently expected to expire in 2036, not including any extensions of term for which we may be eligible and that we may be granted.

The third family includes claims directed to additional read-through inducing compounds and pharmaceutical compositions and uses thereof. As of December 31, 2022, this family included an issued patent in Australia and pending applications in the United States, Europe, Australia, Brazil, Canada, China, EAP0, Hong Kong, India, Israel, Japan, Malaysia, Mexico, New Zealand, Singapore, and South Korea. Patents that have issued or which may issue in the future from this family are currently expected to expire in 2038, not including any extensions of term for which we may be eligible and that we may be granted.

Our licensed and owned patent portfolio also includes patents and applications relating to TURBO-ZM™ compounds that can be optimized to modulate the ribosome in a disease specific manner. The TURBO-ZM™ compounds are macrolides. Most commonly known macrolides are antibiotics such as azithromycin, erythromycin and clarithromycin that are delivered orally and have favorable safety profiles that have been shown to inhibit protein synthesis in bacteria. Until Zikani's TURBO-ZM™ chemistry technology, macrolides were only made semi-synthetically which limited their use to antibiotics.

We have licensed four patent families from the President and Fellows of Harvard College ("Harvard") under the license agreement dated February 10, 2015, and subsequently amended and restated on March 31, 2020, claiming macrolides as well as methods of making and using these macrolides. Patents issuing from these families are expected to expire in 2034, 2035 and 2036, respectively, not including any extensions of term for which we may be eligible and that we may be granted.

We jointly own three patent families with Harvard claiming other macrolides as well as methods of making and using these macrolides. These families include pending applications in the United States, Europe, Australia, Brazil, Canada, China, India, Indonesia, Israel, Japan, Mexico, New Zealand, Singapore, South Africa, and South Korea. Any patents issuing from this family are currently expected to expire in 2038 and 2039, respectively, not including any extensions of term for which we may be eligible and that we may be granted. One of these patent families includes claims directed to ZKN-013, our lead TURBO-ZM™ compound.

Patent Term Extension

The term of a U.S. patent is 20 years from its earliest effective filing date, assuming all maintenance fees are paid, the patent has not been terminally disclaimed, and the patent has not been invalidated through administrative and/or court proceedings. The term of foreign patents varies but is generally also 20 years from the earliest effective filing date. In certain instances, the term of U.S. and certain foreign patents may be extended.

In the United States, patent term may be extended in certain instances by patent term adjustment ("PTA"), which compensates for administrative delays by the U.S. Patent & Trademark Office during examination of the patent. We have received a PTA for one of our exclusively licensed patents relating to ELX-01 and other related read-through inducing compounds, extending the expiration date of that patent from 2027 to 2028. However, we do not know whether any PTA will be granted for any of our future patents.

For pharmaceutical products that have received FDA approval, the term of a U.S. patent covering the approved product, a method of manufacturing the approved product, or an approved method of use of the product may be extended under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act, in certain instances if specific statutory and regulatory requirements are satisfied. The Hatch-Waxman Act provides for a patent term extension, or PTE, of up to five years as compensation for effective patent term lost during product development and the FDA regulatory review process. PTE is only available for the first approval of a particular product, the total patent term including the restoration period must not exceed 14 years from the date of FDA approval, and only one patent may be extended for a particular regulatory review period. In the EU, a similar mechanism exists for extending patent term up to five years through the grant of a Supplementary Protection Certificate ("SPC") following European Medicines Agency (the "EMA") approval. Similar regulatory extensions are available or may be available in the future in other jurisdictions. If and when ELX-02 or other of our read-through inducing compounds are approved by the FDA, EMA, or other foreign regulatory authorities, we will apply for these and other patent term extensions on patents covering the approved products, methods of use, or methods of manufacture if the patents are eligible for such extension. However, we cannot provide any assurance that such extensions will be granted for any of our currently issued or future patents.

Trade Secrets and Know-How

With respect to our ERSG-based technology platform, we primarily rely on trade secrets and know-how to protect the proprietary nature of our platform. However, trade secrets and know-how can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements with our employees,

consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data, know-how and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

License Agreements

Research and License Agreement with Technion Research and Development Foundation Ltd. ("TRDF")

On August 29, 2013, we entered into the Technion Agreement with TRDF, which was further amended and addended to reflect, among other things, the assignment of patents and extension of research periods, with respect to certain technology relating to aminoglycosides and the redesign of aminoglycosides for the treatment of human genetic diseases caused by premature stop mutations and further results of the research of the technology, in order to develop and commercialize products based on such technology. The Technion Agreement provides us with an exclusive, worldwide, non-transferrable license, with a right to grant sublicenses, and royalty-bearing licenses to the TRDF inventions, TRDF patent rights, TRDF's interest in the joint inventions and joint patent rights, and certain materials and research results owned by TRDF, solely with respect to products in the field of prevention, diagnosis or treatment of any human disease or condition therefor. In return for the license we will pay TRDF (i) milestone payments with respect to each licensed product upon the achievement of certain pre-defined goals by us or one of our sublicensees as follows: \$100,000 upon first dosing of a patient in a Phase 2 clinical study (which we paid to TRDF in 2020 for ELX-02); \$1,000,000 upon first dosing of a patient in a pivotal study; and \$5,000,000 upon first filing of a new drug application (NDA); (ii) certain royalties in the low- to mid-single-digit percentages of all net sales (subject to change in the case of (a) sublicensing to a big pharmaceutical or biotechnology company, or (b) payment of royalties to third parties, or (c) commercialization by a third party of an authorized generic to a licensed product); and (iii) a low- to mid-double-digit percentage of any non-royalty sublicense income. In addition to the milestone payments, we undertook to annually fund the research activities under the license, currently in the estimated annual amount of \$0.1 million per year. The Technion Agreement further provides TRDF with an additional pre-emptive right, in force until the first exit event, to invest an amount equal to up to 5% of the amount contemplated to be raised in a proposed investment. TRDF is also entitled, until the closing of an exit event, to appoint an observer to the board under certain restrictions such as confidentiality or conflict of interest. Furthermore, we will reimburse TRDF for all patent filing expenses as of the effective date of the Technion Agreement and for past patent filing expenses in the amount of several hundred thousand New Israeli Shekels upon the occurrence of certain conditions.

Under the Technion Agreement, TRDF reserved the right, for itself, the Technion and other not-for-profit research organizations to utilize the technology solely for educational purposes. Furthermore, Professor Baasov, the principal investigator, had ongoing research programs involving covered compounds (as defined in the agreement) that are being funded by the National Institute of Health in the U.S., or the NIH, under sub-awards from the University of Alabama and the University of Michigan, and it is possible that such research programs will overlap with the research conducted according to the terms of our agreement. In the case of any such overlap, the work product of such research will be subject to the terms and conditions of such sub-awards, including certain obligations under 35 U.S.C. §§ 200-212 or 37 C.F.R. § 401 et seq. in the case of any TRDF inventions that are also "subject invention" as defined in 35 U.S.C. § 201.

The license agreement shall continue in full force and effect on a product-by-product and country-by-country basis until the expiration of all payment obligations for any such licensed product as described above. Upon the expiration, we will have a fully paid-up, worldwide non-exclusive, perpetual, irrevocable license (with the right to grant sublicenses) to use certain materials and the research results, solely with respect to products in the field of prevention, diagnosis or treatment of any human disease or condition.

License Agreement between Zikani and President and Fellows of Harvard College ("Harvard")

On February 10, 2015, Zikani entered into an agreement to license certain patent rights owned by Harvard. This license agreement was subsequently amended and restated on March 31, 2020. Harvard is entitled to receive clinical and regulatory milestone payments totaling up to \$3.6 million in the aggregate per licensed product approved in the United States, European Union, and Japan. The Company is also obligated to make additional royalty payments to Harvard upon the occurrence of certain sales milestones per licensed product up to a mid-single digit royalty percentage. The royalty percentage depends on the product and whether such licensed product is

covered by a valid claim within the certain patent rights that the Company licenses from Harvard. Further, the Company may sub license the patent rights and any income, with the Company obligated to remit to Harvard fees ranging from 20% to 30% of such sublicense income up to the achievement of certain milestone events. There were no royalties recorded in 2022 or 2021.

Under this agreement, the Company has an exclusive, worldwide, royalty-bearing license under Harvard's interest in the Patent Rights, and a non-exclusive, worldwide, royalty-bearing license under Harvard's interest in the Harvard Know-How, solely to develop, make, have made, use, offer for sale, sell, have sold and import and export licensed products solely within the field.

Harvard retains the right, for itself and for other not-for-profit research organizations, to practice the patent rights within the scope of the license granted above, solely for non-commercial research, educational and scholarly purposes; provided, that, nothing herein shall be construed as permitting Harvard or any such not-for-profit research organization to grant any rights to any third party, including any for-profit sponsor, to practice or exploit any of the patent rights for any commercial purpose that would be inconsistent with the terms of the exclusive license of the patent rights, including any right to develop, manufacture, market or sell licensed products for use in the field; and the United States federal government retains rights in the patent rights pursuant to 35 U.S.C. §§ 200-212 and 37 C.F.R. § 401 et seq., and any right granted in this agreement greater than that permitted under 35 U.S.C. §§ 200-212 or 37 C.F.R. § 401 et seq. will be deemed modified.

Manufacturing

ELX-02 is designed to be manufactured under current Good Manufacturing Practice ("cGMP") conditions and is formulated as a sterile frozen liquid or lyophilized powder in glass vials. ELX-02 is designed to be administered by parenteral subcutaneous injection after appropriate dilution or reconstitution, as required.

We do not own or operate manufacturing or distribution facilities for the production of clinical quantities of ELX-02 or for our other preclinical product candidates. We currently rely, and expect to continue to rely, on third parties for the manufacture, packaging, labeling and distribution of clinical supplies of ELX-02 as well as any other candidate that we may develop.

We engage separate manufacturers for drug substance and drug product. We have a relationship with a manufacturer that is capable of providing fill and finish services for our clinical product at the current scale. To support later clinical trials, transfer of the manufacturing and release to a manufacturer with higher lot scale capacity will be needed for our clinical product.

All of our current drug candidates are organic compounds of low molecular weight. We have selected our lead compounds not only on the basis of their potential efficacy and safety but also for their ease of synthesis and reasonable cost of their starting materials. ELX-02 is manufactured in reliable and reproducible synthetic processes. We currently use a single third-party manufacturing source for the production of a key raw material, produced by bacterial fermentation; however, we have identified several other acceptable sources for this production.

We currently obtain clinical supplies of ELX-02 from third-party manufacturers pursuant to agreements that include specific supply timelines and volume expectations. If a manufacturer should become unavailable to us for any reason, we would seek to obtain supply from another manufacturer engaged by us for the applicable product or service. In the event that we were unable to procure the applicable supply from a currently qualified manufacturer, we believe that there are a number of potential replacements for each of our outsourced services; however, we would likely experience delays in our ability to supply ELX-02 in advancing our clinical trials while we identify and qualify replacement suppliers.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing and export and import of drug products. A new drug must be approved by the FDA through the New Drug Application ("NDA") process before it may be legally marketed in the United States. We, along with any third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval of our products and product candidates. 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 financial resources.

U.S. Drug Development Process

In the United States, the FDA regulates drugs under the federal Food, Drug, and Cosmetic Act ("FDCA") and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in accordance with FDA' s Good Laboratory Practice ("GLP") requirements and other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent Institutional Review Board ("IRB") or ethics committee at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices ("GCPs") to establish the safety and efficacy of the proposed drug for its intended use;
- preparation of and submission to the FDA of an NDA after completion of all pivotal trials;
- a determination by the FDA within 60 days of its receipt of an NDA to file the application for review
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the drug' s identity, strength, quality and purity, and of selected clinical investigation sites to assess compliance with GCPs; and
- FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the United States.

The preclinical developmental stage generally involves laboratory evaluations of chemistry, formulation and stability, as well as studies to evaluate the product candidate' s toxicity in animals, in an effort to support subsequent clinical testing. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations, where applicable.

Prior to beginning the first clinical trial with a product candidate in the United States, the trial sponsor must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational drug to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product candidate, chemistry, manufacturing, and controls information, and any available human data or literature to support the use of the product candidate. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

Clinical trials involve the administration of the investigational drug to human subjects under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor' s control, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring subject safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. While the IND is active, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or *in vitro* testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

Furthermore, an independent IRB or ethics committee for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site, and must monitor the study until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study, and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries, including *clinicaltrials.gov*.

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

- Phase 1: The product candidate is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.
- Phase 2: The product candidate is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3: The product candidate is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

In some cases, the FDA may require, or sponsors may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies, may be conducted after initial marketing approval, and may be used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

In addition, 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 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, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the meetings at the end of the Phase 2 trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the new drug.

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

U.S. Review and Approval Process

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, preclinical and other non-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of a use of the product, or from a number of alternative sources, including studies initiated by independent investigators. The submission of an NDA is subject to the payment of substantial user fees, unless a waiver or exemption applies.

In addition, the Pediatric Research Equity Act (“PREA”) requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA 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. Once filed, the FDA has a goal of ten months from the filing date to complete a standard review of an NDA for a drug that is a new molecular entity. 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 sufficient to assure and preserve the product’s identity, strength, quality and purity.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. Before approving an NDA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP and adequate to assure consistent production of the product within required specifications. Additionally, before approving a NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCPs.

After the FDA evaluates an NDA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response Letter (“CRL”). An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A CRL will describe all of the deficiencies that the FDA has identified in the NDA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the CRL without first conducting required inspections and/or reviewing proposed labeling. In issuing the CRL, the FDA may recommend actions that the applicant might take to place the NDA in condition for approval, including requests for new clinical studies or additional information or clarification. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the NDA with a Risk Evaluation and Mitigation Strategy (“REMS”) to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. The FDA may also require one or more Phase 4 post- market studies and surveillance to further assess and monitor the product’s safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

Expedited Development and Review Programs

The FDA offers a number of expedited development and review programs for qualifying product candidates. For example, the Fast Track program is intended to expedite or facilitate the process for reviewing product candidates that are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a Fast Track product candidate has

opportunities for more frequent interactions with the applicable FDA review team during development and, once an NDA is submitted, the product candidate may be eligible for priority review. A Fast Track product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

A product candidate intended to treat a serious or life-threatening disease or condition may also be eligible for Breakthrough Therapy designation to expedite its development and review. A product candidate can receive Breakthrough Therapy designation if preliminary clinical evidence indicates that the product candidate, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers.

Any marketing application for a drug submitted to the FDA for approval, including a product candidate with a Fast Track designation and/or Breakthrough Therapy designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. An NDA is eligible for priority review if the product candidate is designed to treat a serious or life-threatening disease or condition, and if approved, would provide a significant improvement in safety or effectiveness compared to available alternatives for such disease or condition. For new-molecular-entity NDAs, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date, as opposed to ten months under standard review.

Additionally, product candidates studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required post-marketing studies in a timely manner or if such studies fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Fast Track designation, Breakthrough Therapy designation, priority review, and accelerated approval do not change the standards for approval, but may expedite the development or approval process. Even if a product candidate qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Orphan drug designation and exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 individuals in the United States and when there is no reasonable expectation that the cost of developing and making available the drug in the United States will be recovered from sales in the United States for that drug. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same disease or condition for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or, as noted above, if a second applicant demonstrates that its product is clinically superior to the approved product with orphan exclusivity or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Post-approval Requirements

Drug products manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program fees for any marketed products. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

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

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters, or untitled letters;
- clinical holds on clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;

- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of drug products. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe, in their independent professional medical judgment, legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA-approved labelling.

Marketing Exclusivity

Market exclusivity provisions authorized under the FDCA can delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity 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. During the exclusivity period, the FDA may not approve or even accept for review an abbreviated new drug application ("ANDA") or an NDA submitted under Section 505(b)(2) (505(b)(2) NDA) submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, 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 alternatively 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 or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to any preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of marketing exclusivity available in the United States. Pediatric exclusivity provides for an additional six months of marketing exclusivity attached to another period of exclusivity if a sponsor conducts clinical trials in children in response to a written request from the FDA. The issuance of a written request does not require the sponsor to undertake the described clinical trials.

Foreign Regulation

We conduct clinical trials and plan to market our future products in numerous jurisdictions outside the U.S. Most of these jurisdictions have clinical trial, product approval and post-approval regulatory processes that are similar in principle to those in the U.S. Thus, whether or not we obtain FDA approval for a product candidate, we must obtain approval by the comparable regulatory authorities of foreign countries or economic areas, such as the E.U., before we can commence clinical trials or market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Under the E.U. regulatory system, a company may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure, which is compulsory for orphan medicines, medicines produced by biotechnology, and those medicines intended to treat AIDS, cancer, neurodegenerative disorders, or diabetes, and optional for those medicines that are highly innovative, provides for the grant of a single

marketing authorization that is valid for all E.U. member states. In addition to the centralized procedure, the E.U. also has a nationalized procedure, which requires a separate application to and approval determination by each country; a decentralized procedure, whereby applicants submit identical applications to several countries and receive simultaneous approval; and a mutual recognition procedure, where applicants submit an application to one country for review and other countries may accept or reject the initial decision.

Other U.S. Healthcare Laws and Compliance Requirements

Although we currently do not have any products on the market, we are and, upon approval and commercialization, will be subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which we conduct our business. In the United States, such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, price reporting, and transparency laws and regulations regarding payments or other transfers of value made to physicians and other licensed healthcare professionals.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting, or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering, or arranging for the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. In addition, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other. 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 and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing, or recommending 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 of its facts and circumstances.

The federal False Claims Act prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to, or approval by, the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes “any request or demand” for money or property presented to the U.S. government. In addition, 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 False Claims Act.

The U.S. federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), also created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items, or services. Similar to the Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Additionally, the federal Physician Payments Sunshine Act and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid, or the Children’s Health Insurance Program (with certain exceptions) annually report information related to certain payments or other transfers of value made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives) and teaching hospitals, certain ownership and investment interests held by physicians and their immediate family members.

Violation of any of the federal and state healthcare laws described above or any other governmental regulations that apply to us may result in significant penalties, including without limitation, civil, criminal and/or administrative penalties, damages, fines, disgorgement, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, private “qui tam” actions brought by individual whistleblowers in the name of the government, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of operations.

Coverage and Reimbursement

Sales of any pharmaceutical product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Significant uncertainty exists as to the coverage and reimbursement status of any newly approved product, particularly for gene therapy products where the Centers for Medicare & Medicaid Services (“CMS”) and other third-party payors in the United States have not yet established a uniform policy of coverage and reimbursement. Therefore, decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. One third-party payor’s decision to cover a particular product does not ensure that other payors will also provide coverage for the product. As a result, the coverage determination process can require manufacturers to provide scientific and clinical support for the use of a product to each payor separately and can be a time-consuming process, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization.

In addition, third-party payors are increasingly reducing reimbursements for pharmaceutical products and services. The U.S. government and state legislatures have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Third-party payors are more and more challenging the prices charged, examining the medical necessity and reviewing the cost effectiveness of pharmaceutical products, in addition to questioning their safety and efficacy. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of us placing the medicinal product on the market. Pharmaceutical products may face competition from lower-priced products in foreign countries that have placed price controls on pharmaceutical products and may also compete with imported foreign products. Furthermore, there is no assurance that a product will be considered medically reasonable and necessary for a specific indication, will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be established even if coverage is available or that the third-party payors’ reimbursement policies will not adversely affect the ability for manufacturers to sell products profitably.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products and services, implementing reductions in government healthcare programs and other healthcare funding and applying new payment methodologies. For example, in March 2010, the Affordable Care Act, or ACA, was enacted, which affected existing government healthcare programs and resulted in the development of new programs. Among the ACA’s provisions of importance to the pharmaceutical industry, in addition to those otherwise described above, are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;

- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively, and a cap on the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price, or AMP;
- a new Medicare Part D coverage gap discount program, in which manufacturers must now 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 manufacturers' 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, including individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order initiating a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare. It is unclear how other healthcare reform measures of the Biden administration, if any, will impact our business.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes included aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 and a 1% reduction from April 1, 2022 through June 30, 2022, unless additional Congressional action is taken. In addition, on January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. More recently, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, beginning January 1, 2024.

The cost of prescription pharmaceuticals in the United States has also been the subject of considerable discussion. There have been several Congressional inquiries, as well as legislative and regulatory initiatives and executive orders 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 drug products. Members of Congress and the Biden Administration have indicated they will continue to pursue legislative or administrative measures to control prescription drug costs, although the likelihood of such measures being adopted remains uncertain. For example, the Build Back Better Act, if enacted, would introduce substantial drug pricing reforms, including the establishment of a drug price negotiation program within the U.S. Department of Health and Human Services that would require manufacturers to charge a negotiated "maximum fair price" for certain selected drugs or pay an excise tax for noncompliance, and the establishment of rebate payment requirements on manufacturers of certain drugs payable under Medicare Parts B and D. If the Build Back Better Act is not enacted, similar or other drug pricing proposals could appear in future legislation.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical 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.

We anticipate that these new laws will result in additional downward pressure on coverage and the price that we receive for any approved product, and could seriously harm our business. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. In addition, it is possible that there will be further legislation or regulation that could harm our business, financial condition, and results of operations.

Data Privacy and Security Laws

Numerous state, federal and foreign laws, regulations and standards govern the collection, use, access to, confidentiality and security of health-related and other personal information, and could apply now or in the future to our operations or the operations of our partners. In the U.S., numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health-related and other personal information. In addition, certain foreign laws govern the privacy and security of personal data, including health-related data. In particular, the General Data Protection Regulation 2016/679 ("GDPR") and implementing legislation in individual European countries impose specific compliance obligations relating to the processing and transfer of personal data of natural persons, including certain kinds of clinical trial data. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Competition

Our industry is highly competitive and subject to rapid and significant technological change. New therapies and treatments based on innovative discoveries emerge frequently.

Our potential competitors are public and private companies, pharmaceutical companies and biotechnology companies who may be engaged in targeting the same biological processes that our compounds are designed to impact and who may be developing products for the same indications as our investigational drug candidates. Potential competitors could also include academic institutions, government agencies, other public and private research organizations and charitable venture philanthropic organizations that conduct research, seek patent protection and/or establish collaborative arrangements for research, development, manufacturing and commercialization.

Many of our competitors have substantially greater financial resources, technical resources, expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. 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 a result, our competitors may commercialize products more rapidly or effectively than we do, which would affect our competitive position, the likelihood that our drug candidates, if approved, would achieve and maintain market acceptance and our ability to generate meaningful revenues from our products.

Our commercial opportunities could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer side effects, are more convenient or are more affordable than any products that we develop. The key competitive factors affecting the success of ELX-02 and our other product candidates are their impact on the targeted diseases, superiority over competing products, long-term safety, convenience, price and the availability of coverage and reimbursement from government and other third-party payors.

Several companies are involved in researching and developing molecules targeting suppression of nonsense mutations and enhancement of translational read-through. However, we believe that ELX-02 is the only drug candidate in clinical development designed to treat nonsense mutations in CFTR, the underlying cause of cystic fibrosis. Additional competition to ELX-02 may arise from other programs that do not target a specific *CFTR* mutation class but work via other mechanisms.

Employees and Human Capital Management

As of December 31, 2022, we had 15 employees in the United States and three employees in Israel. We believe that we have a good relationship with our employees. In order to achieve our goals, it is crucial that we continue to attract and retain top talent. To facilitate talent attraction and retention, we strive to make our Company a safe and rewarding workplace, with opportunities for our employees to grow and develop in their careers, supported by strong compensation, benefits, health and wellness programs.

We strive to maintain an inclusive environment free from discrimination of any kind, including sexual or other discriminatory harassment. Our employees have multiple avenues available through which inappropriate behavior can be reported, including a confidential hotline.

As of December 31, 2022, 44% of our employees were female and 56% were male. We are committed to creating and maintaining a diverse and inclusive workplace in which all employees have an opportunity to participate and contribute to the success of the business and are valued for their skills, experience, and unique perspectives. We seek and respect different perspectives, points of view, backgrounds, and communication styles.

We frequently benchmark our compensation practices and benefits programs against those of comparable industries and peer companies, and in the geographic areas where our facilities are located. We believe that our compensation and employee benefits are competitive and allow us to attract and retain qualified employees throughout our organization. In addition to salaries, employee benefits include annual discretionary bonuses, equity awards, a 401(k) plan for U.S. employees, healthcare and insurance benefits, health savings and flexible spending accounts, paid time off, family leave, and flexible work schedules, among others.

Other Matters

Corporate Information

We were incorporated under the laws of the State of Delaware. Our principal executive offices are located at 480 Arsenal Way, Watertown, Massachusetts 02472, and our phone number is (781) 577-5300. Our common stock is listed on the Nasdaq Capital Market under the symbol "ELOX."

Information Available on the Internet

Our internet address is www.eloxxpharma.com. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, proxy statements and all amendments to those reports are available to you free of charge through the "Investors-Financials & Filings" section of our website as soon as reasonably practicable after those materials have been electronically filed with, or furnished to, the SEC. The information contained on, or that can be accessed through, our website is not incorporated by reference into, and is not a part of, this Annual Report. In addition, the SEC maintains a website (www.sec.gov) that contains reports, proxy and information statements, and other information regarding issuers that file electronically.

ITEM 1A. RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below, together with all of the other information in this Annual Report on Form 10-K, before you decide to purchase our common stock. If any of the possible adverse events described below actually occurs, we may be unable to conduct our business as currently planned and our financial condition and operating results could be harmed. In addition, the trading price of our common stock could decline due to the occurrence of any of the events described below, and you may lose all or part of your investment. Additional risks that we currently do not know about, or that we currently believe immaterial, may also impair our business.

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

We are heavily dependent on the success of our lead product candidate, ELX-02. If ELX-02 does not achieve positive results during development or suffers any material development delays, it may adversely impact the commercial viability of ELX-02 and our business.

We currently have no products approved for sale. We have invested substantial efforts and financial resources primarily in the research and development of ELX-02, which is currently our only product candidate in clinical development. We have increased investment in our preclinical candidate portfolio but have yet to advance other molecules into clinical development. In September 2022, we announced topline results from our Phase 2 combination clinical trial of ELX-02 for Class 1 CF patients with at least one nonsense mutation. The combination trial of ELX-02 with ivacaftor did not achieve statistical significance for its efficacy endpoints and as a result we have paused all development of ELX-02 in CF. ELX-02 is now being evaluated in a Phase 2 trial in Alport syndrome patients with nonsense mutations. This is the first known clinical study in Alport syndrome and there can be no assurances of its success.

We are heavily dependent on favorable efficacy results from this study in the near term for our continued development and funding for of ELX-02 and the Company. Our ability to achieve and sustain profitability depends on obtaining regulatory approvals for, and successfully commercializing ELX-02 and any future product candidates, either alone or with third parties. The success of ELX-02 and any other product candidates will depend on several factors, including the following:

- our ability to continue our business operations and product candidate research and development, and adapt to any changes in the regulatory approval process, manufacturing supply or clinical trial requirements and timing;
- successful completion of preclinical studies;
- receipt of allowances to proceed under INDs and similar applications outside the United States for our planned clinical trials or future clinical trials;
- successful patient enrollment in and completion of clinical trials;
- safety and efficacy data for our product candidates that are satisfactory to the FDA, European Medicines Agency (“EMA”), or any other comparable foreign regulatory authority for marketing approval;
- receipt of marketing approvals for our product candidates from applicable regulatory authorities;
- completion of any required post-marketing approval commitments to applicable regulatory authorities;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- making arrangements with third-party manufacturers, or establishing manufacturing capabilities, for both clinical and commercial supplies of our product candidates, if any product candidates are approved;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;

- obtaining and maintaining third-party coverage and adequate reimbursement; and
- maintaining a continued acceptable safety profile of our products following any approval.

Many of these factors are beyond our control, and it is possible that we may never obtain regulatory approval for ELX-02 or any other product candidates even if we expend substantial time and resources seeking their development and approval. If we do not achieve regulatory approval in a timely manner or at all, we could experience significant delays or an inability to commercialize our current or future product candidates, which would materially adversely affect our business.

The success of our business, including our ability to finance our Company and generate revenue from products in the future, which we do not expect will occur for several years, if ever, will depend heavily on the successful development and any eventual commercialization of the product candidates we develop. Our current product candidates, and any future product candidates we develop, will require additional preclinical and clinical development, management of clinical, preclinical and manufacturing activities, marketing approval in the United States and other markets, demonstrating cost-effectiveness to pricing and reimbursement authorities, obtaining sufficient manufacturing supply for both clinical development and commercial production in accordance with current Good Manufacturing Practices (“cGMP”) or similar regulatory requirements outside the United States, building of a commercial organization, and substantial investment and significant marketing efforts before we generate any revenue from product sales. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process or transferring that process to commercial partners, which may prevent us from completing our clinical trials or commercializing our product candidates on a timely or profitable basis, if at all. Changes in the manufacturing process or facilities will require further comparability analysis and approval by the FDA before implementation, which could delay our clinical trials and product candidate development, and could require additional clinical trials, including bridging studies, to demonstrate consistent and continued safety and efficacy.

We have not previously submitted a new drug application (“NDA”), to the FDA or similar submissions to a comparable foreign regulatory authority, for any product candidate. An NDA or other relevant regulatory filing must include extensive preclinical and clinical data and supporting information to establish that the product candidate is safe and effective for each desired indication. The NDA or other relevant regulatory filing must also include significant information regarding the chemistry, manufacturing and controls for the product. We cannot be certain that our current or future product candidates will be successful in clinical trials or receive regulatory approval. Further, even if they are successful in clinical trials, our product candidates or any future product candidates may not receive regulatory approval. If we do not receive regulatory approvals for current or future product candidates, we may not be able to continue our operations. Even if we successfully obtain regulatory approval to market a product candidate, our revenue will depend, in part, upon the size of the markets in the territories for which we gain regulatory approval and have commercial rights for each product candidate, as well as the availability of competitive products, whether there is sufficient third-party reimbursement and adoption by physicians.

Preclinical and clinical drug development is a lengthy and expensive process, with an uncertain outcome. Our preclinical and clinical programs may experience delays or may never advance, which would adversely affect our ability to further advance clinical development, obtain regulatory approvals or commercialize our product candidates on a timely basis or at all, which could have an adverse effect on our business.

Before obtaining regulatory approval for the commercial distribution of our therapeutic product candidates, we or a collaborator must conduct extensive preclinical studies and clinical trials to demonstrate the safety and efficacy of our product candidates in humans to the satisfaction of the FDA, EMA and other applicable regulatory agencies in the jurisdictions in which we intend to market our product candidates. Clinical testing is expensive, time-consuming, and subject to uncertainty. Of the large number of drugs in development, only a small percentage successfully complete clinical testing and an even smaller portion obtain FDA or similar foreign regulatory authority approval and are commercialized. Accordingly, even if we are able to obtain the requisite financing to continue to fund our research, development and clinical programs, we cannot assure you that ELX-02, ZKN-013, or any of our future product candidates will be successfully developed or commercialized.

The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical development may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical

trials due to lack of efficacy or safety profiles, notwithstanding promising results in earlier trials. Accordingly, we, or any development partners, may ultimately be unable to provide regulatory agencies with satisfactory data on clinical safety and efficacy sufficient to obtain approval for any indication.

Further, we may experience delays in clinical trials of our product candidates. We do not know whether ongoing clinical trials will be completed on schedule or at all, or whether planned clinical trials will begin on time, need to be redesigned, enroll patients on time or be completed on schedule, if at all. We also cannot be sure that submission of an Investigational New Drug ("IND") or similar application will result in the FDA, or other regulatory authority allowing clinical trials to begin in a timely manner, if at all. Moreover, issues may arise that could cause regulatory authorities to suspend or terminate such clinical trials. Clinical trials can be delayed for a variety of reasons, including delays related to:

- inability to generate sufficient preclinical, toxicology or other in vivo or in vitro data to support the initiation or continuation of clinical trials;
- reaching a consensus with regulatory authorities on study design or implementation of the clinical trials;
- failure in obtaining regulatory authorization to commence a clinical trial;
- reaching agreement on acceptable terms with prospective contract research organizations ("CROs"), and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- obtaining institutional review board ("IRB"), or ethics committee approval at each clinical trial site;
- identifying, recruiting and training suitable clinical investigators;
- manufacturing, testing, releasing, validating or importing/exporting sufficient stable quantities of our product candidates for use in clinical trials;
- insufficient or inadequate supply or quality of product candidates or other materials necessary for use in clinical trials;
- recruiting, screening and enrolling suitable patients to participate in a clinical trial;
- having patients complete a clinical trial or return for post-treatment follow-up;
- clinical trial sites deviating from trial protocol or dropping out of a clinical trial;
- adding new clinical trial sites;
- failure by our CROs, other third parties or us to adhere to clinical trial protocols;
- failure to perform in accordance with the FDA' s good GCPs, or similar regulatory guidelines in other countries;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits, or occurrence of adverse events in clinical trials of the same class of agents conducted by other companies;
- changes in regulatory requirements or guidance that require amending or submitting new clinical trial protocols;
- changes to the standard of care on which a clinical development plan was based, which may require new or additional studies or clinical trials;
- selection of clinical endpoints that require prolonged periods of observation or analyses of resulting data;
- costs of clinical trials of our product candidates being greater than we anticipate;
- clinical trials of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon development of such product candidates;

- transfer of manufacturing processes to larger-scale facilities operated by a contract manufacturing organization (“CMO”) and delays or failure by our CMOs or us to make any necessary changes to such manufacturing processes;
- third parties being unwilling or unable to satisfy their contractual obligations to us; or
- unforeseen factors beyond our control, including public health concerns such as the COVID-19 pandemic.

In addition, disruptions caused by the COVID-19 pandemic, including temporary pauses in our clinical trial enrollment in response to the COVID-19 pandemic have and may in the future increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials. The design of our Phase 2 Alport syndrome trial may not achieve efficacy results in patients, and we cannot provide assurances as to whether we will incur significant additional costs, expend additional resources or be subject to additional regulatory requirements, including COVID-19 related disruptions, any of which may have a material adverse impact on our financial condition and results of operations.

Clinical trials must be conducted in accordance with the FDA and other applicable regulatory authorities’ legal requirements, regulations or guidelines, and are subject to oversight by these governmental agencies and ethics committees or IRBs at the medical institutions where the clinical trials are conducted. We could encounter delays if a clinical trial is suspended or terminated by us, by the data safety monitoring board for such clinical trial or by the FDA or any other regulatory authority, or if the IRBs or ethics committees of the institutions in which such trials are being conducted suspend or terminate the participation of their clinical investigators and sites subject to their review. Such authorities may suspend or terminate a clinical trial 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 product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

In addition, significant adverse events with respect to individuals who are not enrolled in any of our clinical trials but who receive our drug candidate under our compassionate use policy (typically under a single-patient IND administered by the individual’s treating physician) may result in a partial or full clinical hold on our ongoing clinical trials. A clinical hold may result in the inability to enroll new patients in our studies until the hold is removed and may make it more difficult to enroll patients thereafter. Additionally, a clinical hold may also result in, among other things, protocol redesign, changes in eligibility criteria and increased costs, any of which could adversely affect our projected development timelines and jeopardize successful completion of our clinical programs.

Further, conducting clinical trials in foreign countries, as we may do for our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries.

If we experience delays in the completion of any clinical trial of our product candidates, the commercial prospects of our product candidates and the ability to generate revenues may be impaired. In addition, any delays in completing our clinical trials may increase our costs, slow down our product development and approval process and may jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may have an adverse impact on our business, financial condition and prospects. Further, the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

In addition, the FDA’s and other regulatory authorities’ policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the European Union (“EU”) recently evolved. The EU Clinical Trials Regulation (“CTR”) which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate clinical trial application (“CTA”) to be submitted in each member state, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each

member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. For clinical trials whose CTA was made under the Clinical Trials Directive before January 31, 2022, the Clinical Trials Directive will continue to apply on a transitional basis for three years. Additionally, sponsors may still choose to submit a CTA under either the Clinical Trials Directive or the CTR until January 31, 2023 and, if authorized, those will be governed by the Clinical Trials Directive until January 31, 2025. By that date, all ongoing trials will become subject to the provisions of the CTR. Compliance with the CTR requirements by us and our third-party service providers, such as clinical research organizations ("CROs"), may impact our development plans.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may also be impacted.

We and our collaborating partners may be subject, directly or indirectly, to federal and state healthcare fraud and abuse and false claims laws and regulations. If we or our collaborating partners are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Healthcare providers, healthcare facilities and institutions, physicians, and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with our collaborators, healthcare professionals, healthcare facilities and institutions, principal investigators, consultants, customers, and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act, that may constrain the business or financial arrangements and relationships through which we research, sell, market, and distribute any product candidates for which we obtain marketing approval. In addition, we may be subject to transparency laws and regulation with respect to drug pricing payments and other transfers of value made to physicians and other health care professionals by the federal government and by the states and foreign jurisdictions in which we conduct our business. The applicable federal, state, and foreign healthcare laws that affect our ability to operate include, but are not limited to, the following:

- The U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving, or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under any U.S. federal healthcare program, such as Medicare and Medicaid. The term "remuneration" has been broadly interpreted to include anything of value, including stock options. In addition, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. The federal Anti-Kickback Statute has also been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other hand. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, but the exceptions and safe harbors are drawn narrowly and require strict compliance in order to offer protection. Any arrangements with prescribers must be for bona fide services and compensated at fair market value.
- The U.S. federal civil and criminal false claims laws, including without limitation, the civil False Claims Act, which can be enforced by private citizens on behalf of the U.S. federal government through civil whistleblower or qui tam actions, and the federal civil monetary penalties law which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using, or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease, or conceal an obligation to pay money to the U.S. federal government. Pharmaceutical manufacturers can cause false claims to be presented to the U.S. federal government by, among other things, engaging in impermissible marketing practices, such as the off-label promotion of a product for an indication for

which it has not received FDA approval. Further, pharmaceutical manufacturers can be held liable under the civil False Claims Act even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act.

- The U.S. federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items, or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.
- The U.S. Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children’s Health Insurance Program, with specific exceptions, to report annually to CMS information related to certain payments and other transfers of value to physicians (as defined by statute), certain non-physician practitioners (including physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiology assistants, and certified nurse midwives) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- Analogous U.S. state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements, and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and state and local laws requiring the registration of pharmaceutical sales representatives, and similar healthcare laws and regulations in foreign jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is not always possible to identify and deter employee misconduct or business noncompliance, and the precautions we take to detect and prevent inappropriate conduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations.

If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal, and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid, or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations to resolve allegations of noncompliance, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits, and the curtailment or restructuring of our operations. Further, defending against any such actions can be costly, time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

Our product candidates, including ELX-02 and ZKN-013 may cause adverse events or have other properties that could delay or prevent their regulatory approval or limit the scope of any approved label or market acceptance.

Undesirable side effects caused by our product candidates, such as ELX-02 and ZKN-013, could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other comparable foreign regulatory authorities. During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries, and discomforts, to their study doctor. Often, it is not possible to determine whether or not the product candidate being studied caused these conditions. It is possible that as we test

our product candidates in larger, longer and more extensive clinical trials, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in previous trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. Many times, side effects are only detectable after investigational products are tested in large-scale clinical trials or, in some cases, after they are made available to patients on a commercial scale following approval.

It is possible that, during the course of the clinical development of ELX-02, ZKN-013, or other product candidates, results of our clinical trials (or significant adverse events experienced by individuals receiving drug under our compassionate use policy) could reveal an unacceptable severity and prevalence of side effects. For example, in preclinical testing of ELX-02, we observed renal toxicities in the animals we tested following administration of this compound at doses in excess of the doses we expect to administer in our clinical trials. As a result of this or any other side effects, our clinical trials could be suspended or terminated or not even allowed to commence, and the FDA or comparable foreign regulatory authorities could order us to cease further development, or deny approval, of our product candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. If we are required to delay, suspend or terminate any clinical trial or commercialization efforts, the commercial prospects of such product candidates may be harmed, and our ability to generate product revenues from them or other product candidates that we develop may be delayed or eliminated.

Additionally, if one or more of our product candidates receive marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product or impose restrictions on its distribution in the form of a new or modified risk evaluation and mitigation strategy;
- regulatory authorities may require additional labeling, such as additional warnings or contraindications, which may negatively impact sales;
- regulatory authorities may issue safety alerts, letters to healthcare providers, press releases or other communications containing warnings or other safety information about the product;
- we may be required to change the way the product is administered or to conduct additional clinical studies;
- we may be required to create a risk evaluation and mitigation strategy ("REMS") which could include a medication guide outlining the risks of such side effects for distribution to patients;
- we may be subject to fines, injunctions or the imposition of criminal penalties;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

Even though we have received orphan drug designation from the FDA for ELX-02 for the treatment of cystic fibrosis, cystinosis, MPS I, and Rett syndrome, we may not be able to maintain the benefits of orphan drug designation or obtain orphan drug marketing exclusivity for ELX-02 or any of our other product candidates for Alport syndrome or other indications.

Regulatory authorities in some jurisdictions, including the United States ("U.S.") EU, may designate drugs for relatively small patient populations as orphan drugs in the U.S. and orphan medicinal products in the EU. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the U.S., or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. Orphan drug designation must be requested before submitting an NDA.

Similarly, in the EU, a medicinal product may receive orphan designation. This applies to products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition and either the condition affects no more than five in 10,000 persons in the EU when the application is made, or the product, without the benefits derived from orphan status, would unlikely generate sufficient return in the EU to justify the necessary investment. Moreover, in order to obtain orphan designation in the EU, it is necessary to demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition authorized for marketing in the EU, or if such a method exists, that the product will be of significant benefit to those affected by the condition. The applicable exclusivity period is ten years in the EU. The European exclusivity period can be reduced to six years, if, at the end of the fifth year a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified.

The FDA has granted orphan drug designation for ELX-02 for the treatment of cystic fibrosis, MPS I, Rett syndrome, and cystinosis. We may seek orphan drug designation for our other product candidates, and with respect to Alport syndrome and other indications. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and application fee waivers. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA.

In addition, if a drug with an orphan drug designation subsequently receives the first FDA marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same drug for the same disease or condition for that time period. The applicable period is seven years in the U.S. Orphan drug exclusivity may be lost in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity, if the underlying NDA authorizing the sale of the drug is withdrawn, or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the drug candidate from competition because different drugs can be approved for the same disease or condition. In addition, even after an orphan drug is approved, the applicable regulatory authority can subsequently approve the same or a similar drug from another sponsor for the same condition if it concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

A Fast Track Designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.

On August 27, 2021 we received Fast Track Designation for ELX-02 for the treatment of cystic fibrosis patients with nonsense mutations. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply to the FDA for Fast Track Designation. The sponsor of a Fast Track product candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once an NDA is submitted, the product candidate may be eligible for priority review. A Fast Track product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. The FDA has broad discretion whether or not to grant this designation. Even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Many drugs that have received Fast Track Designation have failed to obtain approval.

We may find it difficult to recruit and enroll patients in our clinical trials, which could cause significant delays in the completion of such trials or may cause us to abandon one or more clinical trials.

Successful and timely completion of clinical trials will require that we enroll a sufficient number of subjects. These trials and other trials we conduct may be subject to delays for a variety of reasons, including as a result of enrollment taking longer than anticipated, subject withdrawal or adverse events. These types of developments could cause us to delay the trial or halt further development. Our clinical trials will compete with other clinical trials that are in the same therapeutic areas as our product candidates, and this competition reduces the number and types of patients available to us, as some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. The protocols for our clinical trials generally require that patients may not be enrolled in more than one clinical trial for the same indication, which will limit the pool of available subjects.

In addition to the rarity of some diseases, the eligibility criteria of our clinical studies will further limit the pool of available study participants as we will require that patients have specific characteristics that we can measure and that their disease is not too advanced. Specifically, some of the diseases that our product candidates are designed to treat are rare and ultra-rare and we expect only a subset of the patients with these diseases will be eligible for our clinical trials. Because ELX-02 is designed to target small populations and patient numbers have not been determined definitively, we must be able to identify patients in order to complete our development programs, potentially secure regulatory approval for, and if approved, successfully commercialize ELX-02.

We cannot guarantee that any of our programs will identify a sufficient number of patients to complete clinical development, pursue regulatory approval and market our product candidates, if approved. The combined number of patients in the U.S., Japan and Europe and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with ELX-02, or new patients may become increasingly difficult to identify, all of which would adversely affect our results of operations and our business. An inability to recruit and enroll a sufficient number of patients for any of our current or future clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether, which could impact our ability to develop our product candidates and may have a material adverse effect on our business, results of operations and financial condition. Patient enrollment depends on many factors, including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- eligibility criteria for the trial;
- the proximity of patients to clinical sites;
- the design of the clinical protocol;
- the ability to obtain and maintain patient consents;
- the ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the risk that patients enrolled in clinical trials will drop out of the trials before the administration of our product candidates or trial completion;
- the availability of competing clinical trials;
- the availability of new drugs approved for the indication the clinical trial is investigating; and
- clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies.

In addition, the ongoing COVID-19 pandemic has and may in the future adversely affect enrollment in our clinical trials. We experienced significant delays in our recently completed Phase 2 monotherapy study with ELX-02 in CF as a result of having to pause enrollment in response to the COVID-19 pandemic in order to avoid unnecessary exposure in at-risk populations, to maintain the integrity of our study data and to support global healthcare providers in their commitment to ensure patient safety. On November 1, 2022, we announced that enrollment in our Phase 2 clinical trial in Alport syndrome commenced. We experienced delays in starting the trial related to staffing challenges in our clinical trial sites and related lack of resources at these sites. Any future additional costs as a result of delays in enrollment or failure to complete enrollment in accordance with our objectives could be significant and may have a material adverse impact on our financial condition and results of operations.

Interim, “topline” and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient 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 preliminary or topline data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or 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 evaluate all available data. As a result, the topline or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline and preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the top-line or preliminary data we previously published. As a result, topline and preliminary data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and 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 patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim 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 value of the particular program, the approvability or commercialization of the particular product candidate or product and our Company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine to be material or otherwise appropriate information to include in our disclosure. If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions or interpretations reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could negatively impact our business, operating results, prospects or financial condition.

The regulatory approval processes of the FDA and comparable regulatory authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

The time required to obtain approval by the FDA and comparable regulatory authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate’s clinical development and may vary among jurisdictions. Neither we nor any future collaborator is permitted to market any of our product candidates in the United States until we receive regulatory approval of an NDA from the FDA. Similarly, in the EU, our product candidates can only be placed on the market after obtaining a marketing authorization.

Prior to obtaining approval to commercialize a product candidate in the United States, Europe or other jurisdictions, we or our collaborators must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or other regulatory agencies, that such product candidates are safe and effective for their intended uses. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. The FDA or other regulatory authority may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post-approval, or it may object to elements of our clinical development program.

The FDA or any foreign regulatory authorities or bodies can delay, limit or deny approval of our drug product candidates or require us to conduct additional nonclinical or clinical testing or abandon a program for a variety of reasons, including the following:

- regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the applicable regulatory authority that a product candidate is safe or effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by regulatory authorities for approval;
- serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be acceptable or sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States, the EU, or elsewhere, and we may be required to conduct additional clinical studies;
- the applicable foreign regulatory authority may disagree regarding the formulation, labeling and/or the specifications of our product candidates;
- applicable regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval..

Of the large number of drugs in development, only a small percentage successfully complete the regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations and prospects.

In addition, even if we were to obtain approval, regulatory authorities may approve our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, including Phase 4 clinical trials, and/or the implementation of a REMS program, which may be required to assure safe use of the drug after approval. Regulatory authorities may also approve a product candidate for a more limited indication or patient population than we originally requested, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell any of our product candidates that obtain regulatory approval, we may be unable to generate any revenue.

We have no experience selling and marketing our product candidates or any other products. To successfully commercialize any products that may result from our clinical development programs and obtain regulatory approval, we will need to develop these capabilities, either on our own or with the assistance of others. We may seek to enter into collaborations with other entities to utilize their marketing and distribution capabilities, but we may be unable to do so on favorable terms, if at all. If any future collaborative partners do not commit sufficient resources to commercialize our future products, if any, and we are unable to develop the necessary marketing capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies or successfully commercialize any of our product candidates.

Even if our product candidates receive regulatory approval, they will be subject to significant post- marketing regulatory requirements and oversight.

Any regulatory approvals that we may receive for our product candidates will require the submission of reports to regulatory authorities and surveillance to monitor the safety and efficacy of the product candidate, may contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome post-approval study or risk management requirements. For example, the FDA may require a REMS in order to approve our product candidates, which could entail requirements for a medication guide, physician training and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA, EMA or other regulatory authorities approve our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as ongoing compliance with cGMP requirements and GCPs for any clinical trials that we conduct post-approval. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMP regulations and similar standards. If we or a regulatory authority discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facilities where the product is manufactured, a regulatory authority may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. In addition, failure to comply with applicable regulatory requirements may subject our company to administrative or judicially imposed sanctions, including:

- delays in or the rejection of product approvals;
- restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;
- restrictions on the products, manufacturers or manufacturing process;
- warning or untitled letters;
- civil and criminal penalties;
- injunctions;
- suspension or withdrawal of regulatory approvals;
- product seizures, detentions or import bans;
- voluntary or mandatory product recalls and publicity requirements;
- total or partial suspension of production; and
- imposition of restrictions on operations, including costly new manufacturing requirements.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

In addition, the FDA' s and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may be subject to enforcement action and we may not achieve or sustain profitability.

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

If any of our product candidates are approved and we are found to have improperly promoted off-label uses of those products, we may become subject to significant liability. The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products, such as our product candidates, if

approved. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The U.S. federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

Disruptions at the FDA and other government agencies and foreign regulatory authorities caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA and foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's and foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and foreign regulatory authorities have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies, such as the EMA relocation to Amsterdam and resulting staff changes may also slow the time necessary for new drugs or modifications to approved drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, in March 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, in July 2020, the FDA resumed certain on-site inspections of domestic and foreign manufacturing facilities subject to a risk-based prioritization system. The FDA utilized this risk-based assessment system to assist in determining when and where it was safest to conduct prioritized domestic inspections. Additionally, on April 15, 2021, the FDA issued a guidance document in which the FDA described its plans to conduct voluntary remote interactive evaluations of certain drug manufacturing facilities and clinical research sites, among other facilities. According to the guidance, the FDA may request such remote interactive evaluations where the FDA determines that remote evaluation would be appropriate based on mission needs and travel limitations. In July 2021, the FDA resumed standard inspectional operations of domestic facilities. More recently, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID-19 pandemic. Regulatory authorities outside the United States have adopted similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Developments by competitors may render our products or technologies obsolete or non-competitive which would have a material adverse effect on our business, results of operations and financial condition.

We compete with pharmaceutical companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. Our product candidates will have to compete with existing therapies and potential therapies under development by our competitors. In addition, our commercial opportunities may be reduced or eliminated if our competitors develop and market products that are less expensive, more effective or safer than our product candidates. Other companies have product candidates in various stages of preclinical or clinical development to treat diseases for which we are also seeking to develop product candidates. Some of these potential competing drugs are further advanced in development than our product candidates and may be commercialized earlier. Even if we are successful in developing effective drugs, our products may not compete successfully with products produced by our competitors.

Most of our competitors, either alone or together with their collaborative partners, operate larger research and development programs, staff and facilities, and have substantially greater financial resources than we do, as well as significantly greater experience in:

- developing drugs;
- undertaking preclinical testing and human clinical trials;
- obtaining marketing approvals from the FDA and other regulatory authorities;
- formulating and manufacturing drugs; and
- launching, marketing and selling drugs.

These organizations also compete with us to attract qualified personnel, for acquisitions and joint venture candidates and for other collaborations.

Efforts to compete and the pursuit of activities of our competitors may impose unanticipated costs on our business, which would have a material adverse effect on our business, results of operations and financial condition.

If we are unable to develop and commercialize our product candidates, our business will be adversely affected.

A key element of our strategy is to develop and commercialize a portfolio of new products. We seek to do so through our internal research programs and strategic collaborations for the development of new products. Research programs to identify new product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including:

- a product candidate is not capable of being produced in commercial quantities at an acceptable cost, or at all;
- a product candidate that is developed and approved may not be accepted by patients, the medical community or third-party payors;
- competitors may develop alternatives that render our product candidates obsolete;
- the research methodology used may not be successful in identifying potential product candidates; or
- a product candidate may on further study be shown to have harmful side effects or other characteristics that indicate it is unlikely to be safe or effective or otherwise does not meet applicable regulatory approval requirements.

Any failure to develop or commercialize any of our product candidates may have a material adverse effect on our business, results of operations and financial condition.

Even if we are able to commercialize any product candidate, coverage and adequate reimbursement may not be available or such product candidate may become subject to unfavorable pricing regulations or third-party coverage and reimbursement policies, which would harm our business.

The regulations that govern regulatory approvals, pricing, and reimbursement for drug products vary widely from country to country. Some countries require approval of the sale price of a drug product before it can be marketed. In many countries, the pricing review period begins after marketing approval is granted. In some foreign markets, prescription drug product pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain regulatory approval.

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third-party payors, such as government authorities, private health insurers, and other organizations. Even if we succeed in

bringing one or more products to the market, these products may not be considered cost-effective, and the amount reimbursed for any products may be insufficient to allow us to sell our products on a competitive basis. In the United States, no uniform policy for coverage and reimbursement exists, and coverage and reimbursement can differ significantly from payor to payor. Third-party payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates, but also have their own methods and approval process apart from Medicare determinations. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Decisions regarding the extent of coverage and amount of reimbursement to be provided for any product candidates that we develop will be made on a payor-by-payor basis. One payor's determination to provide coverage for a drug does not assure that other payors will also provide coverage and adequate reimbursement for the drug. There may be significant delays in obtaining reimbursement for newly-approved drug products, and coverage may be more limited than the purposes for which the drug product is approved by the FDA or comparable foreign regulatory authorities.

Moreover, eligibility for reimbursement does not imply that any drugs product will be reimbursed in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Increasingly, the third-party payors who reimburse patients or healthcare providers are requiring that drug companies provide them with predetermined discounts from list prices, and are seeking to reduce the prices charged or the amounts reimbursed for drug products. If the price we are able to charge for any products we develop, or the coverage and reimbursement provided for such products, is inadequate in light of our development and other costs, our return on investment could be affected adversely.

Interim reimbursement levels for new drug products, if applicable, may also be insufficient to cover our costs and may not be made permanent. Reimbursement rates may be based on payments allowed for lower cost drug products that are already reimbursed, may be incorporated into existing payments for other services and may reflect budgetary constraints or imperfections in Medicare data. Net prices for drug products may be reduced by mandatory discounts or rebates required by third-party payors and by any future relaxation of laws that presently restrict imports of drug products from countries where they may be sold at lower prices than in the United States. Obtaining coverage and adequate reimbursement for our product candidates may be particularly difficult because of the higher prices often associated with drugs administered under the supervision of a physician. Similarly, because our product candidates are physician-administered injectables, separate reimbursement for the product itself may or may not be available. Instead, the administering physician may or may not be reimbursed for providing the treatment or procedure in which our product is used.

Our inability to promptly obtain coverage and adequate reimbursement from both third-party payors for the product candidates that we may develop and for which we obtain regulatory approval could have a material and adverse effect on our business, financial condition, results of operations, and prospects.

Current and future legislation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. The Patient Protection and Affordable Care Act, or ACA, which was passed in 2010, substantially changed the way health care is financed by both governmental and private insurers. The ACA, among other things, expanded Medicaid program eligibility and access to commercial health insurance coverage, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and promoted a new Medicare Part D coverage gap discount program. The ACA also appropriated funding to comparative clinical effectiveness research, although it remains unclear how the research will affect Medicare coverage and reimbursement or how new information will influence other third-party payer policies.

Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order initiating a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare. It is unclear how other healthcare reform measures of the Biden administration, if any, will impact our business.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes included aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022. Under current legislation, the actual reduction in Medicare payments varies from 1% from April 1, 2022 through June 30, 2022, up to 3% in the final fiscal year of this sequester unless additional Congressional action is taken. In addition, on January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. More recently, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, beginning January 1, 2024.

Similar developments have occurred outside of the United States, including in the European Union where healthcare budgetary constraints have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. To obtain reimbursement or pricing approval in some European Union member states, we may be required to conduct studies that compare the cost-effectiveness of our product candidates to other therapies that are considered the local standard of care.

It is also possible that additional governmental action is taken in response to address the COVID-19 pandemic. We cannot predict the likelihood, nature, or extent of government regulation that may arise from future legislation or administrative action in the United States, particularly as a result of the recent presidential election, or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant operating losses since our inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future. We may never achieve or maintain profitability.

We have a history of net losses and negative cash flows from operating activities since inception and, as of December 31, 2022, had an accumulated deficit of \$274.4 million. We have financed our operations primarily through equity securities, and to a lesser extent from loans and grants. We have devoted substantially all of our financial resources and efforts to research and development. We expect that it will be several years, if ever, before we receive regulatory approval for commercialization of a product candidate. We expect to continue to incur significant expenses and operating losses for the foreseeable future. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially if and as we:

- advance ELX-02, ZKN-013, and/or other product candidates further into clinical development;
- experience any further delays in enrollment and completion of our clinical trials due to the COVID-19 pandemic or otherwise;
- continue the preclinical development of our research programs and advance candidates into clinical trials;
- pursue regulatory authorization to conduct clinical trials of additional product candidates;
- seek marketing approvals for our product candidates;
- establish a sales, marketing and distribution infrastructure to commercialize any product candidates for which we obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, regulatory, management and scientific personnel;
- add operational, financial and management information systems and personnel;
- acquire or in-license other product candidates and technologies; and
- operate as a public company and maintain our compliance with Nasdaq listing requirements.

We have never generated any revenue from product sales and may never be profitable. To become and remain profitable, we and our collaborators must develop and eventually commercialize one or more product candidates with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those product candidates for which we may obtain marketing approval, securing coverage and reimbursement for those product candidates for which we may obtain marketing approval, and satisfying any post-marketing requirements. We may never succeed in these activities and, even if we do, may never generate revenue that is significant or large enough to achieve profitability. Our failure to become and remain profitable would decrease the value of the company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of the company could also cause investors to lose all or part of their investment.

We will need substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, continue and initiate clinical trials of, and seek marketing approval for ELX-02, and as we become obligated to make milestone payments pursuant to our outstanding license agreements. In addition, if we obtain marketing approval for any of our current or future product candidates, we expect to incur significant commercialization expenses related to sales, marketing, manufacturing and distribution of the approved product. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of drug discovery, clinical development, laboratory testing and clinical trials for ELX-02, ZKN-013, and other product candidates;
- the costs, timing and outcome of any regulatory review of ELX-02, ZKN-013, and other product candidates;
- the cost of any other product candidate programs we pursue;
- the costs and timing of commercialization activities, including manufacturing, marketing, sales and distribution, and securing coverage and reimbursement for any product candidates that receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our ability to establish and maintain collaborations on favorable terms, if at all; and
- the extent to which we acquire or in-license other product candidates and technologies.

Identifying potential product candidates and conducting preclinical studies and clinical trials are time consuming, expensive and uncertain processes that take years to complete, and we may never generate the necessary data or results required to obtain marketing approval or achieve product sales for any of our current or future product candidates. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenue, if any, will be derived from sales of products that we do not expect to be commercially available for several years, if at all.

Accordingly, despite our prior public equity offerings and debt financings, we will need substantial additional funding in connection with our continuing operations and to achieve our goals. However, our existing cash and cash equivalents may prove to be insufficient for these activities. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs, product portfolio expansion or future commercialization efforts. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional financing due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our operating plans. If we are unable to obtain adequate financing, we will evaluate options, which may include reducing or deferring operating expenses, including by downsizing our workforce and curtailing certain development programs, which could have a material adverse effect on our operations and financial results.

Changing circumstances and market conditions, some of which may be beyond the Company's control, could impair our ability to access our existing cash and cash equivalents and investments and to timely pay key vendors and others.

We maintain our cash and cash equivalents in accounts with major financial institutions, and our deposits these institutions can and do exceed insured limits. Market conditions can impact the viability of these institutions. In the event of failure of any of the financial institutions where we maintain our cash and cash equivalents, we could lose our deposits in excess of the federally insured or protected amounts and there can be no assurance that we will be able to access uninsured funds in a timely manner or at all. Any inability to access or delay in accessing these funds could adversely affect our business and financial position.

Our recurring losses from operations raise substantial doubt regarding our ability to continue as a going concern.

For the year ended December 31, 2022, our net losses were \$36.1 million and as of December 31, 2022, we had an accumulated deficit of \$274.4 million. We anticipate operating losses to continue for the foreseeable future due to, among other things, costs related to research, development of our product candidates, conducting preclinical studies and clinical trials, and our administrative organization. We will require substantial additional financing to fund our operations and to continue to execute our strategy, and we will pursue a range of options to secure additional capital. We believe that our cash and cash equivalents at December 31, 2022 are not sufficient to fund our current and planned operations for at least the next twelve months. These conditions raise substantial doubt about our ability to continue as a going concern within one year after the date of the issuance of the consolidated financial statements included in this Annual Report on Form 10-K.

We are exploring various sources of funding such as strategic collaborations and the issuance of equity to fund our operations. If we raise additional funds through strategic collaborations and alliances, which may include existing collaboration partners, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms that are not favorable to us. To the extent that we raise additional capital through the sale of equity, the ownership interest of our existing stockholders will be diluted and other preferences may be necessary that adversely affect the rights of existing stockholders. If we are unable to raise sufficient capital through the transactions discussed above, we may need to curtail expenses contemplated by our current operating plan, and we may be required to delay, limit, reduce or terminate our product development efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. If the foregoing plans are unsuccessful and we are unable to continue as a going concern, you could lose all or part of your investment in the Company.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity and debt financings, as well as entering into new collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity, such as our public offering of shares of our common stock in May 2021 or issuances of common stock under our at-the-market program ("ATM Program"), or convertible debt securities, an investor' s ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that may adversely affect an investor' s rights as a common stockholder. Debt 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, and may be secured by all or a portion of our assets. Further, the availability of funding under the Hercules Term Loan is conditioned on us meeting certain clinical and equity milestones during defined time periods. For example, because the Company did not meet the milestone requirements for the Tranche 2 Advance under the Hercules Term Loan as of August 15, 2022, this funding was not available to the Company. Any debt agreements we may enter into in the future may contain similar restrictions on funding. If we raise funds by entering into new collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or 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 through collaborations, strategic alliances or licensing arrangements when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

We may not be able to maintain compliance with our debt covenants in the future.

The Hercules Term Loan Agreement contains customary affirmative and negative covenants which, among other things, required the Company to maintain at all times a minimum qualified cash balance equaling amounts ranging from \$6.3 million to \$10.0 million (\$10.0 million effective as of August 15, 2022 and at December 31, 2022) and limits our ability to (i) incur additional indebtedness, (ii) pay dividends or make certain distributions, (iii) dispose of our assets, grant liens or encumber our assets or (iv) fundamentally alter the nature of our business. These covenants are subject to a number of exceptions and qualifications. Subsequent to year end, on March 7, 2023, this minimum qualified cash balance was reduced to \$2.25 million as of March 7, 2023 with the amendment of the terms and our repayment of \$7.5 million of principal. If we breach these financial covenants and fail to secure a waiver or forbearance from the third-party lender, such breach or failure could accelerate the repayment of the outstanding borrowings under the Hercules Term Loan or the exercise of other rights or remedies the third-party lender may have under applicable law. No assurance can be provided a waiver or forbearance will be granted or the outstanding borrowings under the Hercules Term Loan, will be successfully refinanced on terms that are acceptable to the Company.

We do not intend to pay dividends for the foreseeable future.

We have never declared or paid any dividends on our common stock and do not intend to pay any dividends in the foreseeable future. We anticipate that we will retain all of our future earnings for use in the operation of our business and for general corporate purposes. Further, the terms of the Hercules Term Loan Agreement limit us from paying dividends or making certain distributions. Any determination to pay dividends in the future will be at the discretion of our board of directors.

Our indebtedness and debt service obligations may adversely affect our cash flow.

We intend to fulfill our debt service obligations, including repayment of the principal of the Hercules Term Loan, from cash generated from our future operations, from our existing cash, and potential additional cash proceeds from our ATM Program or other future equity financings. Our indebtedness could have significant additional negative consequences, including requiring the dedication of a substantial portion of our expected cash flow to service our indebtedness, thereby reducing the amount of our expected cash flow available for other purposes and limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete. If we are unable to generate sufficient cash to meet these obligations and need to use existing cash in order to fund our debt service obligations, including repayment of the principal, we may have to delay or curtail research and development programs.

Risks Related to Our Business and Operations

We continue to seek opportunities to expand our business through strategic initiatives. Our efforts to identify opportunities or complete transactions that satisfy our strategic criteria may not be successful, and we may not realize the anticipated benefits of any completed acquisition, collaboration or other strategic transaction.

Our business strategy includes expanding our product candidates and capabilities. We regularly evaluate potential merger, acquisition, partnering and in-license opportunities that we expect will expand our pipeline or product offerings, and enhance our research or development programs.

We may engage in future strategic transactions that could cause us to incur additional liabilities, commitments or significant expense. Any such transactions will be dependent on our ability to appropriately evaluate the potential risks and uncertainties, integrate any new technology, product and/or business, and generate revenues (including through up-front payments, milestones and/or royalties) sufficient to meet our underlying objectives.

Any strategic transaction undertaken may result in unforeseen development costs, timeline delays, regulatory approval challenges and uncertainties relating to the commercial market opportunity, any of which could cause us to fail to realize the anticipated value of the transaction and may have a material adverse effect on our business and financial condition.

To manage effectively our current and future potential growth, we must also continue to enhance and develop our global employee base, and our operational and financial processes. Supporting our growth strategy will

require significant capital expenditures and management resources, including investments in research, development, sales and marketing, manufacturing and other areas of our operations. The development or expansion of our business, any acquired business or any acquired or in-licensed products may require a substantial capital investment by us. We may not have these necessary funds, or they might not be available to us on acceptable terms or at all. We may also seek to raise funds by selling shares of our capital stock, or securities convertible into our capital stock, which could dilute current stockholders' ownership interest in our Company.

Our business could be affected by litigation, government investigations and enforcement actions.

We operate in many jurisdictions in a highly regulated industry and we could be subject to litigation, government investigation and enforcement actions on a variety of matters in the U.S. or foreign jurisdictions, including, without limitation, intellectual property, regulatory, product liability, environmental, whistleblower, Qui Tam, false claims, privacy, anti-kickback, anti-bribery, securities, commercial, employment, and other claims and legal proceedings which may arise from conducting our business. Any of these actions or proceedings may result in significant costs, fines, penalties or imposition of burdensome restrictions on the company, any of which could have a material adverse effect on our business, results of operations and financial condition.

We could be subject to additional tax liabilities.

We are subject to federal, state and local taxes in the United States and Israel. Significant judgment is required in evaluating our tax positions and our worldwide provision for taxes. During the ordinary course of business, there are many activities and transactions for which the ultimate tax determination is uncertain. In addition, our tax obligations and effective tax rates could be adversely affected by changes in the relevant tax, accounting and other laws, regulations, principles and interpretations, including those relating to income tax nexus, by our earnings being lower than anticipated in jurisdictions where we have lower statutory rates and higher than anticipated in jurisdictions where we have higher statutory rates, by changes in foreign currency exchange rates, or by changes in the valuation of our deferred tax assets and liabilities. We may be audited in various jurisdictions, and such jurisdictions may assess additional taxes against us. Although we believe our tax estimates are reasonable, the final determination of any tax audits or litigation could be materially different from our historical tax provisions and accruals, which could have a material adverse effect on our operating results or cash flows in the period or periods for which a determination is made.

Our business could be adversely affected by the effects of widespread public health epidemics and other factors beyond our control.

Public health epidemics or widespread outbreaks of contagious diseases could adversely impact our business. Any outbreak of contagious diseases, and other adverse public health developments, such as the COVID-19 pandemic, could impact our operations depending on future developments, which are highly uncertain, largely beyond our control and cannot be predicted with certainty. These uncertain factors include the duration of the outbreak, new information which may emerge concerning the severity of the disease and the actions to contain or treat its impact, could adversely impact our operations, including among others, conduct of our clinical trials, employee mobility and productivity, temporary closure of facilities, including clinical trial sites, our manufacturing capabilities, and third party service providers such as CROs, any of which could have an adverse impact on our business and our financial results. The COVID-19 pandemic has also adversely affected the conduct of our clinical trials. For example, on March 25, 2020, we announced that enrollment in our clinical trials had been paused temporarily in response to the COVID-19 pandemic in order to avoid unnecessary exposure in at-risk populations, to maintain the integrity of our study data and to support global healthcare providers in their commitment to ensure patient safety. On June 17, 2020, we announced that enrollment in our Phase 2 clinical trial in cystic fibrosis had resumed in Israel and Europe, and on August 12, 2020, had resumed in the United States. As the COVID-19 pandemic continues in the United States and elsewhere, we may experience additional disruptions that could severely impact our business, preclinical studies and clinical trials.

We may be subject to numerous and varying privacy and security laws, and our failure to comply could result in penalties and reputational damage, and adversely affect our financial condition and results of operations.

We are subject to laws and regulations covering data privacy and the protection of personal information including health information. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues which may affect our business. In the U.S., we may be subject to state security breach notification laws, state health information privacy laws and

federal and state consumer protections laws which impose requirements for the collection, use, disclosure and transmission of personal information. Each of these laws is subject to varying interpretations by courts and government agencies, creating complex compliance issues for us. Any actual or perceived failure by us to comply with applicable laws and regulations could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our business, financial condition and results of operation.

As our operations and business grow, we may become subject to or affected by new or additional data protection laws and regulations and face increased scrutiny or attention from regulatory authorities. In the U.S., HIPAA as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and regulations promulgated thereunder (collectively, “HIPAA”) imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. While we do not believe that we are currently acting as a “covered entity” or “business associate” as such terms are defined under HIPAA, and therefore are not directly regulated under HIPAA, we could be subject to penalties or sanctions, including criminal penalties if we knowingly obtain individually identifiable health information from a covered entity in a manner that is not authorized or permitted by HIPAA or for aiding and abetting the violation of HIPAA.

Further, certain states have also adopted privacy and security laws and regulations, which govern the privacy, processing and protection of health-related and other personal information. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. For example, the California Consumer Privacy Act of 2018 (“CCPA”) went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Further, the California Privacy Rights Act (“CPRA”) recently passed in California. The CPRA significantly amends the CCPA and will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. Similar laws have passed in Virginia, Utah, Connecticut, and Colorado, and have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

Numerous other countries have also developed, or are developing, laws governing the collection, use and transmission of personal information. EU member states and other jurisdictions have adopted data protection laws and regulations, which impose significant compliance obligations. For example, in May 2018, the General Data Protection Regulation (“GDPR”) went into effect, which imposes strict requirements for processing the personal data of individuals within the European Economic Area (“EEA”). Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States; in July 2020, the Court of Justice of the EU (“CJEU”) limited how organizations could lawfully transfer personal data from the EU/EEA to the United States by invalidating the Privacy Shield for purposes of international transfers and imposing further restrictions on the use of standard contractual clauses (“SCCs”). The European Commission issued revised SCCs on June 4, 2021 to account for the decision of the CJEU and recommendations made by the European Data Protection Board. The revised SCCs must be used for relevant new data transfers from September 27, 2021; existing standard contractual clauses arrangements must be migrated to the revised clauses by December 27, 2022. The new SCCs apply only to the transfer of personal data outside of the EEA and not the United Kingdom. The United Kingdom’s Information Commissioner’s Office has published new data transfer standard contracts for transfers from the United Kingdom under the United Kingdom GDPR. This new documentation will be mandatory for relevant data transfers from September 21, 2022; existing standard contractual clauses arrangements must be migrated to the new documentation by March 21, 2024. There is some uncertainty around whether the revised clauses can be used for all types of data transfers, particularly whether they can be relied on for data transfers to non-EEA entities subject to the GDPR. As supervisory authorities issue further guidance on

personal data export mechanisms, including circumstances where the SCCs cannot be used, and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results.

Since the beginning of 2021, after the end of the transition period following the United Kingdom's departure from the EU, we are also subject to the United Kingdom GDPR ("UK GDPR"), which together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR imposes separate but similar obligations to those under the GDPR and comparable penalties, including fines of up to £17.5 million or 4% of a noncompliant company's global annual revenue for the preceding financial year, whichever is greater. The relationship between the United Kingdom and the EU in relation to certain aspects of data protection law remains unclear, and the European Commission adopted an adequacy decision in favor of the United Kingdom, enabling data transfers from EU member states to the United Kingdom without additional safeguards. However, the United Kingdom adequacy decision will automatically expire in June 2025 unless the European Commission re-assesses and renews or extends that decision. In September 2021, the United Kingdom government launched a consultation on its proposals for wide-ranging reform of United Kingdom data protection laws following Brexit and the response to this consultation was published in June 2022. There is a risk that any material changes which are made to the United Kingdom data protection regime could result in the European Commission reviewing the United Kingdom adequacy decision, and the United Kingdom losing its adequacy decision if the European Commission deems the United Kingdom to no longer provide adequate protection for personal data. As we continue to expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business.

The EU has also proposed a Regulation on Privacy and Electronic Communications, ("ePrivacy Regulation"), which, if adopted, would impose new obligations on the use of personal data in the context of electronic communications, particularly with respect to online tracking technologies and direct marketing. Additionally, the EU adopted the EU Clinical Trials Regulation, which came into effect on January 31, 2022. This regulation imposes new obligations on the use of data generated from clinical trials and enables European patients to have the opportunity to access information about clinical trials. Failure or perceived failure to comply with the GDPR, the UK GDPR, the ePrivacy Regulation, the EU Clinical Trials Regulations, and other countries' privacy or data security-related laws, rules or regulations could result in significant regulatory penalties and fines, affect our compliance with contracts entered into with our partners, collaborators and other third-party payors, and could have an adverse effect on our reputation, business and financial condition.

Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, collaborators, or other third parties to comply with such requirements or adequately address privacy and security concerns, even if unfounded, could result in additional cost and liability to us, damage our reputation, and adversely affect our business, financial condition and results of operations.

Security breaches, cyber-attacks, or other disruptions could expose us to liability and affect our business and reputation.

We are increasingly dependent on our information technology systems and infrastructure for our business. We collect, store, and transmit sensitive information including intellectual property, proprietary business information and personal information in connection with business operations. The secure maintenance of this information is critical to our operations and business strategy. Some of this information could be an attractive target of criminal attack by third parties with a wide range of motives and expertise, including organized criminal groups, "hacktivists," patient groups, disgruntled current or former employees, and others. Cyber-attacks are of ever-increasing levels of sophistication, and despite our security measures, our information technology systems and those of our third-party service providers, strategic partners and other contractors or consultants are vulnerable to attack and damage or interruption from computer viruses and malware (e.g. ransomware), malicious code, natural disasters, terrorism, war, telecommunication and electrical failures, hacking, cyberattacks, phishing attacks and other social engineering schemes, employee theft or misuse, human error, fraud, denial or degradation of service attacks, sophisticated nation-state and nation-state-supported actors or unauthorized access or use by persons inside our organization, or persons with access to systems inside our organization.

The COVID-19 pandemic has caused us to modify our business practices, including permitting our employees to work from home. As a result, we are increasingly dependent upon our information technology systems to operate our business and our ability to effectively manage our business depends on the security, reliability and adequacy of our information technology systems and data, which includes use of cloud technologies. This increased remote usage of information systems increases the risks that our business may be disrupted due to a variety of reasons, including security breaches, power outages, unavailability of employees, use of non-company secured equipment and increased phishing and hack activity. However, despite these measures, and due to the ever-changing information cyber-threat landscape, we may be subject to data breaches through cyber-attacks. Any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost or stolen. If our systems become compromised, we may not promptly discover the intrusion. Even if a compromise were identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence.

Like other companies in our industry, we and our service providers are from time to time subject to cyberattacks and security incidents, including malware and computer viruses. While we do not believe that we have experienced any significant system failure, accident, or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in patient and other data and information becoming compromised, and we could lose sales for approved products, if any, and suffer reputational damage and loss of confidence by patients, investors and business partners. Such incidents may result in notification obligations to affected individuals and government agencies, legal claims or proceedings, and liability under federal and state laws that protect the privacy and security of personal information. Any one of these events, or similar events occurring through one of our vendors that maintain such information on our behalf, could cause our business to be materially harmed and our results of operations to be adversely impacted.

Our existing general liability and cyber liability insurance policies may not cover, or may cover only a portion of, any potential claims related to security breaches to which we are exposed or may not be adequate to indemnify us for all or any portion of liabilities that may be imposed. We also cannot be certain that our existing insurance coverage will continue to be available on acceptable terms or in amounts sufficient to cover the potentially significant losses that may result from a security incident or breach or that the insurer will not deny coverage of any future claim. Accordingly, if our cybersecurity measures, and those of our service providers, fail to protect against unauthorized access, attacks (which may include sophisticated cyberattacks) and the mishandling of data by our employees and third-party service providers, then our reputation, business, results of operations and financial condition could be adversely affected.

We currently rely, and plan to rely on in the future, third parties to conduct and support our preclinical studies and clinical trials. If these third parties do not properly and successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval of or commercialize our product candidates.

We have utilized and plan to continue to utilize and depend upon independent investigators and collaborators, such as medical institutions, CROs, CMOs, consultants and strategic partners to conduct and support our preclinical studies and clinical trials. As a result, we will have less direct control over the conduct, timing and completion of these preclinical studies and clinical trials and the management of data developed. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP regulations, 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 our marketing applications. We cannot assure you that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the GCP regulations. In addition, our clinical trials must be conducted with pharmaceutical product produced under cGMP regulations. Our failure or any failure by these third parties to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Further, these investigators and CROs are not our employees and we will not be able to control, other than by contract, the amount of resources, including time, which they devote to our product candidates and clinical trials. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If independent investigators or CROs fail to devote sufficient resources to the development of our product candidates, or if CROs 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 obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed or precluded entirely.

Our CROs have the right to terminate their agreements with us in the event of an uncured material breach. In addition, some of our CROs have an ability to terminate their respective agreements with us if it can be reasonably demonstrated that the safety of the subjects participating in our clinical trials warrants such termination, if we make a general assignment for the benefit of our creditors or if we are liquidated. If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional 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. Additionally, CROs may lack the capacity to absorb higher workloads or take on additional capacity to support our needs. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar 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 contract with third parties for the manufacture of our product candidates for preclinical studies and our ongoing clinical trials, and expect to continue to do so for additional clinical trials and ultimately for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or drugs or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not currently have the infrastructure or internal capability to manufacture supplies of our product candidates for use in development, or if approved, eventual commercialization. We rely, and expect to continue to rely, on third-party manufacturers for the production of our product candidates for preclinical studies and clinical trials. We do not have long-term supply agreements with these manufacturers. Furthermore, the raw materials for our product candidates are sourced, in some cases, from a single-source supplier. If we were to experience an unexpected loss of supply of any of our product candidates or any of our future product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing clinical trials. For example, the extent to which the COVID-19 pandemic impacts our ability to procure sufficient supplies for the development of our products and product candidates will depend on the severity and duration of the spread of the virus, and the actions undertaken to contain COVID-19 or treat its effects.

We expect to continue to rely on third-party manufacturers for the commercial supply of any of our product candidates for which we obtain marketing approval. We may be unable to maintain or establish required agreements with third-party manufacturers or to 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:

- the failure of the third party to manufacture our product candidates according to our schedule;
- the reduction or termination of production or deliveries by suppliers, or the raising of prices or renegotiation of terms;
- the termination or nonrenewal of agreements at a time that is costly or inconvenient for us;
- the failure to comply with contractual obligations;
- the failure to comply with applicable regulatory requirements;
- the failure to manufacture our product candidates according to our specifications;

- clinical supplies not being delivered to clinical sites on time;
- disruptions to the operations of our third-party manufacturers or suppliers, testing facilities, or research sites caused by conditions unrelated to our business or operations, including unrelated regulatory action against or the bankruptcy of the manufacturer or supplier, testing facility, or research site, or the unavailability of essential personnel to conduct or complete our research or clinical trials, such as, for example, a result of the COVID-19 pandemic; and
- the misappropriation of our proprietary information, including our trade secrets and know-how.

We do not have complete control over all aspects of the manufacturing process of, and are dependent on, our contract manufacturing partners for compliance with cGMP regulations for manufacturing both active drug substances and finished drug products. Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. 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/or maintain marketing approval for their manufacturing facilities. In addition, we do not have control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA, EMA or comparable regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing approval for or market our product candidates, if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates or drugs and harm our business and results of operations. Our current and anticipated future dependence upon others for the manufacture of our product candidates or drugs may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis.

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

The success of our business is dependent in large part on our continued ability to attract and retain our senior management, and other highly qualified personnel in our scientific, clinical, manufacturing and commercial organizations. Intense competition exists in the biopharmaceutical industry for these types of personnel. Our business is specialized and global and we must attract and retain highly qualified individuals across many geographies. We may not be able to continue to attract and retain the highly qualified personnel necessary for developing, manufacturing and commercializing our product candidates. If we are unsuccessful in our recruitment and retention efforts, or if our recruitment efforts take longer than anticipated, our business may be harmed. We may face difficulty in attracting and retaining key talent for a number of reasons, including management changes, the underperformance or discontinuation of one or more late-stage programs, recruitment by competitors or delays in the recruiting and hiring process as a result of the COVID-19 pandemic or otherwise. We cannot ensure that we will be able to hire or retain the personnel necessary for our operations or that the loss of any such personnel will not have a material impact on our financial condition and results of operations.

We are highly dependent on principal members of our senior management. While we have entered into employment agreements or offer letters with each of our executive officers, any of them could leave our employment at any time. Recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel, will also be critical to our success. Competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, failure to succeed in preclinical studies or clinical trials may make it more challenging to recruit and retain qualified personnel. The inability to recruit or loss of the services of any executive, key employee, consultant or advisor may impede the progress of our research, development and commercialization objectives. If we fail to attract and retain highly qualified personnel, we may not be able to successfully develop, manufacture or commercialize our product candidates.

We have experienced recent changes in management and other key personnel in critical functions across our organization, including in connection with the Zikani Merger. Changes in management and other key personnel have the potential to disrupt our business, and any such disruption could adversely affect our operations, programs, growth, financial condition or results of operations. In addition, new members of management may have different perspectives on programs and opportunities for our business, which may cause us to focus on new business opportunities or reduce or change emphasis on our existing business programs. Further, if members of our management and other key personnel in critical functions across our organization are unable to perform their duties, we may not be able to execute on our business strategy and/or our operations may be negatively impacted.

Risks Related to Intellectual Property

If we fail to adequately protect or enforce our intellectual property rights or secure rights to third party patents, the value of our intellectual property rights would diminish, and our business, competitive position and results of operations would suffer.

As of December 31, 2022, we owned or licensed 66 issued patents and 101 pending patent applications in the U.S. and abroad, not including U.S. provisional applications. However, with regard to the pending applications, the filing of a patent application does not mean that we will be issued a patent, or that any patent eventually issued will be as broad as requested in the patent application or sufficient to protect our technology. Any modification required to a currently pending patent application may delay the approval of such patent application which could have a material adverse effect on our business, results of operations and financial condition. In addition, there are a number of factors that could cause our current or future issued patents to become invalid or unenforceable or that could cause our pending patent applications to not be granted, including known or unknown prior art, deficiencies in the patent application or lack of originality of the technology. Our competitive position and future revenue will depend in part on our ability and the ability of our licensors and collaborators to obtain and maintain patent protection for our product candidates, methods, processes and other technologies, to preserve our trade secrets, to prevent third parties from infringing on our proprietary rights and to operate without infringing the proprietary rights of third parties. However, we cannot predict:

- the degree and range of protection any patents will afford us against competitors and those who infringe upon our patents, including whether third parties will find ways to invalidate or otherwise circumvent our licensed patents;
- if and when patents will issue;
- whether or not others will obtain patents claiming aspects similar to those covered by our owned or licensed patents and patent applications; or
- whether we will need to initiate litigation or administrative proceedings, which may be costly, and whether we win or lose.

If patent rights covering our products or technologies are not sufficiently broad, they may not provide us with sufficient proprietary protection or competitive advantages against competitors with similar products and technologies. Furthermore, if the U.S. Patent and Trademark Office or foreign patent offices issue patents to us or our licensors, others may challenge the patents or circumvent the patents, or the patent office or the courts may invalidate the patents. Thus, any patents we own or license from or to third parties may not provide any protection against our competitors and those who infringe upon our patents.

Furthermore, the lives of our patents are limited. With regard to our lead compound ELX-02, patents that have issued or that may issue in the future from our primary composition of matter patent family are currently set to expire in 2031. We have pending patent families directed to specific methods of manufacturing ELX-02 and using ELX-02 to treat various ocular conditions, and any patents that may issue from these families would be expected to expire in 2038 and 2039, respectively. However, these applications may not issue, and even if they do issue the resultant patents may not provide adequate coverage to meaningfully block competitors from launching their products. We will likely pursue additional patent protection relating to ELX-02 in the future, including for example additional methods of use or manufacture, specific formulations, or combinations of ELX-02 with other therapeutic agents. However, as with our pending patent families, any applications we file in the future may not issue or may not result in adequate coverage to adequately protect our assets.

Depending upon the timing, duration, and conditions of any FDA marketing approval for ELX-02, one or more of our patents may be eligible for patent term extension of up to five years under the Hatch-Waxman Act. However, we may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, fail to apply for an extension within applicable deadlines, or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. Only one patent per approved product can be extended, the extension cannot extend the total patent term beyond 14 years from approval and only those claims covering the approved drug, an approved method of using the approved drug, or a method of manufacturing the approved drug may be extended. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for ELX-02 will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be reduced. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case, and our business could be harmed.

If we cannot obtain new patents, maintain our existing patents and protect the confidentiality and proprietary nature of our trade secrets and other intellectual property, our business and competitive position may be harmed.

Our success will depend in part on our ability to obtain and maintain patent and regulatory protections for our product candidates, to preserve our trade secrets and other proprietary rights, to operate without infringing the proprietary rights of third parties, and to prevent third parties from circumventing our rights. Due to the time and expense of bringing new product candidates through development and regulatory approval to the marketplace, there is particular importance in obtaining patent and trade secret protection for significant new technologies, products and processes.

We have and may in the future obtain patents or the right to practice patents through ownership or license. Our patent applications may not result in the issue of patents in the U.S. or other countries. Our patents may not afford adequate protection for our products. Third parties may challenge our patents. If any of our patents are narrowed, invalidated or become unenforceable, competitors may develop and market products similar to ours that do not conflict with or infringe our patents rights, which could have a material adverse effect on our financial condition. We may also finance and collaborate in research conducted by government organizations, hospitals, universities or other educational or research institutions. Such research partners may be unwilling to grant us exclusive rights to technology or products developed through such collaborations. There is also a risk that disputes may arise as to the rights to technology or products developed in collaboration with other parties. Our product candidates are expensive and time-consuming to test and develop. Even if we obtain and maintain patents, our business may be significantly harmed if the patents are not broad enough to protect our products from copycat products.

Significant legal questions exist concerning the extent and scope of patent protection for biopharmaceutical products and processes in the U.S. and elsewhere. Accordingly, there is no certainty that patent applications owned or licensed by us will issue as patents, or that our issued patents will afford meaningful protection against competitors. Once issued, patents are subject to challenge through both administrative and judicial proceedings in the U.S. and other countries. Such proceedings include re-examinations, inter partes reviews, post-grant reviews and interference proceedings before the U.S. Patent and Trademark Office, as well as opposition proceedings before the European Patent Office and other non-U.S. patent offices. Litigation may be required to enforce, defend or obtain our patent and other intellectual property rights. Any administrative proceeding or litigation could require a significant commitment of our resources and, depending on outcome, could adversely affect the scope, validity or enforceability of certain of our patent or other proprietary rights.

In addition, our business requires using sensitive technology, techniques and proprietary compounds that we protect as trade secrets. However, we may also rely heavily on collaboration with, or discuss the potential for collaboration with, suppliers, outside scientists and other biopharmaceutical companies. Collaboration and discussion of potential collaboration present a strong risk of exposing our trade secrets. If our trade secrets were exposed, it would help our competitors and adversely affect our business prospects.

If we are found to be infringing on patents owned by others, we may be forced to pay damages to the patent owner and/or obtain a license to continue the manufacture, sale or development of our product candidates. If we cannot obtain a license, we may be prevented from the manufacture, sale or development of our product candidates, which would adversely affect our business.

If we infringe the rights of third parties, we could be prevented from selling products, forced to pay damages and required to defend against litigation which could result in substantial costs and may have a material adverse effect on our business, results of operations and financial condition.

We have not received to date any claims of infringement by any third parties. However, as our product candidates progress into clinical trials and commercialization, if at all, our public profile and that of our product candidates may be raised and generate such claims. Defending against such claims, and occurrence of a judgment adverse to us, could result in unanticipated costs and may have a material adverse effect on our business and competitive position. If our products, methods, processes and other technologies infringe the proprietary rights of other parties, we may incur substantial costs and we may have to:

- obtain licenses, which may not be available on commercially reasonable terms, if at all;
- redesign our products or processes to avoid infringement, which could significantly impede development and impair or block our ability to secure regulatory approval of any redesigned product or process;
- stop using the subject matter claimed in the patents held by others, which could cause us to lose the use of one or more of our product candidates;
- defend litigation or administrative proceedings that may be costly whether we win or lose, and which could result in a substantial diversion of management resources; or
- pay damages.

Any costs incurred in connection with such events or the inability to develop or sell our products may have a material adverse effect on our business, results of operations and financial condition.

We rely on confidentiality agreements that could be breached and may be difficult to enforce which could have a material adverse effect on our business and competitive position.

Our policy is to enter agreements relating to the non-disclosure of confidential information with third parties, including our contractors, consultants, advisors and research collaborators, as well as agreements that purport to require the disclosure and assignment to us of the rights to the ideas, developments, discoveries and inventions of our employees and consultants while we employ them. However, these agreements can be difficult and costly to enforce. Moreover, to the extent that our contractors, consultants, advisors and research collaborators apply or independently develop intellectual property in connection with any of our projects, disputes may arise as to the proprietary rights to the intellectual property. If a dispute arises, a court may determine that the rights belong to a third party, and enforcement of our rights can be costly and unpredictable. In addition, we rely on trade secrets and proprietary know-how that we seek to protect in part by confidentiality agreements with our employees, contractors, consultants, advisors and other third parties. Despite the protective measures we employ, we still face the risk that:

- these agreements may be breached;
- these agreements may not provide adequate remedies for the applicable type of breach; or
- our trade secrets or proprietary know-how will otherwise become known.

Any breach of our confidentiality agreements or our failure to effectively enforce such agreements may have a material adverse effect on our business and competitive position.

If we cannot meet requirements under our license agreement, we could lose the rights to our product candidates, which could have a material adverse effect on our business.

We depend on the license agreement with TRDF to maintain the intellectual property rights to certain of our product candidates. Our license agreement requires us to make payments and satisfy performance obligations in order to maintain our rights under this agreement. This agreement lasts either throughout the life of the patents that are the subject of the agreement, or with respect to other licensed technology, for a number of years after the first commercial sale of the relevant product.

In addition, we are responsible for the cost of filing and prosecuting certain patent applications and maintaining certain issued patents licensed to us. If we do not meet our obligations under our license agreement in a timely manner, we could lose the rights to our proprietary technology, which could have a material adverse effect on our business, results of operations and financial condition.

We may become involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time consuming and unsuccessful and have an adverse effect on the success of our business.

Competitors or other third parties may infringe, misappropriate or otherwise violate our patents or other intellectual property. If we or one of our licensors were to initiate legal proceedings against a third party to enforce a patent covering one of our products or product candidates, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States and in Europe, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness, lack of written description, or non-enablement. Third parties might allege unenforceability of our patents because during prosecution of the patent an individual connected with such prosecution withheld relevant information or made a misleading statement. 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. The outcome of proceedings involving assertions of invalidity and unenforceability during patent litigation is unpredictable. 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 products and product candidates, which may allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or could require us to obtain license rights from the prevailing party in order to be able to manufacture or commercialize our products, product candidates or technologies without infringing third-party patent rights. Even if a defendant does not prevail on a legal assertion of invalidity or unenforceability, our patent claims may be construed in a manner that would limit our ability to enforce such claims against the defendant and others. Moreover, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize our product candidates. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon, misappropriating or otherwise violating our intellectual property rights. Thus, even if we were to ultimately prevail, or to settle at an early stage, such litigation could burden us with substantial unanticipated costs. Our patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without infringing our patents or other intellectual property rights.

We may be subject to third-party claims including infringement, interference or derivation proceedings, post-grant review and inter partes review before the USPTO or similar adversarial proceedings or litigation in other jurisdictions. Even if we believe such claims are without merit, a court could hold that these third-party patents are valid, enforceable and infringed, and the holders of any such patents may be able to block our ability to commercialize the applicable product or product candidates unless we obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our products, product candidates or technologies may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court to cover aspects of our products, product candidates or technologies, the holders of any such patents may be able to prohibit our commercialization of the applicable product or product candidate until such patent expires or is finally determined to be invalid or unenforceable or unless we obtained a license.

In addition, defending such claims would cause us to incur substantial expenses and, if successful, could cause us to pay substantial damages if we are found to be infringing a third party's patent rights. These damages potentially include royalties, increased damages (possibly treble damages) and attorneys' fees if we are found to have infringed such rights willfully. Further, if a patent infringement suit is brought against us, our development, manufacturing or sales activities relating to the product, product candidate or technology that is the subject of the suit may be delayed or terminated, as parties making claims against us may obtain injunctive or other equitable relief. As a result of patent infringement claims, or in order to avoid potential infringement claims, we may choose to seek, or be required to seek, a license from the third party, which may require payment of substantial royalties or fees, or require us to grant a cross-license under our intellectual property rights. These licenses may not be available on reasonable terms or at all. If we are unable to enter into a license on acceptable terms, we could be prevented

from commercializing one or more of our products or product candidates, or forced to modify such products or product candidates, or to cease some aspect of our business operations, which could harm our business significantly. We might also be forced to redesign or modify our products, product candidates or technologies so that we no longer infringe the third-party intellectual property rights, which may result in significant cost or delay to us, or which redesign or modification could be impossible or technically infeasible.

Even if we were ultimately to prevail, any of these events could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business. Intellectual property litigation, regardless of its outcome, may cause negative publicity, adversely impact prospective customers, cause product shipment delays, or prohibit us from manufacturing, importing, marketing or otherwise commercializing our products or product candidates. Such litigation or proceedings could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have an adverse effect on our ability to compete in the marketplace and could have an adverse impact on our business and financial condition.

Risks Related to Our Regional Operations

Potential political and economic instability in regions where we conduct business may adversely affect our results of operations.

In addition to our operations in the United States, we currently conduct certain research and clinical development activities through our regional operations located in Israel. We also maintain a legal presence and contract with vendors located in Australia. We may, in the future, expand our presence and operations to other locations as circumstances require. Accordingly, political and economic conditions in any other country or region where we do business may directly affect our operations.

In particular, regional instability in the Middle East may lead to a deterioration in the political and trade relationship that exists between countries in the region, making it more difficult to conduct operations. In addition, our insurance does not cover losses that may occur as a result of an event associated with the security situation in the Middle East or for any resulting disruption in our operations. Although the Israeli government has in the past covered the reinstatement value of direct damages that were caused by terrorist attacks or acts of war, we cannot provide assurance that this government coverage will be maintained or, if maintained, will be sufficient to compensate us fully for damages incurred.

Furthermore, in the past, Israel and Israeli companies have been subjected to economic boycotts. Several countries still restrict business with Israel and with Israeli companies. These restrictive laws and policies, even though we are a U.S.-based company, may have an adverse impact on our operating results, financial conditions or the expansion of our business.

We received Israeli government grants for our research and development activities and programs. The terms of such grants may require us, in the future, to pay royalties and under certain circumstances, penalties in addition to payment of royalties.

Our research and development efforts were initially financed, in part, through royalty-bearing grants from the Israel Innovation Authority, or IIA. We received an aggregate of \$2.6 million from the IIA for the development of our technologies. With respect to such grants we are required to pay certain royalties (including accrued interest) up to \$2.8 million. We are required to comply with the requirements of the Israeli Encouragement of Research, Development and Technological Innovation in the Industry Law, 5744-1984, as amended, and related regulations ("the R&D Law") with respect to these past grants. If we fail to comply with the R&D Law, we may be required to refund certain grants previously received and/or to pay interest and penalties and we may become subject to criminal charges.

With respect to such grants we are obligated to pay royalties at a rate in the low to middle single digit percentage from the revenue generated from the sale of any products or services developed using IIA grants up to a maximum amount equal to repayment of the grant proceeds received plus accrued interest. We have not commenced

the payment obligation of these royalties since we have not yet generated revenue, and we have a contingent obligation with respect to such future royalty payments including interest, of \$2.8 million.

The R&D Law and terms of the prior grants restrict the transfer of certain know-how, and the transfer of manufacturing or manufacturing rights of products developed with grant funds, outside of Israel, without the prior approval of the IIA. Therefore, if aspects of our technologies are deemed to have been developed with IIA funding according to the R&D Law, the discretionary approval of the IIA may be required for any assignment and/or transfer to third parties inside or outside of Israel of know-how or transfer outside of Israel of manufacturing or manufacturing rights and may result in payment of increased royalties and/or payment of additional amounts to the IIA. Furthermore, the IIA may impose certain conditions on any arrangement under which it permits us to transfer technology or development outside of Israel. Such approvals may not be granted by the IIA and any conditions imposed may not be acceptable to the Company.

The R&D Law and the regulations promulgated thereunder provide that the transfer of IIA-supported technology or know-how outside of Israel may involve the payment of additional amounts depending upon the value of the transferred technology or know-how, the amount of IIA support, the time of completion of the IIA-supported research project and other factors, up to a maximum of six times the amount of grants received. These restrictions and requirements for payment may impair our ability to sell our technology assets outside of Israel or to outsource or transfer development or manufacturing activities with respect to any product or technology outside of Israel. Furthermore, the consideration available to our stockholders in a transaction involving the transfer outside of Israel of technology or know-how developed with IIA funding may be reduced by any amounts that we are required to pay to the IIA. Our obligations and limitations pursuant to the R&D Law are not limited in time and may not be terminated by us at will. As of the date hereof, we have not been required to pay any royalties with respect to the IIA grants.

We may become subject to claims for remuneration or royalties for assigned service invention rights by our employees, which could result in litigation and adversely affect our business.

We enter into agreements with our employees pursuant to which they agree that any inventions created in the scope of their employment or engagement are assigned to us or owned exclusively by us, without the employee retaining any rights. A significant portion of our intellectual property has been developed by our employees in the course of their employment for us. Under the Israeli Patent Law, 5727-1967 (the "Patent Law"), inventions conceived by an employee during the scope of his or her employment with a company are regarded as "service inventions," which belong to the employer, absent a specific agreement between the employee and employer giving the employee service invention rights. The Patent Law also provides that if there is no such agreement between an employer and an employee, the Israeli Compensation and Royalties Committee (the "Committee"), a body constituted under the Patent Law, shall determine whether the employee is entitled to remuneration for his or her inventions. Previous decisions by the Committee have created uncertainty in this area regarding whether the right to receive remuneration for service inventions can be voluntarily waived by an employee and whether such waiver is enforceable. In addition, the Committee determined that even if such right to receive compensation and royalties for service inventions may be waived, the waiver should be specific. Subsequent court cases have not provided significant clarity on these matters.

Risks Related to Our Common Stock

Our stock price may be volatile, and purchasers of our common stock could incur substantial losses.

The trading price of our common stock has been volatile and may continue to be volatile and subject to wide fluctuations in the future. Many factors could have an impact on our stock price, including fluctuations in our or our competitors' operating results, clinical trial results or adverse events associated with our product candidates, product development by us or our competitors, changes in laws, including healthcare, regulatory, tax or intellectual property laws, intellectual property developments, acquisitions or other strategic transactions, changes in financial or operational estimates or projections and the perceptions of our investors that we are not performing or meeting expectations. The trading price of the common stock of many biopharmaceutical companies, including ours, has experienced extreme price and volume fluctuations, which have at times been unrelated to the operating performance of the companies whose stocks were affected. In addition, the securities market has from time-to-time experienced significant price and volume fluctuations that are not related to the operating performance of particular companies. These market fluctuations may also materially and adversely affect the market price of shares of our common stock.

Our failure to meet the continued listing requirements of The Nasdaq Capital Market could result in a delisting of our common stock.

If we fail to satisfy the continued listing requirements of The Nasdaq Capital Market, such as the minimum closing bid price requirement, Nasdaq may take steps to delist our common stock.

For example, on January 3, 2022, we received a letter from the Listing Qualifications Department of The Nasdaq Stock Market ("Nasdaq Listing Qualifications") notifying us that, for the last 30 consecutive business days, the closing bid price for our common stock has been below the minimum \$1.00 per share required for continued listing on The Nasdaq Global Market pursuant to Nasdaq Listing Rule 5450(a)(1) (the "Minimum Bid Price Requirement"). Under Nasdaq Listing Rule 5810(c)(3)(A), the Company was granted a 180 calendar day grace period, or until July 5, 2022, to regain compliance with the minimum bid price requirement. The minimum bid price requirement will be met if our common stock has a minimum closing bid price of at least \$1.00 per share for a minimum of 10 consecutive business days during the 180 calendar day grace period. Because the Company did not regain compliance with the Minimum Bid Price Requirement before July 5, 2022, the Company applied to transfer its listing to the Nasdaq Capital Market and for an extension of an additional 180 calendar days, or until January 2, 2023 to regain compliance with the Minimum Bid Price Requirement. On July 7, 2022, Nasdaq notified us that our application for listing on the Nasdaq Capital Market was approved and that Nasdaq had approved the Company's extension request.

On December 1, 2022, we effected a 1-for-40 reverse stock split of our common stock (the "Reverse Stock Split"). At a special meeting of stockholders held on November 30, 2022 (the "Special Meeting"), the stockholders of the Company approved a proposal to authorize the Company's Board of Directors, in its discretion following the Special Meeting to amend the Company's Amended and Restated Certificate of Incorporation, as amended (the "Certificate of Incorporation"), to effect a reverse stock split of all of the outstanding shares of the Company's common stock. On November 30, 2022, following the Special Meeting, the Company's Board of Directors approved the Reverse Stock Split at a ratio of 1-for-40. On December 1, 2022, the Company filed with the Secretary of State of the State of Delaware a certificate of amendment (the "Certificate of Amendment") with the Secretary of State of the State of Delaware to amend the Company's Certificate of Incorporation to effect the Reverse Stock Split. The Reverse Stock Split became effective at 5:00 p.m., Eastern Time, on December 1, 2022.

On December 19, 2022, we were notified by Nasdaq Listing Qualifications that the closing bid price of the our common stock had been at \$1.00 per share or greater for the 11 consecutive business days, from December 2, 2022 to December 16, 2022. Accordingly, the Company has regained compliance with Listing Rule 5550(a)(2) and this matter is now closed. Although we regained compliance with Listing Rule 5550(a)(2) there can be no guarantee that we can continue to remain compliant.

Further, on October 11, 2022, we received a letter from Nasdaq Listing Qualifications notifying us that for the last 30 consecutive business days, the Company's Minimum Value of Listed Securities, as defined by Nasdaq ("MVLS"), has been below the minimum \$35 million requirement for continued listing on The Nasdaq Capital Market under Nasdaq Listing Rule 5500(b)(2) (the "Minimum Market Value Requirement"). Under Nasdaq Listing Rule 5810(c)(3)(C), the Company has 180 calendar days, or until April 10, 2023, to regain compliance with the Minimum Market Value Requirement. The Minimum Market Value Requirement will be met if our minimum MVLS closes at \$35 million or more for a minimum of ten (10) consecutive business days during the compliance period ending April 10, 2023. If we do not regain compliance with the Minimum Market Value Requirement during the compliance period ending April 10, 2023, Nasdaq will provide written notification that the Company's common stock will be subject to delisting. At that time, the Company may appeal any such delisting determination to the Panel. We are actively monitoring our MVLS and evaluating available options to regain compliance with the Minimum Market Value Requirement. However, there is no assurance that we will be able to regain compliance with the Minimum Market Value Requirement during the 180-day compliance period.

The delisting of our common stock from Nasdaq may make it more difficult for us to raise capital on favorable terms in the future. Such a delisting would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so. Further, if we were to be delisted from Nasdaq, our common stock would cease to be recognized as covered securities and we would be subject to regulation in each state in which we offer our securities. Moreover, there is no assurance that any actions that we take to restore our compliance with the Minimum Market Value Requirement required for continued listing or prevent future non-compliance with Nasdaq's listing requirements. There is also no assurance that we will maintain compliance with the other listing requirements of The Nasdaq Capital Market.

General Risk Factors

Maintaining and improving our financial controls and the requirements of being a public company may strain our resources, divert management's attention and affect our ability to attract and retain qualified board members.

As a public company, we are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act of 2002 (the "Sarbanes-Oxley Act"), and Nasdaq stock market rules. The requirements of these rules and regulations have increased and will continue to significantly increase our legal and financial compliance costs, including costs associated with the hiring of additional personnel, making some activities more difficult, time-consuming or costly, and may also place undue strain on our personnel, systems and resources. The Exchange Act requires, among other things, that we file annual, quarterly and current reports with respect to our business and financial condition.

The Sarbanes-Oxley Act requires, among other things, that we maintain disclosure controls and procedures and internal control over financial reporting. Ensuring that we have adequate internal financial and accounting controls and procedures in place, as well as maintaining these controls and procedures, is a costly and time-consuming effort that needs to be re-evaluated frequently. Section 404 of the Sarbanes-Oxley Act, or Section 404, requires that we annually evaluate our internal control over financial reporting to enable management to report on the effectiveness of those controls. In connection with the Section 404 requirements, we test our internal controls and could, as part of that documentation and testing, identify material weaknesses, significant deficiencies or other areas for further attention or improvement.

Implementing any appropriate changes to our internal controls may require specific compliance training for our directors, officers and employees, require the hiring of additional finance, accounting and other personnel, entail substantial costs to modify our existing accounting systems, and take a significant period of time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and could materially impair our ability to operate our business. Moreover, adequate internal controls are necessary for us to produce reliable financial reports and are important to help prevent fraud. As a result, our failure to satisfy the requirements of Section 404 could result in the loss of investor confidence in the reliability of our financial statements, which in turn could cause the market value of our common stock to decline.

Our ability to use our net operating losses to offset future taxable income may be subject to certain limitations.

As of December 31, 2022, we had U.S. federal and state net operating loss carryforwards ("NOLs"), of \$159.2 million and \$25.9 million, respectively, and federal research tax credit carryforwards of \$8.1 million. Certain U.S. NOLs will begin to expire, beginning in 2023 through 2037, and research tax credits will expire beginning in 2026 through 2041. Included in these U.S. federal NOLs are \$84.1 million of NOLs generated after the effective date of the Tax Cuts and Jobs Act of 2017 ("TCJA") which are not subject to expiration. Under the TCJA, Federal NOLs generated in 2018 and future years may be carried forward indefinitely but may not be carried back and are only eligible to offset up to a maximum of 80% of taxable income generated in a given year. It is uncertain if and to what extent various U.S. states will conform their net operating loss rules to the TCJA.

In general, under Section 382 of the U. S. Internal Revenue Code of 1986, as amended, (the "Code"), a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-ownership change NOLs to offset future taxable income. We may have experienced ownership changes in the past. We may experience additional ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. Although we have not completed our analysis, it is reasonably possible that our federal NOLs available to offset future taxable income could materially decrease. This reduction will be offset by an adjustment to the existing valuation allowance for an equal and offsetting amount. Additionally, our state NOLs available to offset future state income could similarly decrease which would also be offset by an equal and offsetting adjustment to the existing valuation allowance. Given the offsetting adjustments to the existing valuation allowance, any ownership change is not expected to have a material adverse effect on our consolidated financial statements. As of December 31, 2022, we had Israeli NOLs of \$101.0 million, which carry forward indefinitely.

Our ability to utilize our NOLs is dependent on attaining profitability sufficient to offset such available NOLs prior to their expiration. In addition, we may not be able to utilize a portion of the NOLs even if we attain profitability.

Our directors, executive officers, principal stockholders and affiliated entities own a significant percentage of our capital stock, and they may make decisions that an investor may not consider to be in the best interests of our stockholders.

Our directors, executive officers, principal stockholders and affiliated entities beneficially own, in the aggregate, a significant percentage of our common stock, giving effect to options and other derivative securities that are held by such persons. As a result, if some or all of them acted together, they would have the ability to exert substantial influence over the election of our board of directors and the outcome of issues requiring approval by our stockholders. This concentration of ownership may have the effect of delaying or preventing a change in control of our company that may be favored by other stockholders. This could prevent the consummation of transactions favorable to other stockholders, such as a transaction in which stockholders might otherwise receive a premium for their shares over current market prices.

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

Additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities or our ATM Program pursuant to which we may sell up to \$50.0 million of our common stock, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner, we determine from time to time. If we sell common stock, convertible securities or other equity securities in one or more transactions, existing investors may be materially diluted by subsequent sales, and new investors could gain rights superior to our existing stockholders.

Pursuant to our 2018 Equity Incentive Plan, our management is authorized to grant stock options and other equity-based awards to our employees, directors and consultants. As of December 31, 2022, individuals held share awards to purchase or receive an aggregate of 249,403 shares of our common stock. If our board of directors elects to increase the number of shares available for future grant by the maximum amount each year (5% of the outstanding common stock), our stockholders may experience additional dilution, which could have a negative effect on our share price.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Our principal executive offices are currently located at 480 Arsenal Way, Watertown, Massachusetts, and consist of approximately 9,000 square feet of office space under lease until February 2024, with an option to extend the lease period for an additional three years. We also lease additional office space in Rehovot, Israel. We believe that our existing facilities are adequate to meet current business needs, and that suitable additional or substitute space will be available as needed to accommodate our future office space needs.

ITEM 3. LEGAL PROCEEDINGS

From time to time, we may become involved in various lawsuits and legal proceedings, which arise in the ordinary course of business, which may include, without limitation, actions related to or based on our intellectual property and its use, customer claims, employment practices and employee complaints and other events arising out of our operations. We are currently unaware of any material pending legal proceedings to which we are party or of which our property is the subject. However, we may at times in the future become involved in litigation in the ordinary course of business. When appropriate in management's estimation, we will record adequate reserves in our financial statements for pending litigation. Litigation is subject to inherent uncertainties, and an adverse result in any such matters could adversely impact our reputation, operations, and our financial operating results or overall financial condition. Additionally, any litigation to which we may become subject could also require significant involvement of our senior management and may divert management's attention from our business and operations.

ITEM 4. MINE SAFETY DISCLOSURES

None.

PART II

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

Market Information for Common Stock

From July 7, 2022, our common stock has traded on The NASDAQ Capital Market under the symbol "ELOX." From April 26, 2018 to July 6, 2022, our common stock traded on The NASDAQ Global Market under the symbol "ELOX." Prior to April 26, 2018, our common stock traded on the OTCQB market under the symbol "ELOX".

Holders

As of March 21, 2023, there were approximately 90 holders of record of our common stock. This number does not include "street name" or beneficial holders, whose shares are held of record by banks, brokers, financial institutions and other nominees.

Recent Sales of Unregistered Securities

None.

Purchases of Equity Securities by the Issuer or Affiliated Purchaser

There were no repurchases of shares of our common stock during the fourth quarter ended December 31, 2022.

Dividend Policy

We have not paid dividends on our common stock since inception and we do not intend to pay any dividends in the foreseeable future. We expect that any earnings which we may realize will be retained to finance the growth of our Company. The declaration of dividends in the future will be at the election of our board of directors and will depend upon our earnings, capital requirements, financial position, general economic conditions, and other factors the board of directors deems relevant.

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 together with our consolidated financial statements and related notes and other financial information appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. Please see "Special Note Regarding Forward-Looking Statements." As a result of many factors, including those factors set forth in "Part I, Item 1A - Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described in, projected or implied by the forward-looking statements contained in the following discussion and analysis.

Our discussion and analysis of our financial condition and results of operations for 2022 as compared to 2021 are discussed below. For a discussion of our financial condition and results of operations for 2021 as compared to 2020, please refer to Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our 2021 Annual Report on Form 10-K, except as set forth below.

Company Overview

We are a clinical-stage biopharmaceutical company engaged in the science of ribosome modulation, leveraging both our innovative TURBO-ZM™ chemistry technology platform and our library of novel aminoglycosides to develop novel oral small molecule Ribosome Modulating Agents ("RMAs") and Eukaryotic Ribosome Selective Glycosides ("ERSGs"), for the treatment of rare and ultra-rare genetic diseases where patients have point nonsense genetic mutations that result in premature stop codons and less than full length proteins. "Nonsense mutations result in premature stop codons in the impacted messenger RNA ("mRNA") which in turn disrupt protein synthesis from that mRNA leading to less than full length proteins. Patients with these mutations have significantly worse outcomes than with missense mutations.

We have multiple programs in our pipeline including a clinical program for the treatment of Alport syndrome with ELX-02 (subcutaneous delivery), preclinical programs in investigational new drug ("IND") enabling stages in Recessive Dystrophic ("RDEB") and Junctional Epidermolysis Bullosa ("JEB") and Familial Adenomatous Polyposis ("FAP") with ZKN-013, and IND enabling stage program with inhaled delivery of ELX-02 in Class 1 cystic fibrosis ("CF"). We also have various earlier discovery stage programs in Cystic fibrosis and oncology. As our programs advance, we plan to actively look to expand our pipeline by seeking new indications in other rare diseases for compounds designed with our platforms. The U.S. Food and Drug Administration ("FDA") has granted Fast Track designation for ELX-02 for the treatment of CF patients with nonsense mutations. In addition, the FDA granted ELX-02 Orphan Drug Designation for the treatment of CF in July 2020 and based on the European Medicines Agency' s ("EMA") positive opinion, the European Commission granted ELX-02 orphan medicinal product designation in September 2018.

In March 2022, we announced our decision to advance ELX-02 delivered subcutaneously for the restoration of Collagen IV protein for the treatment of Alport syndrome patients. Alport syndrome with nonsense mutations is a genetic kidney disorder that occurs in 1 in 50,000 newborns in the United States. It is caused by the loss of one of three collagen IV subtypes. This disease is characterized by blood (hematuria) and protein (proteinuria) in the patient's urine, and results in progressive kidney disease, hearing loss, and eye abnormalities. In November 2022, we began a Phase 2 monotherapy clinical trial for ELX-02 for the potential treatment of Alport syndrome and in January 2023, we announced that the first patients had been enrolled. ELX-02 treatment has demonstrated restoration of full-length protein in multiple preclinical models, including collagen IV and collagen VII in cells, and also clinical activity in our Phase 2 cystic fibrosis trial. We believe our results, previously conducted in vivo studies showing improvement of kidney function with collagen IV restoration and the ability to achieve high kidney drug levels at tolerable doses support the clinical development of ELX-02 in Alport syndrome. This Phase 2 trial is targeting dosing of up to eight Alport syndrome patients with nonsense mutations in the COL4 gene. Patients will be dosed for two months with a three month follow-up. In addition to the primary endpoint of safety, the key secondary efficacy endpoint of proteinuria will be measured every two weeks. For eligible patients, induction of COL IV will also be measured at the end of two months. Topline results are expected in the first half of 2023.

We are also advancing ZKN-013, as an oral agent for the treatment of RDEB/JEB and FAP patients with nonsense mutations. RDEB and JEB are rare skin diseases characterized by mutations in Collagen VII (RDEB) and

LAMB3(JEB) proteins. We estimate that there are approximately 4,000 patients with nonsense mutations in these diseases in the major markets of the US, Japan and Western Europe. Patients suffer from severe skin bruising, wounds and internal lesions resulting in increased risk of skin cancer and severe malnourishment. FAP patients have mutations in the APC gene that result in a proliferation of polyps in the colon that if untreated can lead to colon and other related cancers. There are currently no approved disease modifying therapies for these diseases. ZKN-013 has demonstrated robust collagen VII restoration in patient cells comparable to 5-10% of protein restoration across a range of mutations. We have also seen in two separate studies, that treatment of APCMin mice, a validated model for evaluating potential treatment effects in FAP patients, with ZKN-013 for eight weeks reduced polyp number, polyp size and meaningfully improved survival. We submitted an IND for ZKN-013 on March 24, 2023 for the treatment of RDEB.

In September 2022, in consultation with the Cystic Fibrosis Foundation (“CFF”), we terminated the development of ELX-02 delivered subcutaneously, for the treatment of cystic fibrosis (“CF”) patients with at least one nonsense (“Class 1 CF”) mutations. This decision was made after our Phase 2 trial of ELX-02 in combination with ivacaftor, an approved drug currently marketed for the treatment of certain CF patients under the trade name “Kalydeco”, did not meet the secondary efficacy endpoint of reduction from baseline in sweat chloride concentration (SCC) or improvement from baseline in percent forced expiratory volume (FEV1). Encouragingly, we continued to see strong evidence of biological activity similar to that in our previously completed Phase 2 study that reported in November 2021 a reduction in sweat chloride concentration from baseline after one week of treatment with ELX-02. We believe that the lack of statistically significant clinical benefit in Class 1 CF patients was due to drug concentration in the lung tissue being significantly below that required for effect consistent with our preclinical studies. ELX-02 was well tolerated in the Phase 2 trial with no drug related adverse events even at the clinical dose of 1.5mg/kg. Going forward, we plan to only develop that ELX-02 as an inhaled therapy for Class 1 CF patients because the achievable drug concentrations are more than one-hundred times higher in the lung tissue than when given subcutaneously. We have completed the IND enabling studies for inhaled ELX-02 in Class 1 CF but further clinical development is contingent upon funding from the CFF.

Acquisition of Zikani Therapeutics, Inc.

On April 1, 2021, the Company acquired Zikani Therapeutics, Inc. (“Zikani” and such acquisition, the “Zikani Merger”), a company in preclinical development and engaged in the science of ribosome modulation, leveraging its innovative TURBO-ZM™ chemistry technology platform to develop novel RMAs as potential therapeutics for diseases with limited treatment options. The TURBO-ZM™ platform is designed to enable rapid synthesis of novel compounds that can be optimized to modulate the ribosome in a disease specific manner. The TURBO-ZM™ synthetic chemistry platform can design oral novel macrolide-based small molecules that are potent oral modulators with favorable therapeutic indices. Macrolides are antibiotics that inhibit protein synthesis in bacteria.

Under the terms of the Agreement and Plan of Merger, the Company issued 189,920 shares of common stock in exchange for all of the issued and outstanding equity interests of Zikani (the “Merger Consideration”). The Zikani Merger was accounted for as an asset acquisition with acquired in-process research and development which was immediately expensed.

Results of Operations

Comparison of the Years Ended December 31, 2022 and 2021

Dollar amounts in the following table are in thousands:

	Year ended December 31,		2022 / 2021	
	2022	2021	\$ Change	% Change
Operating expenses:				
Research and development	\$ 23,727	\$ 22,899	\$ 828	4 %
General and administrative	10,692	20,449	(9,757)	(48) %
In process research and development	–	22,670	(22,670)	(100) %
Total operating expenses	34,419	66,018	(31,599)	(48) %
Loss from operations	(34,419)	(66,018)	(31,599)	(48) %
Other expense, net	1,646	709	937	132 %
Net loss	<u>\$ (36,065)</u>	<u>\$ (66,727)</u>	<u>\$ (30,662)</u>	<u>(46) %</u>

Research and development expenses

Research and development expenses were \$23.7 million for the year ended December 31, 2022 compared to \$22.9 million for the year ended December 31, 2021, an increase of \$0.8 million. The increase was primarily related to a \$0.1 million increase in clinical trial expenses related primarily to Alport and CFF funded activities and a \$0.8 million increase in facility and research and development related overhead expenses, offset by a \$0.1 million decrease in expenses related to subcontractors, advisors, and lab supplies in connection with preclinical research and development activities.

General and administrative expenses

General and administrative expenses were \$10.7 million for the year ended December 31, 2022 compared to \$20.4 million for the year ended December 31, 2021, a decrease of \$9.8 million. The decrease was primarily related to a \$3.4 million decrease in salaries and other personnel related costs, offset by an increase of \$0.1 million in expenses attributable to professional and consulting fees as the Company reduced headcount and outsourced certain functions, a decrease of \$6.1 million in stock-based compensation expense due primarily to option modifications of former executives in 2021, and a \$0.4 million decrease in facility and other general and administrative overhead costs.

Acquired in-process research and development

Acquired in-process research and development ("IPR&D") expense of \$22.7 million for the year ended December 31, 2021 consists of the estimated fair value of the assets acquired and consideration given in connection with the acquisition of the Zikani' s IPR&D. As the assets acquired were in the research and development phase and were determined to not have any alternative future use, such assets were expensed as acquired IPR&D. There was no such expense for the year ended December 31, 2022.

Other expense (income), net

We recorded \$1.6 million in other expense, net, for the year ended December 31, 2022 compared to \$0.7 million for the year ended December 31, 2021, an increase of \$0.9 million. The increase in 2022 as compared to 2021 was primarily due to the Company recognizing an increase of \$0.7 million of interest expense due to the increased interest rate and debt principal offset by increased interest income of \$0.3 million and net Australian research and development tax credits of \$0.1 million. During 2021, the Company recognized a \$0.8 million gain on extinguishment of debt related to the forgiveness of the PPP Loan (defined below), offset by a \$0.3 million loss on extinguishment of debt related to the repayment of the amounts outstanding under our previous term loan from SVB in September 2021.

Liquidity, Capital Resources and Going Concern

Since our inception, we have incurred significant operating losses. Our net losses were \$(36.1) million and \$(66.7) million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of \$(274.4) million. To date, we have financed our operations primarily through equity capital investments, and to a lesser extent, from loans and grants. We have devoted substantially all of our financial resources and efforts to research and development. We expect that it may be several years, if ever, before we receive regulatory approval and have a product candidate ready for commercialization. We expect to continue to incur significant expenses and operating losses for the foreseeable future due to, among other things, costs related to research, development of our product candidates, conducting preclinical studies and clinical trials, and our administrative organization. A successful transition to profitable operations is dependent upon achieving a level of revenue adequate to support our cost structure. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses may increase if, and as, we:

- advance ELX-02 and/or other product candidates further into clinical development;
- experience additional delays in enrollment and completion of our clinical trials due to the COVID-19 pandemic or otherwise;
- continue the preclinical development of our research programs and advance candidates into clinical trials;
- pursue regulatory authorization to conduct clinical trials of additional product candidates;
- seek marketing approvals for our product candidates;
- establish a sales, marketing and distribution infrastructure to commercialize any product candidates for which we obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;

- hire additional clinical, regulatory, management and scientific personnel;
- add operational, financial and management information systems and personnel;
- acquire or in-license other product candidates and technologies; and
- operate as a public company including costs associated with maintaining Nasdaq compliance.

We may never achieve profitability, and unless and until we do, we will continue to need to raise additional cash to fund our operations. We believe that our cash and cash equivalents of \$19.2 million at December 31, 2022, is not sufficient to maintain our current and planned operations for at least the next twelve months following the filing of this Annual Report on Form 10-K. We will need to raise additional capital to finance our operations, which cannot be assured. We have concluded that these conditions, in aggregate, raise substantial doubt about our ability to continue as a going concern through one year after the date these consolidated financial statements are issued. Our independent registered public accounting firm, in its report on our consolidated financial statements for the year ended December 31, 2022, has also expressed substantial doubt about our ability to continue as a going concern. The financial statements included elsewhere in this Annual Report have been prepared assuming the Company will continue as a going concern and do not include any adjustments that might result from the outcome of this uncertainty.

In addition, as previously noted, we entered into a Loan and Security Agreement with Hercules for an aggregate principal amount of up to \$30.0 million of which \$12.5 million had been funded as of December 31, 2022. Of the remaining tranches, \$7.5 million was only available through August 15, 2022, and is no longer available to us, and \$10.0 million may be available until April 1, 2023 subject to approval by the Hercules' investment committee in its sole discretion. The term loan contains customary affirmative and negative covenants, which among others requires us to maintain at all times a minimum qualified cash balance equaling amounts ranging from \$6.3 million to \$10.0 million (\$10.0 million effective as of August 15, 2022 and as of December 31, 2022) plus qualified accounts payable. Subsequent to year end, on March 7, 2023, we amended the terms of the Loan and Security Agreement, whereby we repaid \$7.5 million of the outstanding principal and the minimum qualified cash balance requirement was reduced to \$2.25 million as of March 7, 2023. We will be required to make principal payments on the remaining \$5.0 million outstanding principal balance of the Term Loan Advances commencing on September 1, 2023, plus interest, with a final maturity date of April 1, 2025.

As previously noted, in March 2022, we entered into an agreement with the Cystic Fibrosis Foundation ("CFF") for an award of up to \$15.9 million to fund the ongoing global Phase 2 clinical development of ELX-02 in CF. We received an upfront payment of \$7.0 million in March 2022 and an additional milestone payment of \$1.5 million in September 2022. In September 2022, the CFF determined not to fund further development of the program and the remaining \$7.4 million of the award and all further development of ELX-02 delivered subcutaneously was terminated.

Management intends to fund future operations through private or public debt or equity financing transactions and may seek additional capital through arrangements with strategic partners or from other sources. The availability of sufficient funding to alleviate the conditions that raise substantial doubt are not within management' s control and cannot be assessed as being probable of occurring. If we are unable to obtain adequate financing, we will evaluate alternatives which may include curtailing expenses contemplated by our current operating plan, and we may be required to delay, limit, reduce or terminate our product development efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves, which may have a material adverse effect on our operations and future prospects.

Principal Financing Activities

Borrowing Activities

On September 30, 2021, we entered into a loan and security agreement (the "Hercules Term Loan Agreement") with Hercules Capital, Inc., ("Hercules" or the "Lender"), Hercules agreed to extend term loans (the "Hercules Term Loan") to the Company in an aggregate principal amount of up to \$30.0 million, comprised of three tranches, of which \$12.5 million had been funded as of December 31, 2022. Of the remaining tranches, \$7.5 million was only available through August 15, 2022, and is no longer available to the Company, and \$10.0 million may be available until April 1, 2023 subject to approval by the Hercules' investment committee in its sole discretion. We are required to pay interest only on the outstanding principal on a monthly basis for the first 18 months of the agreement, which may be extended for an additional 12 months upon the achievement of certain milestones. Any amounts outstanding under the term loan advances, if not repaid sooner, are due and payable on April 1, 2025. On

any date that we partially repay the outstanding obligations, the Company shall pay the Lenders a charge equal to 6.55% of the original principal amount.

The Hercules Term Loan Agreement contains customary affirmative and negative covenants, which among others requires us to maintain at all times a minimum qualified cash balance ranging from \$6.3 million to \$10.0 million (\$10.0 million effective as of August 15, 2022 and as of December 31, 2022) plus qualified accounts payable. As of December 31, 2022 we were in compliance with all debt covenants, however, the inherent uncertainties described above may impact our ability to remain in compliance with these covenants over the next twelve months. If we breach our financial covenants and fail to secure a waiver or forbearance from the third-party lender, such breach or failure could accelerate the repayment of the outstanding borrowings under the Hercules Term Loan or the exercise of other rights or remedies the third-party lender may have under applicable law. No assurance can be provided that a waiver or forbearance will be granted or that the outstanding borrowings under the Hercules Term Loan, will be successfully refinanced on terms that are acceptable to the Company.

On March 7, 2023, we entered into an amendment to the Hercules Term Loan Agreement. As a condition to entering into the amendment, we repaid \$7.5 million of the outstanding principal (without incurring a prepayment premium), reducing the remaining outstanding Term Loan Advances to \$5.0 million. We will be required to make principal payments on the remaining \$5.0 million outstanding principal balance of the Term Loan Advances commencing on September 1, 2023, plus interest, with a final maturity date of April 1, 2025. Additionally, the debt covenant that required us to maintain at all times a minimum qualified cash balance equaling amounts ranging from \$6.3 million to \$10.0 million (\$10.0 million as of December 31, 2022) plus qualified accounts payable, was decreased to \$2.25 million as of March 7, 2023, and may be further reduced to \$0 if the Company has raised at least \$20.0 million in equity investments on or prior to May 31, 2023.

In March 2022, we entered into an agreement with the CFF, amending our prior funding award with CFF, for an award of up to \$15.9 million to fund the ongoing global Phase 2 clinical development of ELX-02 in CF. We received an upfront payment of \$7.0 million in March 2022 and an additional milestone payment of \$1.5 million in September 2022. In September 2022, the CFF determined not to continue funding the program and the remaining \$7.4 million of the award will not be available to the Company under the current agreement. Upon the successful commercialization of ELX-02 delivered subcutaneously for the treatment of CF, we will pay the CFF sales milestones and royalties based on future sales tiered on the actual level of funding from the CFF. As of December 31, 2022, we were eligible to receive up to \$2.1 million in funding from the CFF related to the 2021 Agreement.

On January 30, 2019, we entered into a Loan and Security Agreement (the "Loan Agreement") with Silicon Valley Bank ("SVB"), and WestRiver Innovation Lending Fund VIII, L.P. (together with SVB, the "Lenders"). Pursuant to the terms and conditions of the Loan Agreement, the Lenders extended a term loan to us of \$15.0 million. We commenced making payments on the outstanding principal balance of the loan on February 1, 2020, which was payable in 36 equal monthly installments. Amounts outstanding under the loan were due and payable on January 1, 2023. On September 30, 2021, in connection with the funding of the Hercules Term Loan Tranche 1 Advance, the Company voluntarily repaid in full the carrying value of the outstanding loan consisting of \$6.7 million of principal, a final maturity payment of \$0.9 million, and early termination fees of \$0.1 million from funds received under the Hercules Loan Agreement. The debt issuance costs, the valuation of the warrants, and the final maturity payment of \$0.9 million, had been recorded as a debt discount which were being accreted to interest expense through the maturity date of the loan. The remaining unamortized debt discount of \$0.2 million and early termination fees were accounted for as a loss on debt extinguishment and included in other income and expense in the statement of operations for the year ended December 31, 2021.

In April 2020, we entered into a loan agreement with SVB under the U.S. Small Business Administration (the "SBA") Paycheck Protection Program (the "PPP") pursuant to the Coronavirus Aid, Relief and Economic Security Act of 2020 (the "CARES Act") and received loan proceeds of \$0.8 million (the "PPP Loan"). We used the loan proceeds for payroll and other covered costs in accordance with the relevant terms and conditions of the CARES Act. The PPP Loan has an interest rate of 1.0% per annum. Under the terms of the PPP, on September 3, 2021, the PPP Loan was forgiven in full and the Company recognized a gain on extinguishment of debt of \$0.8 million during the year ended December 31, 2021.

Equity Financings

On September 30, 2021, we entered into a Sales Agreement with SVB Leerink, LLC ("SVB Leerink") pursuant to which the Company may offer and sell up to \$50.0 million of shares of its common stock (the "ATM Shares") from time to time, through an "at the market offering" program (the "ATM Program"), under which SVB Leerink will act as sales agent. Pursuant to the Sales Agreement, the Company will set the parameters for the sale of

ATM Shares, including the number of ATM Shares to be issued, the time period during which sales are requested to be made, limitations on the number of ATM Shares that may be sold in any one trading day and any minimum price below which sales may not be made. The Company is not obligated to make any sales of Shares under the ATM Program. The Company had not sold any shares under the ATM Program as of December 31, 2022.

On May 13, 2021, we completed an underwritten public offering of 958,333 shares of common stock at a price of \$54.00 per share and received gross proceeds of approximately \$51.8 million, before deducting underwriting discounts and commissions of \$3.1 million and offering expenses of \$0.8 million.

Government Grants from the Israeli Innovation Authority ("IIA")

To date, we have received research and development grants from the IIA totaling \$2.6 million. We did not receive any grants for the years ended December 31, 2022 or 2021.

Under the research and development agreements with the IIA and pursuant to applicable law, we are required to pay royalties at the rate of 3% on sales to end customers of product candidates developed with funds provided by the IIA, up to an amount equal to 100% of the IIA research and development grants received, plus interest based on the 12-month LIBOR rate. If we do not generate sales of product candidates developed with funds provided by the IIA, we are not obligated to pay royalties or repay the grants.

As of December 31, 2022, we have not commenced the payment obligation of the royalties and have a contingent obligation with respect to royalty-bearing participation received or accrued, amounting to \$2.8 million, including accrued LIBOR interest.

Cash Flows

The following table summarizes our sources and uses of cash for each of the periods presented (in thousands):

	Year ended December 31,	
	2022	2021
Net cash used in operating activities	\$ (31,845)	\$ (35,001)
Net cash (used in) provided by investing activities	\$ (66)	\$ 2,056
Net cash provided by financing activities	\$ 8,812	\$ 50,788

Our operating activities used cash of \$31.8 million and \$35 million for the years ended December 31, 2022 and 2021, respectively. Cash used in operations resulted primarily from our net losses adjusted for non-cash items and changes in working capital. During the year ended December 31, 2022, our net loss was \$36.1 million, partially offset by non-cash charges primarily related to \$3.0 million related to stock-based compensation expense, \$0.1 million of depreciation expense, \$0.6 million of amortization of lease assets, and \$0.5 million of debt discount amortization. During the year ended December 31, 2021, our net loss was \$66.7 million, partially offset by non-cash charges primarily related to \$22.7 million of acquired in-process research and development from the Zikani Merger, \$9.2 million related to stock-based compensation expense, \$0.1 million of depreciation expense, \$0.8 million of amortization of lease assets, and \$0.4 million of debt discount amortization.

Cash provided by investing activities during the year ended December 31, 2021, was primarily related to \$2.1 million of cash acquired as part of the Zikani Merger. There were no material investing activities during the year ended December 31, 2022 other than purchase of equipment for less than \$0.1 million.

Our financing activities provided cash of \$8.8 million and \$50.8 million for the years ended December 31, 2022 and 2021, respectively. For the year ended December 31, 2022, net cash provided by financing activities consisted primarily of \$8.8 million in advances received from collaboration partners. For the year ended December 31, 2021, net cash provided by financing activities consisted primarily of net proceeds of \$47.7 million from our public offering of common stock in May 2021, \$2.9 million in advances received from collaboration partners, \$11.9 million of net cash received from the Hercules term loan, offset by \$11.3 million in SVB term loan principal and repayments and final loan payment, and \$0.3 million related to the settlement of taxes upon vesting of restricted stock units.

Critical Accounting Policies and Significant Judgments and Estimates

Our discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements and the notes thereto included elsewhere in this Annual Report, which have been prepared in accordance with accounting principles generally accepted in the United States ("U.S. GAAP"). The preparation of

these annual consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the expenses during the reporting period. We evaluate our estimates and judgments on an ongoing basis. These items are monitored and analyzed by us for changes in facts and circumstances, and material changes in these estimates could occur in the future. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 2 of the Notes to Consolidated Financial Statements appearing elsewhere in this Annual Report, we believe that the following accounting policies related to accrued expenses and accrued clinical trial costs and contract research liabilities are the most critical accounting policies for fully understanding and evaluating our financial condition and results of operations.

Accrued Expenses and Accrued Clinical Trial Costs and Contract Research Liabilities

As part of the process of preparing our financial statements, we are required to estimate accrued expenses. This process involves identifying services which have been performed on our behalf and estimating the level of service performed and the associated cost incurred for such service as of each balance sheet date in our financial statements. Given our current business, the primary area of uncertainty concerning accruals which could have a material effect on our operating results is with respect to service fees paid to contract manufacturers in conjunction with the production of clinical drug supplies, and to contract research organizations in connection with our pre-clinical research and clinical trials. In connection with all of the foregoing service fees, our estimates are most affected by our understanding of the status and timing of services provided. The majority of our service providers, including contract research organizations, invoice us in arrears for services performed. In the event that we do not identify some costs which have begun to be incurred, or we underestimate or overestimate the level of services performed or the costs of such services in a given period, our reported expenses for such period would be understated or overstated. We currently reflect the effects of any changes in estimates based on changes in facts and circumstances directly in our statement of operations in the period such change becomes known.

Our arrangements with contract research organizations in connection with clinical trials often provide for payment prior to commencing the project or based upon predetermined milestones throughout the period during which services are expected to be performed. We recognize expense relating to these arrangements based on the various services provided over the estimated time to completion. The date on which services commence, the level of services performed on or before a given date, and the cost of such services are often determined based on subjective judgments. We make these judgments based upon the facts and circumstances known to us based on the terms of the contract and our ongoing monitoring of service performance. During the years ended December 31, 2022 and 2021, we had arrangements with multiple contract research organizations whereby these organizations commit to performing services for us over multiple reporting periods. We recognize the expenses associated with these arrangements based on our expectation of the timing of the performance of components under these arrangements by these organizations. Generally, these components consist of the costs of setting up the trial, monitoring the trial, closing the trial and preparing the resulting data. Costs related to patient enrollment in clinical trials are accrued as patients are enrolled in the trial.

With respect to financial reporting periods presented in this Annual Report, the timing of our actual costs incurred have not differed materially from our estimated timing of such costs. In light of the foregoing, we do not believe our practices for estimating future expenses and making judgments concerning the accrual of expenses are reasonably likely to change in the future.

Off-Balance Sheet Arrangements

As of December 31, 2022 and 2021, we did not have any off-balance sheet arrangements, as such term is defined under Item 303 of Regulation S-K, that have or are reasonably likely to have a current or future effect on our financial condition, changes in financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources that is material to investors.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURE ABOUT MARKET RISK

Not required pursuant to the scaled disclosure requirements available to smaller reporting companies, as defined in Item 10(f)(1) of Regulation S-K

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The consolidated financial statements and supplementary data required by this Item are set forth indicated in Item 15 of this Annual Report and are incorporated by reference into this Item.

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

The information required by this Item was previously provided in and is hereby incorporated under this Item by reference to the Company's Current Report on [Form 8-K filed with the SEC on July 15, 2022.](#)

ITEM 9A. CONTROLS AND PROCEDURES

Limitations on Effectiveness of Controls and Procedures

We maintain disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, to allow timely decisions regarding required disclosure.

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

Management's Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and interim Chief Financial Officer, evaluated, as of the end of the period covered by this Annual Report, the effectiveness of our disclosure controls and procedures. Based on that evaluation, our Chief Executive Officer and interim Chief Financial Officer concluded that our disclosure controls and procedures were effective at December 31, 2022 at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over our financial reporting, as such term is defined in Rule 13a-15(f) and 15d-15(f) under the Exchange Act. Because of its inherent limitations, internal controls 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. Our management, under the supervision and with the participation of our principal executive officer and principal financial officer, conducted an assessment of the effectiveness of our internal control over financial reporting as of December 31, 2022, based on the criteria set forth in "Internal Control - Integrated Framework (2013)" issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on this assessment, our management concluded that, as of December 31, 2022, our internal control over financial reporting was effective at the reasonable assurance level.

Attestation Report of the Registered Public Accounting Firm

This Annual Report does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting due to our status as a non-accelerated filer.

Changes in Internal Control over Financial Reporting

There were no changes in our internal controls over financial reporting (as defined in Rules 13a-15(f) and 15(d)-15(f) under the Exchange Act) during the quarter ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS.

Not Applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The following information with respect to our board of directors and executive officers is presented as of March 30, 2023:

Name	Age	Position at Eloxx Pharmaceuticals, Inc.	Principal Employment
Sumit Aggarwal	50	President and Chief Executive Officer and director	Same
Daniel E. Geffken	65	Interim Chief Financial Officer	Danforth Advisors, Inc.
Vijay Modur	55	Head of Research and Development	Same
Tomer Kariv	62	Chairman of the Board of Directors	Chief Executive Officer and Co-Founder of The Pontifax Group
Lindsay Androski, JD, MBA	51	Director	Founder, President and CEO of Roivant Social Ventures
Steven Rubin	62	Director	Executive Vice President – Administration of OPKO Health, Inc.
Alan Walts, Ph.D.	63	Director	US-based Venture Partner with Advent Life Sciences

Other information required by this Item 10 is incorporated by reference to our definitive proxy statement for our 2023 Annual Meeting of Stockholders to be filed within 120 days after the end of the fiscal year covered by this Annual Report.

ITEM 11. EXECUTIVE AND DIRECTOR COMPENSATION

The information required by this Item 11 will be included in our definitive proxy statement for our 2023 Annual Meeting of Stockholders to be filed within 120 days after the end of the fiscal year covered by this Annual Report.

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

The information required by this Item 12 will be included in our definitive proxy statement for our 2023 Annual Meeting of Stockholders to be filed within 120 days after the end of the fiscal year covered by this Annual Report.

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

The information required by this Item 13 will be included in our definitive proxy statement for our 2023 Annual Meeting of Stockholders to be filed within 120 days after the end of the fiscal year covered by this Annual Report.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this Item 14 will be included in our definitive proxy statement for our 2023 Annual Meeting of Stockholders to be filed within 120 days after the end of the fiscal year covered by this Annual Report.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

Item 15(a)

(1) Financial Statements

The financial statements required by this item are submitted in a separate section beginning on page F-1 of this Annual Report.

(2) Financial Statement Schedules

Schedules have been omitted because of the absence of conditions under which they are required or because the required information is included in the financial statements or notes thereto beginning on page F-1 of this Annual Report.

(3) Exhibits:

The exhibits listed in the Exhibit Index at the end of this Annual Report are filed or incorporated by reference as part of this Annual Report.

Item 15(b) Exhibits

See (a)(3) above.

Item 15(c) Financial Statement Schedules

See (a)(2) above.

ITEM 16. FORM 10-K SUMMARY

Not applicable.

EXHIBIT INDEX

Exhibit No.	Description of Exhibit
2.1◇	<u>Agreement and Plan of Merger, dated April 1, 2021, by and among Eloxx Pharmaceuticals, Inc., Delta Merger Sub Acquisition Corporation and Zikani Therapeutics, Inc. (incorporated by reference to Exhibit 2.1 of our Current Report on Form 8-K filed on April 1, 2021, SEC File No. 001-31326).</u>
3.1	<u>Amended and Restated Certificate of Incorporation of Senesco Technologies, Inc. filed with the State of Delaware on January 22, 2007. (incorporated by reference to Exhibit 3.1 of our Quarterly Report on Form 10-Q filed on February 14, 2007, SEC File No. 001-31326).</u>
3.2	<u>Certificate of Amendment to the Amended and Restated Certificate of Incorporation of Senesco Technologies, Inc. filed with the State of Delaware on December 13, 2007. (incorporated by reference to Exhibit 3.1 of our Quarterly Report on Form 10-Q filed on February 14, 2008, SEC File No. 001-31326).</u>
3.3	<u>Certificate of Amendment to the Amended and Restated Certificate of Incorporation of Senesco Technologies, Inc. filed with the State of Delaware on September 22, 2009. (incorporated by reference to Exhibit 3.3 of our Annual Report on Form 10-K filed on September 28, 2009, SEC File No. 001-31326).</u>
3.4	<u>Certificate of Amendment to the Amended and Restated Certificate of Incorporation of Senesco Technologies, Inc. filed with the State of Delaware on May 25, 2010. (incorporated by reference to Exhibit 3.1 to our Current Report on Form 8-K filed on May 28, 2010, SEC File No. 001-31326).</u>
3.5	<u>Certificate of Amendment to the Amended and Restated Certificate of Incorporation of Senesco Technologies, Inc. filed with the State of Delaware on December 22, 2011. (incorporated by reference to Exhibit 3.1 to our Quarterly Report on Form 10-Q filed on February 14, 2011, SEC File No. 001-31326).</u>
3.6	<u>Certificate of Amendment to the Amended and Restated Certificate of Incorporation of Senesco Technologies, Inc. filed with the State of Delaware on April 1, 2013. (incorporated by reference to Exhibit 3.1 to our Quarterly Report on Form 10-Q filed on May 15, 2013, SEC File No. 001-31326).</u>
3.7	<u>Certificate of Amendment to the Company' s Amended and Restated Certificate of Incorporation, as filed with the Secretary of State of the State of Delaware on October 16, 2013. (incorporated by reference to Exhibit 3.1 of our Current Report on Form 8-K filed on October 21, 2013, SEC File No. 001-31326).</u>
3.8	<u>Certificate of Amendment to the Company' s Amended and Restated Certificate of Incorporation, as filed with the Secretary of State of the State of Delaware on September 29, 2014. (incorporated by reference to Exhibit 3.1 of our Current Report on Form 8-K filed on October 3, 2014, SEC File No. 001-31326).</u>
3.9	<u>Certificate of Amendment to the Company' s Amended and Restated Certificate of Incorporation, as filed with the Secretary of State of the State of Delaware on December 19, 2017. (incorporated by reference to Exhibit 3.1 of our Current Report on Form 8-K filed on December 22, 2017, SEC File No. 001-31326).</u>
3.10	<u>Certificate of Amendment to the Company' s Amended and Restated Certificate of Incorporation, as filed with the Secretary of State of the State of Delaware on December 19, 2017. (incorporated by reference to Exhibit 3.2 of our Current Report on Form 8-K filed on December 22, 2017, SEC File No. 001-31326).</u>
3.11	<u>Certificate of Designations to the Company' s Certificate of Incorporation. (Series A) (incorporated by reference to Exhibit 3.1 to our Current Report on Form 8-K filed on March 29, 2010, SEC File No. 001-31326).</u>

Exhibit No.	Description of Exhibit
3.12	<u>Certificate of Designations to the Company' s Certificate of Incorporation. (0% Series C Convertible Preferred Stock) (incorporated by reference to Exhibit 3.1 of our Current Report on Form 8-K filed on May 6, 2015, SEC File No. 001-31326).</u>
3.13	<u>Certificate of Amendment to Amended and Restated Certificate of Incorporation of Eloxx Pharmaceuticals, Inc., as filed with the Secretary of State of the State of Delaware on December 1, 2022[A1] (incorporated by reference to Exhibit 3.12of the Company' s Current Report on Form 8-K filed on December 1, 2022, SEC File No. 001-31326).</u>
3.14	<u>Amended and Restated Bylaws of Eloxx Pharmaceuticals, Inc. (incorporated by reference to Exhibit 3.2 of the Company' s Current Report on Form 8-K filed on December 27, 2017, SEC File No. 001-31326).</u>
4.1	<u>Specimen of Common Stock Certificate (incorporated by reference to Exhibit 4.1 of our Annual Report on Form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>
4.2	<u>Description of Registered Securities.</u>
10.1 ‡	<u>Research and License Agreement by and between Technion Research and Development Foundation Ltd. and Eloxx Pharmaceuticals Ltd., dated August 29, 2013 (incorporated by reference to Exhibit 10.1 of our Annual Report on Form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>
10.2 ‡	<u>First Amendment to Research and License Agreement by and between Technion Research and Development Foundation Ltd. and Eloxx Pharmaceuticals Ltd., dated November 26, 2013 (incorporated by reference to Exhibit 10.2 of our Annual Report on form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>
10.3	<u>Second Amendment to Research and License Agreement by and between Technion Research and Development Foundation Ltd. and Eloxx Pharmaceuticals Ltd., dated January 14, 2014 (incorporated by reference to Exhibit 10.3 of our Annual Report on form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>
10.4	<u>Third Amendment to Research and License Agreement by and between Technion Research and Development Foundation Ltd. and Eloxx Pharmaceuticals Ltd., dated June 9, 2014 (incorporated by reference to Exhibit 10.4 of our Annual Report on form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>
10.5	<u>First Addendum to Research and License Agreement by and between Technion Research and Development Foundation Ltd. and Eloxx Pharmaceuticals Ltd., dated August 3, 2014 (incorporated by reference to Exhibit 10.5 of our Annual Report on form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>
10.6	<u>Second Addendum to Research and License Agreement by and between Technion Research and Development Foundation Ltd. and Eloxx Pharmaceuticals Ltd., dated January 21, 2015 (incorporated by reference to Exhibit 10.6 of our Annual Report on form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>
10.7	<u>Third Addendum to Research and License Agreement by and between Technion Research and Development Foundation Ltd. and Eloxx Pharmaceuticals Ltd., dated February 9, 2015 (incorporated by reference to Exhibit 10.7 of our Annual Report on form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>
10.8	<u>Fourth Addendum to Research and License Agreement by and between Technion Research and Development Foundation Ltd. and Eloxx Pharmaceuticals Ltd., dated April 29, 2015 (incorporated by reference to Exhibit 10.8 of our Annual Report on form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>
10.9	<u>Fifth Addendum to Research and License Agreement by and between Technion Research and Development Foundation Ltd. and Eloxx Pharmaceuticals Ltd., dated June 2, 2015 (incorporated by reference to Exhibit 10.9 of our Annual Report on form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>

Exhibit No.	Description of Exhibit
10.10	<u>Sixth Addendum to Research and License Agreement by and between Technion Research and Development Foundation Ltd. and Eloxx Pharmaceuticals Ltd., dated January 11, 2016 (incorporated by reference to Exhibit 10.10 of our Annual Report on form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>
10.11	<u>Seventh Addendum to Research and License Agreement by and between Technion Research and Development Foundation Ltd. and Eloxx Pharmaceuticals Ltd., dated March 6, 2016 (incorporated by reference to Exhibit 10.11 of our Annual Report on form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>
10.12	<u>Eighth Addendum to Research and License Agreement by and between Technion Research and Development Foundation Ltd. and Eloxx Pharmaceuticals Ltd., dated July 16, 2017 (incorporated by reference to Exhibit 10.12 of our Annual Report on form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>
10.13	<u>Ninth Addendum to Research and License Agreement by and between Technion Research and Development Foundation Ltd. and Eloxx Pharmaceuticals Ltd., dated July 16, 2017 (incorporated by reference to Exhibit 10.13 of our Annual Report on form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>
10.14	<u>Amendment to Research and License Agreement, by and among Eloxx Pharmaceuticals, Inc., Eloxx Pharmaceuticals Ltd. and Technion Research & Development Foundation Ltd., dated as of June 13, 2018 (incorporated by reference to Exhibit 10.1 of our Current Report on Form 8-K filed on June 14, 2018, SEC File No. 001-31326).</u>
10.15 #	<u>Consulting Agreement, dated December 1, 2014, by and between Eloxx Pharmaceuticals Ltd. and Dr. Silvia Noiman (incorporated by reference to Exhibit 10.1 of our Current Report on Form 8-K filed on December 22, 2017, SEC File No. 001-31326).</u>
10.16 #	<u>Memorandum of Understanding, dated March 13, 2018, by and between Eloxx Pharmaceuticals, Inc. and Dr. Silvia Noiman (incorporated by reference to Exhibit 10.15 of our Quarterly Report on Form 10-Q filed on May 10, 2018, SEC File No. 001-31326).</u>
10.17 #	<u>Employment Agreement, dated as of December 26, 2017, between Eloxx Pharmaceuticals, Inc. and Robert E. Ward (incorporated by reference to our Current Report on Form 8-K filed on December 27, 2017, SEC File No. 001-31326).</u>
10.18 #	<u>Employment Agreement, dated as of March 12, 2018, between Eloxx Pharmaceuticals Inc. and Gregory Weaver (incorporated by reference to Exhibit 10.19 of our Annual Report on Form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>
10.19 #	<u>Form of Indemnification Agreement (incorporated by reference to Exhibit 10.4 of our Current Report on Form 8-K filed on December 22, 2017, SEC File No. 001-31326).</u>
10.20 #	<u>Amended and Restated Senesco Technologies, Inc. 2008 Incentive Compensation Plan. (incorporated by reference to Exhibit 10.3 of our Quarterly Report on Form 10-Q for the period ended March 31, 2014, SEC File No. 001-31326)</u>
10.21 #	<u>Form of Stock Option Agreement under the Senesco Technologies, Inc. 2008 Stock Incentive Plan. (incorporated by reference to Exhibit 10.5 of our Quarterly Report on Form 10-Q for the period ended September 30, 2009, SEC File No. 001-31326).</u>
10.22 #	<u>Eloxx Pharmaceuticals Share Ownership and Option Plan (2013) (incorporated by reference to Exhibit 10.24 of our Annual Report on Form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>
10.23 #	<u>Forms of Option Agreement, Stock Option Grant Notice and Notice of Exercise under the Eloxx Pharmaceuticals Share Ownership and Option Plan (2013) (incorporated by reference to Exhibit 10.25 of our Annual Report on Form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>
10.24 #	<u>Performance Stock Option Grant Notice and Stock Option Agreement (Inducement Grant) between Eloxx Pharmaceuticals, Inc. and Robert E. Ward, dated March 5, 2018 (incorporated by reference to Exhibit 10.25 of our Annual Report on Form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>

Exhibit No.	Description of Exhibit
10.25	<u>Restricted Stock Unit Grant Notice and Restricted Stock Unit Agreement (Inducement Grant) between Eloxx Pharmaceuticals, Inc. and Robert E. Ward, dated March 5, 2018 (incorporated by reference to Exhibit 10.25 of our Annual Report on Form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>
10.26 #	<u>Performance Restricted Stock Unit Grant Notice and Restricted Stock Unit Agreement (Inducement Grant) between Eloxx Pharmaceuticals, Inc. and Robert E. Ward, dated March 5, 2018 (incorporated by reference to Exhibit 10.25 of our Annual Report on Form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>
10.27 #	<u>Stock Option Grant Notice and Stock Option Agreement (Inducement Grant) between Eloxx Pharmaceuticals, Inc. and Robert E. Ward, dated March 5, 2018 (incorporated by reference to Exhibit 10.25 of our Annual Report on Form 10-K filed on March 16, 2018, SEC File No. 001-31326).</u>
10.28 #	<u>Retention Policy (incorporated by reference to Exhibit 10.1 of our Current Report on Form 8-K filed on October 15, 2012, SEC File No. 001-31326).</u>
10.29 #	<u>Eloxx Pharmaceuticals, Inc. 2018 Equity Incentive Plan (incorporated by reference to Exhibit 10.1 of our Current Report on Form 8-K filed on March 30, 2018, SEC File No. 001-31326).</u>
10.30 #	<u>Form of Stock Option Grant Notice, Option Agreement and Notice of Exercise under the Eloxx Pharmaceuticals, Inc. 2018 Equity Incentive Plan (incorporated by reference to Exhibit 10.2 of our Current Report on Form 8-K filed on March 30, 2018, SEC File No. 001-31326).</u>
10.31 #	<u>Form of Restricted Stock Unit Grant Notice for non-Israeli employees (incorporated by reference to Exhibit 99.5 of our Registration Statement on Form S-3 filed on May 11, 2018, SEC File No. 333-224860).</u>
10.32 #	<u>Israeli Sub-Plan under the Eloxx Pharmaceuticals, Inc. 2018 Equity Incentive Plan (incorporated by reference to Exhibit 10.3 of our Current Report on Form 8-K filed on March 30, 2018, SEC File No. 001-31326).</u>
10.33 #	<u>Form of Israeli Stock Option Grant Package under the Israeli Sub-Plan under the Eloxx Pharmaceuticals, Inc. 2018 Equity Incentive Plan (incorporated by reference to Exhibit 10.4 of our Current Report on Form 8-K filed on March 30, 2018, SEC File No. 001-31326).</u>
10.34 #	<u>Form of Restricted Stock Unit Grant Notice for Israeli employees (incorporated by reference to Exhibit 10.6 of our Quarterly Report on Form 10-Q filed on August 10, 2018, SEC File No. 001-31326).</u>
10.35	<u>Loan and Security Agreement, dated as of September 30, 2021, by and among Hercules Capital, Inc., the Company, Zikani Therapeutics, Inc. and the other parties thereto. (incorporated by reference to Exhibit 10.1 of our Quarterly Report on Form 10-Q filed on November 8, 2021, SEC File No. 001-31326).</u>
10.36	<u>First Amendment, dated March 7, 2023, to the Loan and Security Agreement, dated as of September 30, 2021, by and among Hercules Capital, Inc., the Company, Zikani Therapeutics, Inc. and the other parties thereto.</u>
10.37	<u>Change in Control Severance Benefit Plan, dated September 17, 2019 (incorporated by reference to Exhibit 10.1 of our Quarterly Report on Form 10-Q filed on November 6, 2019, SEC File No. 001-31326).</u>
10.38 #	<u>Executive Employment Agreement between Eloxx Pharmaceuticals, Inc. and Gregory C. Williams dated as of February 25, 2020 (incorporated by reference to Exhibit 10.42 of our Annual Report on Form 10-K filed on March 6, 2020, SEC File No. 001-31326).</u>
10.39 #	<u>Executive Employment Agreement between Eloxx Pharmaceuticals, Inc. and Neil Belloff dated as of February 25, 2020 (incorporated by reference to Exhibit 10.43 of our Annual Report on Form 10-K filed on March 6, 2020, SEC File No. 001-31326).</u>

Exhibit No.	Description of Exhibit
10.40	<u>Employment offer letter between Eloxx Pharmaceuticals, Inc. and Stephen G. MacDonald dated as of September 24, 2019 (incorporated by reference to Exhibit 10.44 of our Annual Report on Form 10-K filed on March 6, 2020, SEC File No. 001-31326).</u>
10.41	<u>Employment Agreement, dated as of April 1, 2021, by and between Sumit Aggarwal and Eloxx Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.1 of our Current Report on Form 8-K filed on April 1, 2021, SEC File No. 001-31326).</u>
10.42	<u>Employment Agreement, dated as of April 1, 2021, by and between Vijay Modur and Eloxx Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.4 of our Current Report on Form 8-K filed on April 1, 2021, SEC File No. 001-31326).</u>
10.43	<u>Lease agreement by and between Zikani Therapeutics, Inc. and ARE-480 Arsenal Street, LLC, dated July 28, 2015 (incorporated by reference to Exhibit 10.4 of our Quarterly Report on Form 10-Q filed on May 7, 2021, SEC File No. 001-31326).</u>
10.44	<u>Lease agreement by and between Zikani Therapeutics, Inc. and ARE-480 Arsenal Street, LLC, dated July 28, 2015(incorporated by reference to Exhibit 10.5 of our Quarterly Report on Form 10-Q filed on May 7, 2021, SEC File No. 001-31326).</u>
21.1*	<u>List of Subsidiaries of the Company.</u>
23.1*	<u>Consent of Baker Tilly, LLP, Independent Registered Public Accounting Firm.</u>
23.2*	<u>Consent of Deloitte & Touche LLP, Independent Registered Public Accounting Firm.</u>
31.1*	<u>Certification of the Company' s Chief Executive Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities and Exchange Act of 1934, as amended, pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</u>
31.2*	<u>Certification of the Company' s Principal Financial Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities and Exchange Act of 1934, as amended, pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</u>
32.1**	<u>Certification of the Company' s Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</u>
32.2**	<u>Certification of the Company' s Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</u>
101.INS	Inline XBRL Instance Document - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the XBRL document.
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Labels Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Link Document
104*	Cover Page Interactive Data File (embedded within the Inline XBRL document)

* Filed herewith.

** Furnished herewith.

‡ Confidential treatment requested under 17 C.F.R. § 200.80(b)(4) and 24b-2. The confidential portions of this exhibit have been omitted and are marked accordingly. The confidential portions have been filed separately with the Securities and Exchange Commission pursuant to the confidential treatment request.

Indicates a management contract or compensatory plan or arrangement required to be filed pursuant to Item 15(b) of Form 10-K

◇ Schedules have been omitted pursuant to Item 601(b)(2) of Regulation S-K. Eloxx hereby agrees to furnish supplementally a copy of any of the omitted schedules upon request by the SEC.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities and 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.

ELOXX PHARMACEUTICALS, INC.

(Registrant)

Date: March 31, 2023

/s/ Sumit Aggarwal

Sumit Aggarwal

*President, Chief Executive Officer and Director
(On behalf of the Registrant and as Principal Executive Officer)*

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
<u>/s/ Sumit Aggarwal</u> Sumit Aggarwal	President, Chief Executive Officer and Director (Principal Executive Officer)	March 31, 2023
<u>/s/ Daniel E. Geffken</u> Daniel E. Geffken	Interim Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	March 31, 2023
<u>/s/ Tomer Kariv</u> Tomer Kariv	Chairman of the Board of Directors	March 31, 2023
<u>/s/ Lindsay Androski, JD</u> Lindsay Androski	Director	March 31, 2023
<u>/s/ Steven D. Rubin</u> Steven D. Rubin	Director	March 31, 2023
<u>/s/ Alan Walts</u> Alan Walts, Ph.D.	Director	March 31, 2023

ELOXX PHARMACEUTICALS, INC. AND SUBSIDIARIES
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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the stockholders and the Board of Directors of Eloxx Pharmaceuticals, Inc. and subsidiaries

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheet of Eloxx Pharmaceuticals, Inc. and subsidiaries. (the “Company”) as of December 31, 2022, and the related consolidated statements of operations, stockholders’ equity, and cash flows for the year then ended, and the related notes (collectively referred to as the “consolidated financial statements”). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022, and the results of its operations and its cash flows for the year then ended, in conformity with accounting principles generally accepted in the United States of America.

The financial statements of the Company for the year ended December 31, 2021, before the effects of the retrospective adjustments to apply the change in presentation related to the reverse stock split discussed in Note 2 to the consolidated financial statements, were audited by other auditors whose report, dated March 30, 2022, expressed an unqualified opinion on those statements. We have also audited the adjustments to the 2021 financial statements to retrospectively apply the change in presentation for the reverse stock split, as discussed in Note 2 to the consolidated financial statements. In our opinion, such retrospective adjustments are appropriate and have been properly applied. However, we were not engaged to audit, review, or apply any procedures to the 2021 consolidated financial statements of the Company other than with respect to the retrospective adjustments, and accordingly, we do not express an opinion or any other form of assurance on the 2021 consolidated financial statements as a whole.

Going Concern Uncertainty

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As described in Note 1 to the consolidated financial statements, the Company has a history of net losses and negative cash flows from operating activities and also has an accumulated deficit at December 31, 2022. The Company expects to continue to incur net losses and negative cash flows from its operations for the foreseeable future and needs additional working capital to support its operations and debt covenants for at least the next twelve months past the date the consolidated financial statements are issued. The inherent uncertainties described above may impact the Company’s ability to remain in compliance with debt covenants over the next twelve months. These matters raise substantial doubt about its ability to continue as a going concern. Management’s plans in regard to these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

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

Our audit 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 audit also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audit provides a reasonable basis for our opinion.

Critical Audit Matter

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 (1)

relates to accounts or disclosures that are material to the financial statements and (2) 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.

Accrued Research and Development Expenses – Clinical Trial Costs and Contract Research Liabilities

As described in Note 2 to the consolidated financial statements, the Company is required to estimate accrued clinical trial costs and contract research liabilities incurred for research and development expenses incurred in connection with its pre-clinical and clinical trials. The Company recognizes and measures these costs based on the date on which services commence and the level of services performed on or before December 31, 2022. The cost of such services are often determined based on subjective judgements and requires management to make certain estimates to the progress of completion.

We identified the accounting for the accrued research and development expenses, specifically clinical trial costs and contract research liabilities related to contract research organizations as a critical audit matter. This includes both the evaluation of the various significant estimates and assumptions management makes to measure these accrued liabilities. This evaluation required a high amount of auditor judgement and an increased extent of effort when performing audit procedures to evaluate the reasonableness of management's methods of data collection, including the identification of services provided by contract research organizations, and assumptions underlying the accrued clinical trial costs and contract research liabilities.

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, among others:

- Obtaining an understanding and evaluating the design and implementation of the Company's controls over accrued clinical trial costs and contract research liabilities.
- Evaluating management's assessment of the level of services performed by clinical research organizations by obtaining corroborating evidence related to the percentage of completion of individual projects and comparing the estimates to management's clinical research progress reports, research milestone specifications and contract research agreements.
- Evaluating the reasonableness of management's method for identification of services provided by contract research organizations and the development of assumptions for estimating accrued clinical trial costs and contract research liabilities by
 - o inspecting third-party documents such as service contracts, status reports, and other correspondence,
 - o testing the mathematical accuracy of the analysis used to create the accrual,
 - o testing the completeness and accuracy of the underlying data used in the analysis.

/s/ Baker Tilly US, LLP

We have served as the Company's auditor since 2022.

Tewksbury, Massachusetts
March 31, 2023

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the stockholders and the Board of Directors of Eloxx Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited, before the effects of the retrospective adjustments related to the reverse stock split discussed in Note 2 to the consolidated financial statements, the consolidated balance sheet of Eloxx Pharmaceuticals, Inc. and subsidiaries (the "Company") as of December 31, 2021, the related consolidated statements of operations and comprehensive loss, stockholder's equity, and cash flows, for the year ended December 31, 2021, and the related notes (collectively referred to as the "financial statements") (the 2021 financial statements before the effects of the retrospective adjustments related to the reverse stock split discussed in Note 2 to the financial statements are not presented herein). In our opinion, before the effects of the retrospective adjustments related to the reverse stock split discussed in Note 2 to the financial statements, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021, and the results of its operations and its cash flows for the year ended December 31, 2021, in conformity with accounting principles generally accepted in the United States of America.

We were not engaged to audit, review, or apply any procedures to the retrospective adjustments related to the reverse stock split discussed in Note 2 to the financial statements, and accordingly, we do not express an opinion or any other form of assurance about whether such retrospective adjustments are appropriate and have been properly applied. Those retrospective adjustments were audited by other auditors.

Basis for Opinion

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

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

Going Concern

The 2021 financial statements were prepared assuming that the Company would continue as a going concern. As of December 31, 2021, the Company had incurred recurring losses from operations and was at risk of being unable to remain in compliance with certain financial covenants required by its term loan, which raised substantial doubt about its ability to continue as a going concern. The 2021 financial statements did not include any adjustments that might result from the outcome of this uncertainty.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 30, 2022

We have served as the Company's auditor since 2018. In 2022 we became the predecessor auditor.

ELOXX PHARMACEUTICALS, INC. AND SUBSIDIARIES

CONSOLIDATED BALANCE SHEETS
(Amounts in thousands, except share and per share data)

	December 31,	
	2022	2021
Assets		
Current assets:		
Cash and cash equivalents	\$ 19,207	\$ 42,268
Restricted cash	261	299
Prepaid expenses and other current assets	661	913
Total current assets	20,129	43,480
Property and equipment, net	169	216
Operating lease right-of-use asset	825	1,443
Total assets	\$ 21,123	\$ 45,139
Liabilities and Stockholders' (Deficit) Equity		
Current liabilities:		
Accounts payable	\$ 3,020	\$ 1,379
Accrued expenses	2,799	4,196
Current portion of long-term debt	3,980	-
Advances from collaboration partners	12,535	3,723
Current portion of operating lease liability	712	657
Derivative liabilities	45	-
Total current liabilities	23,091	9,955
Long-term debt	8,557	11,996
Operating lease liability	135	804
Total liabilities	31,783	22,755
Commitments and contingencies		
Stockholders' (deficit) equity:		
Preferred stock, \$0.01 par value per share, 5,000,000 shares authorized, no shares issued or outstanding as of December 31, 2022 and 2021	—	—
Common stock, \$0.01 par value per share, 500,000,000 shares authorized, 2,166,356 and 2,176,783 shares issued, and 2,166,356 and 2,166,248 shares outstanding as of December 31, 2022 and 2021, respectively	22	22
Common stock in treasury, at cost, 0 and 10,535 shares as of December 31, 2022 and 2021, respectively	-	(2,190)
Additional paid-in capital	263,706	262,875
Accumulated deficit	(274,388)	(238,323)
Total stockholders' (deficit) equity	(10,660)	22,384
Total liabilities and stockholders' (deficit) equity	\$ 21,123	\$ 45,139

See accompanying notes to consolidated financial statements

ELOXX PHARMACEUTICALS, INC. AND SUBSIDIARIES**CONSOLIDATED STATEMENTS OF OPERATIONS**
(Amounts in thousands, except share and per share data)

	Year ended December 31,	
	2022	2021
Operating expenses:		
Research and development	\$ 23,727	\$ 22,899
General and administrative	10,692	20,449
In process research and development	—	22,670
Total operating expenses	34,419	66,018
Loss from operations	(34,419)	(66,018)
Other expense, net	1,646	709
Net loss	<u>\$ (36,065)</u>	<u>\$ (66,727)</u>
Net loss per share, basic and diluted	<u>\$ (16.65)</u>	<u>\$ (38.15)</u>
Weighted average number of shares of common stock used in computing net loss per share, basic and diluted	<u>2,166,311</u>	<u>1,749,071</u>

See accompanying notes to consolidated financial statements

ELOXX PHARMACEUTICALS, INC. AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' (DEFICIT) EQUITY
(Amounts in thousands, except share data)

	<u>Common Stock</u>			<u>Treasury Stock</u>		<u>Accumulat ed deficit</u>	<u>Total stockhold ers' (deficit) equity</u>
	<u>Shares</u>	<u>Amou nt</u>	<u>Additional paid-in capital</u>	<u>Shares</u>	<u>Amount</u>		
Balance as of December 31, 2020	1,003,930	\$ 10	\$ 183,644	(4,844)	\$ (1,828)	\$ (171,596)	\$ 10,230
Exercise of stock options	587	—	23	—	—	—	23
Vesting of restricted stock units	13,478	—	—	(5,691)	(362)	—	(362)
Stock-based compensation expense	—	—	9,167	—	—	—	9,167
Issuance of common stock in connection with merger	189,920	2	22,333	—	—	—	22,335
Issuance of shares upon public offering, net of offering costs	958,333	10	47,708	—	—	—	47,718
Net loss	—	—	—	—	—	(66,727)	(66,727)
Balance as of December 31, 2021	2,166,248	\$ 22	\$ 262,875	(10,535)	\$ (2,190)	\$ (238,323)	\$ 22,384
Vesting of restricted stock units	157	—	—	—	—	—	—
Stock-based compensation expense	—	—	3,021	—	—	—	3,021
Retirement of treasury stock	—	—	(2,190)	10,535	2,190	—	—
Effect of reverse stock split	(49)	—	—	—	—	—	—
Net loss	—	—	—	—	—	(36,065)	(36,065)
Balance as of December 31, 2022	2,166,356	\$ 22	\$ 263,706	—	\$ —	\$ (274,388)	\$ (10,660)

See accompanying notes to consolidated financial statements.

ELOXX PHARMACEUTICALS, INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF CASH FLOWS
(Amounts in thousands)

	Year ended December 31,	
	2022	2021
Cash flows from operating activities:		
Net loss	\$ (36,065)	\$ (66,727)
Adjustments to reconcile net loss to net cash used in operating activities:		
Acquired in-process research and development	—	22,670
Stock-based compensation	3,021	9,167
Depreciation and amortization	77	114
Impairment of property and equipment	36	—
Amortization of operating lease right-of-use asset	618	846
Amortization of debt discount	541	420
Loss (gain) on sales and disposals of property and equipment	—	84
Change in fair value of derivative liabilities	45	—
Gain on extinguishment of PPP debt	—	(808)
Loss on extinguishment of term debt	—	268
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	252	582
Accounts payable	1,641	(320)
Accrued expenses	(1,397)	535
Merger related costs paid	—	(1,003)
Operating lease liabilities	(614)	(829)
Net cash used in operating activities	<u>(31,845)</u>	<u>(35,001)</u>
Cash flows from investing activities:		
Purchase of property and equipment	(66)	(89)
Cash acquired in merger activities	—	2,145
Net cash (used in) provided by investing activities	<u>(66)</u>	<u>2,056</u>
Cash flows from financing activities:		
Proceeds from advances from collaboration partners	8,812	2,918
Proceeds from underwritten public offering, net of issuance costs	—	47,718
Proceeds from debt financing obligation	—	11,874
Repayment of term loan principal	—	(11,383)
Proceeds from exercises of stock options	—	23
Payment for settlement of taxes upon vesting of restricted stock units	—	(362)
Net cash provided by financing activities	<u>8,812</u>	<u>50,788</u>
Increase (decrease) in cash, cash equivalents and restricted cash	(23,099)	17,843
Cash, cash equivalents and restricted cash at the beginning of the year	42,567	24,724
Cash, cash equivalents and restricted cash at the end of the year	<u>\$ 19,468</u>	<u>\$ 42,567</u>
Reconciliation of cash, cash equivalents and restricted cash to consolidated balance sheet:		
Cash and cash equivalents	\$ 19,207	\$ 42,268
Restricted cash	261	299
Total cash, cash equivalents and restricted cash	<u>\$ 19,468</u>	<u>\$ 42,567</u>
Supplemental disclosure of cash flow activities:		
Cash paid for interest	<u>\$ 1,365</u>	<u>\$ 728</u>
Supplemental disclosure of non-cash financing activities:		
Right-of-use assets obtained in exchange for lease liabilities	<u>\$ 64</u>	<u>\$ —</u>

See accompanying notes to consolidated financial statements

ELOXX PHARMACEUTICALS, INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of the Business

Eloxx Pharmaceuticals, Inc., together with its subsidiaries (collectively “Eloxx” or the “Company”), is a clinical-stage biopharmaceutical company engaged in the science of ribosomal modulation. The Company is developing novel small molecule drug candidates from its library of unique Ribosome Modulating Agents (“RMAs”) and Eukaryotic Ribosomal Selective glycosides (“ERSGs”), for the treatment of a subset of rare and ultra-rare diseases and cancers characterized by genetic mutations that cause defects in protein translation. Specifically, the Company is targeting restoration of functional proteins in patients with premature stop codon mutations and ribosomal mutations. Premature stop codons are point mutations that disrupt the stability of the impacted messenger RNA (mRNA) and the protein synthesis from that mRNA. Additionally, certain mutations of the ribosome disrupt normal protein translation and are drivers of a subset of cancers. On April 1, 2021, the Company acquired Zikani Therapeutics, Inc. (“Zikani”), a preclinical stage biopharmaceutical company engaged in the science of ribosome modulation, leveraging its innovative TURBO-ZM™ chemistry technology platform to develop novel ribosome modulating agents (“RMAs”). The TURBO-ZM™ platform is designed to enable rapid synthesis of novel macrolides that can be optimized to modulate the human, bacterial or viral ribosomes to treat rare diseases and cancers with certain ribonucleic acid (“RNA”) and ribosomal mutations.

On December 1, 2022, the Company effected a 1-for-40 reverse split of its common stock (the “Reverse Stock Split”). Proportional adjustments for the Reverse Stock Split were made to the Company’s outstanding stock options, warrants, and equity incentive plans. All share and per-share data and amounts have been retroactively adjusted as of the earliest period presented in the consolidated financial statements to reflect the Reverse Stock Split. In conjunction with the Reverse Stock Split, the Company cancelled all shares of treasury stock.

The Company is headquartered in Watertown, Massachusetts, with additional operations in Israel and Australia.

Liquidity and Going Concern

The Company has a history of net losses and negative cash flows from operating activities since inception, and as of December 31, 2022, had an accumulated deficit of \$274.4 million. The Company expects to continue to incur net losses and negative cash flows from its operations for the foreseeable future. The Company has not generated revenue from the sale of any product or service and does not expect to generate significant revenue unless it obtains marketing approval for and commercializes one or more of its product candidates currently in development. Successful transition to profitable operations is dependent upon achieving a level of revenue adequate to support the Company’s cost structure.

The Company has financed its operations primarily from the sale of equity securities and to a lesser extent, loans and grants. The Company may never achieve profitability, and unless and until it does, the Company will continue to need to raise additional capital to fund its operations. In addition, as disclosed in Note 7, in September 2021, the Company entered into the Hercules Term Loan (as defined below) for an aggregate principal amount of \$30.0 million of which \$12.5 million had been funded as of December 31, 2022. The second tranche of \$7.5 million expired August 15, 2022 and the third tranche of \$10.0 million is only available at the sole discretion of Hercules’ investment committee. The Hercules Term Loan Agreement contains customary affirmative and negative covenants, which among others further described in Note 7, require the Company to maintain at all times a minimum qualified cash balance ranging from \$6.3 million to \$10.0 million (\$10.0 million effective as of August 15, 2022 and as of December 31, 2022) plus qualified accounts payable (as defined in the Hercules Term Loan Agreement). Subsequent to year end, on March 7, 2023, the Company repaid \$7.5 million of principal and the minimum qualified cash balance debt covenant was decreased to \$2.25 million as of March 7, 2023, and may be further reduced to \$0 if the Company has raised \$20.0 million in equity investments prior to May 31, 2023.

As of December 31, 2022, the Company was in compliance with all debt covenants. However, the inherent uncertainties described above may impact the Company's ability to remain in compliance with these covenants over the next 12 months. If the Company breaches its financial covenants and fails to secure a waiver or forbearance from the third-party lender, such breach or failure could accelerate the repayment of the outstanding borrowings under the Hercules Term Loan Agreement or the exercise of other rights or remedies the third-party lender may have under applicable law. No assurance can be provided a waiver or forbearance will be granted or the outstanding borrowings under the Hercules Term Loan Agreement, will be successfully refinanced on terms that are acceptable to the Company.

The Company believes that its cash and cash equivalents of \$19.2 million at December 31, 2022 will not be sufficient to maintain its current and planned operations for at least the next twelve months following the filing of this Annual Report on Form 10-K. The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern, which contemplates the realization of assets and settlement of liabilities in the normal course of business. However, based on the Company's current working capital, anticipated operating expenses and net losses and the uncertainties surrounding its ability to raise additional capital as needed, as discussed below, the Company believes that these conditions, in aggregate, raise substantial doubt about its ability to continue as a going concern for one year after the date these consolidated financial statements are issued.

Management intends to fund future operations through private or public debt or equity financing transactions and may seek additional capital through arrangements with strategic partners or from other sources. The availability of sufficient funding to alleviate the conditions that raise substantial doubt are not within management's control and cannot be assessed as being probable of occurring. If the Company is unable to obtain adequate financing, it will evaluate options which may include reducing or deferring operating expenses, which may have a material adverse effect on the Company's operations and future prospects.

2. Summary of Significant Accounting Policies

Basis of Presentation

The Company has prepared its consolidated financial statements in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP") as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASUs") promulgated by the Financial Accounting Standards Board ("FASB").

Reverse Stock Split

On December 1, 2022, the Company effected a 1-for-40 reverse stock split of its common stock (the "Reverse Stock Split"). As further described below, at a special meeting of stockholders held on November 30, 2022 (the "Special Meeting"), the stockholders of the Company approved a proposal to authorize the Company's Board of Directors, in its discretion following the Special Meeting to amend the Company's Amended and Restated Certificate of Incorporation, as amended (the "Certificate of Incorporation"), to effect a reverse stock split of all of the outstanding shares of the Company's common stock, par value \$0.01 per share, at a ratio ranging from any whole number between 1-for-2 and 1-for-40, as determined by the Company's Board of Directors in its discretion. On November 30, 2022, following the Special Meeting, the Company's Board of Directors approved the Reverse Stock Split at a ratio of 1-for-40. On December 1, 2022, the Company filed with the Secretary of State of the State of Delaware a certificate of amendment to amend the Company's Certificate of Incorporation to effect the Reverse Stock Split. The Reverse Stock Split became effective at 5:00 p.m., Eastern Time, on December 1, 2022.

As a result of the Reverse Stock Split, every 40 shares of the Company's common stock issued or outstanding were automatically reclassified into one validly issued, fully-paid and nonassessable new share of common stock, subject to the treatment of fractional shares as described below, without any action on the part of the holders. Proportionate adjustments will be made to the exercise prices and the number of shares underlying the Company's outstanding equity awards, as applicable, and warrants exercisable for shares of common stock, as well as to the number of shares issuable under the Company's equity incentive plans and certain existing agreements. The common stock issued pursuant to the Reverse Stock Split remain fully paid and non-assessable. The Reverse Stock Split did not affect the number of authorized shares of common stock or the par value of the common stock.

No fractional shares were issued in connection with the Reverse Stock Split. Stockholders of record who would otherwise have been entitled to receive fractional shares as a result of the Reverse Stock Split received a cash payment in lieu thereof at a price equal to the fraction to which the stockholder would otherwise be entitled multiplied by the closing sales price per share of the common stock (as adjusted for the Reverse Stock Split) on The Nasdaq Capital Market on November 30, 2022, the last trading day immediately preceding the effective time of the Reverse Stock Split.

All share and per share amounts in the accompanying financial statements, related footnotes, and management's discussion and analysis have been adjusted retroactively to reflect the reverse stock split as if it had occurred at the beginning of the earliest period presented. Effective December 2, 2022, trading of the Company's common stock on The Nasdaq Capital Market commenced on a split-adjusted basis, under the existing trading symbol "ELOX."

Principles of Consolidation

The consolidated financial statements include the accounts of the Company and its subsidiaries. Intercompany balances and transactions have been eliminated upon consolidation.

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates, judgments and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. On an ongoing basis, the Company's management evaluates its estimates, which include, but are not limited to, estimates related to accrued expenses, including clinical trials and other research and development related accruals, derivative liabilities, and stock-based compensation expense. The Company bases its estimates on historical experience and other market specific or other relevant assumptions that it believes to be reasonable under the circumstances. Actual results could materially differ from those estimates.

Foreign Currency

The functional currency of the Company and its subsidiaries is the U.S. dollar. Accordingly, monetary accounts maintained in other currencies are re-measured into U.S. dollars in accordance with ASC Topic 830, "Foreign Currency Matters". All foreign currency transaction gains and losses arising from transactions denominated in foreign currencies, whether realized or unrealized, are recorded in the statements of operations as other income or expenses.

Cash and Cash Equivalents

The Company considers all highly liquid investments purchased with an original maturity of three months or less to be cash equivalents. The Company's cash and cash equivalents include holdings in checking and overnight sweep accounts. The Company's cash equivalents, which are money market funds held in a sweep account, are measured at fair value on a recurring basis. As of December 31, 2022 and 2021 the balances of cash and cash equivalents were \$19.2 million and \$42.3 million, respectively, which approximate fair value and were determined based upon Level 1 inputs. The sweep account is valued using quoted market prices with no valuation adjustments applied. Accordingly, these financial instruments are categorized as Level 1.

Marketable Securities

The Company classifies all investment instruments with an original maturity date, when purchased, in excess of three months but less than one year as current marketable securities. Marketable securities are classified as available-for-sale and are carried at fair value. The Company periodically assesses its portfolio of securities to determine whether to record any estimated allowances for credit losses in the statement of operations. This assessment includes considering whether the Company intends to sell a security, whether it is more likely than not that the Company will have to sell a security before recovery of its amortized cost, and whether a decline in a security's fair value below its amortized cost is credit-related or non-credit-related. The Company records non-credit-related unrealized gains and losses on available-for-sale securities in accumulated other comprehensive income, which is a separate component of stockholders' equity on its consolidated balance sheet. Gains or losses realized upon sales of available-for-sale securities are recorded in other income. The cost of securities sold is based on the specific identification method. To date, the Company has recorded no allowances for credit losses, and no realized gains or losses upon sales of securities.

Restricted Cash

At December 31, 2022, and 2021, restricted cash consisted of bank guarantees related to corporate facilities leases and credit card programs.

Concentrations of Credit Risk and Off-Balance Sheet Risk

Financial instruments that potentially subject the Company to credit risk consist primarily of cash and cash equivalents. The Company mitigates its risk with respect to cash and cash equivalents by maintaining its deposits and investments at high-quality financial institutions. The Company invests any excess cash in money market funds and the management of these investments is not discretionary on the part of the financial institution. Substantially all of the Company's cash and cash equivalents are held at Silicon Valley Bank (SVB), and the amounts frequently exceed federally insured limits. On March 10, 2023, the Federal Deposit Insurance Corporation (FDIC) announced that SVB had been closed by the California Department of Financial Protection and Innovation. The United States Department of the Treasury announced in a joint statement with the Federal Reserve and FDIC that depositors of SVB would have access to all of their money starting March 13, 2023, including funds exceeding federally insured limits. The Company is exposed to credit risk in the event of default by the financial institutions holding its cash and cash equivalents. If the Company is unable to access its cash and cash equivalents as needed, its financial position and ability to operate its business will be adversely affected.

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

Property and Equipment

Property and equipment are recorded at cost, less accumulated depreciation and amortization. Leasehold improvements are amortized over the lesser of the estimated useful life or the expected term of the related lease. Costs associated with maintenance and repairs are expensed as incurred. Depreciation expense is computed on a straight-line method over the estimated useful lives of the respective assets, as follows:

	Estimated Useful Life
Computers and software	3 years
Office furniture and equipment	5 to 12 years
Laboratory equipment	5 years
Leasehold improvement	Over the shorter of the expected remaining lease term or estimated useful life

Upon sale or disposition of property and equipment, the cost and related accumulated depreciation and amortization are eliminated from the accounts and any resultant gain or loss is credited or charged to operations.

Impairment of Long-Lived Assets

Property and equipment subject to depreciation are reviewed for impairment in accordance with ASC Topic 360, "Accounting for the Impairment or Disposal of Long-Lived Assets," whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. If such assets are considered to be impaired, the impairment to be recognized is measured as the amount by which the carrying amount of the assets exceeds their fair value. The Company continually evaluates whether events or circumstances have occurred that indicate that the remaining useful life of its long-lived assets may warrant revision or that the carrying value of these assets may be impaired. 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.

Evaluation of recoverability of the asset or asset group is based on an estimate of undiscounted future cash flows resulting from the use of the asset or asset group and its eventual disposition. In the event that such cash flows are not expected to be sufficient to recover the carrying amount of the asset or asset group, the assets are written down to their estimated fair value. 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. As of each balance sheet date presented, none of the Company's long-lived assets were impaired. The Company has not recorded any impairment losses to date other than to property and equipment.

Legal and Other Contingencies

The Company accounts for its contingent liabilities in accordance with ASC Topic 450, "Contingencies". A provision is recorded when it is both probable that a liability has been incurred and the amount of the loss can be reasonably estimated. With respect to legal matters, provisions are reviewed and adjusted to reflect the impact of negotiations, estimated settlements, legal rulings, advice of legal counsel and other information and events pertaining to a particular matter. For the years ended December 31, 2022 and 2021, the Company was not a party to any litigation that was reasonably possible to have a material adverse effect on the Company's business, financial position, results of operations or cash flows (see also Note 9, "Legal and Other Contingencies"). Legal costs incurred in connection with loss contingencies are expensed as incurred.

Research and Development Expenses

Research and development expenses are comprised of costs incurred in performing research and development activities, including salaries, stock-based compensation and benefits for employees performing such activities, certain allocated facilities and support costs, depreciation, third-party license fees, and external costs of vendors engaged to conduct preclinical development activities and clinical trials. Research and development expenses are expensed as incurred and include the Company's costs of performing services in connection with its collaboration agreements and research grants.

Non-refundable prepayments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized in prepaid expenses and other current assets. Such amounts are recognized as an expense as the goods are delivered or the related services are performed, or until it is no longer expected that the goods will be delivered, or the services rendered.

The Company enters into arrangements with contract research organizations in connection with clinical trials. Such arrangements often provide for payment prior to commencing the project or based upon predetermined milestones throughout the period during which services are expected to be performed. As part of the process of preparing the Company's financial statements, management is required to estimate prepaid and accrued clinical trial expenses. The date on which services commence, the level of services performed on or before a given date, and the cost of such services are often determined based on subjective judgments informed by the facts and circumstances known to management from the terms of the contract and the Company's ongoing monitoring of service performance. The Company makes these judgments based upon the facts and circumstances known to management based on the terms of the contract and the Company's ongoing monitoring of service performance.

Fair Value of Financial Instruments

Fair value is determined based on the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal market for the asset or liability in an orderly transaction between market participants. U.S. GAAP specifies a hierarchy of valuation techniques based upon whether the inputs to those valuation techniques reflect assumptions other market participants would use based upon market data obtained from independent sources (observable inputs) or reflect the Company's own assumptions of market participant valuation (unobservable inputs).

The fair value hierarchy consists of three levels:

Level 1 - Quoted prices (unadjusted) in active markets that are unadjusted and accessible at the measurement date for identical, unrestricted assets or liabilities.

Level 2 - Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3 - Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

Financial assets and liabilities are classified within the fair value hierarchy based on the lowest level of input that is significant to the fair value measurement. The authoritative guidance requires the use of observable market data if such data is available without undue cost and effort. When available, the Company uses unadjusted quoted market prices to measure fair value and classify such items within Level 1. If quoted market prices are not available, fair value is based upon internally developed models that use, where possible, current market-based or independently-sourced market parameters, such as interest and currency rates and comparable transactions. Items valued using internally generated models are classified according to the lowest level input or value driver that is significant to the valuation. Thus, items may be classified in Level 3 even though there may be inputs that are readily observable. If quoted market prices are not available, the valuation model used generally depends on the specific asset or liability being valued. The Company did not have any transfers of financial assets between Level 2 and 3 during 2022 or 2021.

Some assets and liabilities are required to be recorded at fair value on a recurring basis, while other assets and liabilities are recorded at fair value on a nonrecurring basis. The carrying amounts of current financial instruments, which include cash and cash equivalents, restricted bank deposits, accounts payable, accrued expenses, lease obligation liability and debt, approximate their fair values due to the short-term nature of these instruments.

Stock-Based Compensation

The Company accounts for stock-based compensation in accordance with ASC Topic 718, "Compensation-Stock Compensation" ("ASC 718"), which requires companies to estimate the fair value of equity-based payment awards on the date of grant using an option-pricing model. The Company recognizes compensation expenses for the value of its awards granted based on the straight-line method over the requisite service period of each of the awards or over the implicit service period when a performance condition affects the vesting, and it is considered probable that the performance condition will be achieved.

The Company determines the fair value of each stock option award at its grant date using the Black-Scholes option pricing model for options awarded in 2022 and 2021. The Company determines the fair value of each restricted stock unit, or RSU, at its grant date based on the closing market price of the Company' s common stock on that date.

Warrants

The Company accounts for warrants on capital stock based on guidelines provided in ASC Topic 815, Derivatives and Hedging—Contracts in Entity' s Own Equity ("ASC 815"), which provides guidance on contracts that are settled in the Company' s own shares as either a liability or as an equity instrument depending on the warrant agreement. The Company' s warrants are all classified as equity instruments. As such, the Company uses the Black-Scholes pricing model, depending on the applicable terms of the warrant agreement, to value the warrants at the issuance date.

Income Taxes

The Company accounts for income taxes in accordance with ASC Topic 740, "Income Taxes" ("ASC 740"), which prescribes the use of the asset and liability method whereby deferred tax assets and liability account balances are determined based on differences between financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to be recovered or settled. The Company provides a valuation allowance, if necessary, to reduce deferred tax assets to their estimated realizable value if it is more likely than not that a portion or all of the deferred tax assets will not be realized. The Company considers many factors when assessing the likelihood of future realization of deferred tax assets, including recent earnings results, expectations of future taxable income, carryforward periods available and other relevant factors. The Company records changes in the required valuation allowance in the period that the determination is made.

Based on ASC 740, a two-step approach is used to recognize and measure uncertain tax positions. The first step is to evaluate the tax position taken or expected to be taken in a tax return by determining if the weight of available evidence indicates that it is more likely than not that, on an evaluation of the technical merits, the tax position will be sustained on audit, including resolution of any related appeals or litigation processes. The second step is to measure the tax benefit as the largest amount that is more than 50% likely to be realized upon ultimate settlement. As of December 31, 2022 and 2021, no liability for unrecognized tax positions has been recorded. Accordingly, no interest or penalties related to uncertain tax positions are recorded. The Company' s policy is to record any interest or penalties associated with unrecognized tax positions as a component of income tax expense.

Net Loss per Share, Basic and Diluted

Basic loss per share is computed by dividing the loss for the period applicable to ordinary shareholders by the weighted average number of ordinary shares outstanding during the period. In computing diluted income per share, weighted average shares used in computing basic earnings per share are adjusted to reflect the potential dilution that could occur upon the exercise of outstanding stock options and upon conversion of restricted stock units and warrants issued to investors and service providers using the “treasury stock method”.

Leases

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease. Leases with a term greater than one year are recognized on the consolidated balance sheet as a right-of-use (“ROU”) asset and current and non-current lease liabilities, as applicable. The Company has made an accounting policy election, known as the short-term lease recognition exemption, which allows the Company to not recognize ROU assets and lease liabilities that arise from short-term leases (12 months or less); The Company has applied this election to all classes of underlying assets. The Company typically only includes an initial lease term in its assessment of a lease arrangement. Options to renew or options to cancel a lease are not included in the Company’ s assessment unless there is reasonable certainty that the Company will renew or will not cancel, respectively. The Company monitors its material leases on a quarterly basis.

Operating lease liabilities and their corresponding ROU assets are recorded based on the present value of future lease payments over the expected remaining lease term. Lease cost for operating leases is recognized on a straight-line basis over the lease term as an operating expense. Certain adjustments to the ROU asset may be required for items such as lease prepayments or incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. The Company has elected to account for the lease and non-lease components together for all leases.

Recent Accounting Pronouncements

In March 2020, the FASB issued ASU 2020-04, Reference Rate Reform (Topic 848): Facilitation of the Effects of Reference Rate Reform on Financial Reporting, which provides optional expedients and exceptions to applying the guidance on contract modifications, hedge accounting, and other transactions, to simplify the accounting for transitioning from the London Interbank Offered Rate (“LIBOR”), and other interbank offered rates expected to be discontinued, to alternative reference rates. The guidance in this Update was effective upon its issuance. If elected, the guidance is to be applied prospectively through December 31, 2022. The adoption of this ASU did not have a material impact on our consolidated financial statements, including but not limited to our research and development grant agreements with the Israel Innovation Authority, discussed in additional detail Note 9, Commitments and Contingencies. While this agreement continues to use LIBOR as of December 31, 2022, any future change to an alternate interest rate is not expected to be material.

Although the FASB has issued several other ASUs for which adoption dates are pending, the Company does not expect any of them to have any impacts on its consolidated financial statements.

3. Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following (in thousands):

	December 31,	
	2022	2021
Research and development	\$ 366	\$ 413
Insurance	93	123
Other	202	377
Totals	<u>\$ 661</u>	<u>\$ 913</u>

4. Property and Equipment, net

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

	December 31,	
	2022	2021
Computers and software	\$ 26	\$ 31
Office furniture and equipment	15	27
Laboratory equipment	251	221
Leasehold improvements	57	88
Assets in progress	–	20
Total property and equipment, at cost	349	387
Less: Accumulated depreciation and amortization	(180)	(171)
Property and equipment, net	<u>\$ 169</u>	<u>\$ 216</u>

Depreciation expense was \$77 thousand and \$114 thousand for the years ended December 31, 2022 and 2021, respectively. During the year ended December 31, 2022, the Company recognized an impairment loss of equipment of \$36 thousand.

5. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31,	
	2022	2021
Research and development	\$ 1,544	\$ 1,849
Payroll, bonus and other employee-related expenses	750	1,615
Professional services	225	489
Interest on debt	146	102
Other	134	141
Total	<u>\$ 2,799</u>	<u>\$ 4,196</u>

6. Leases

Operating lease costs under the leases for the years ended December 31, 2022 and 2021 were approximately \$0.7 million and \$1.1 million, respectively. The weighted average remaining lease term at December 31, 2022 was 1.18 years and the weighted average incremental borrowing rate was 5.4%.

In January 2022, the Company entered into a new lease agreement for office space in Israel for an initial period of 24 months and with the option to extend the lease for an additional 24 months. The lease commenced on April 1, 2022 at the rate of approximately \$36 thousand per year, billed monthly, plus the Company's share of utilities, common area expenses, and taxes. Upon commencement of the lease, the Company recognized a right-of-use asset and related liability of \$64 thousand.

The following table summarizes the Company's maturities of operating lease liabilities as of December 31, 2022 (in thousands):

2023	\$ 740
2024	134
2025	2
Total lease payments	876
Less imputed interest	(29)
Total operating lease liabilities	847
Less: current portion	(712)
Long-term portion	<u>\$ 135</u>

7. Debt

Hercules Term Loan

On September 30, 2021, the Company entered into a Loan and Security Agreement, dated as of September 30, 2021 (the “Hercules Loan Agreement”) with Hercules Capital, Inc., (“Hercules” or the “Lender”).

The Hercules Term Loan Agreement provided for term loans in an aggregate principal amount of up to \$30.0 million, comprised of (i) a tranche 1 advance of \$12.5 million (the “Tranche 1 Advance”), (ii) a tranche 2 advance of \$7.5 million (the “Tranche 2 Advance”) and (iii) a tranche 3 advance of \$10.0 million (the “Tranche 3 Advance”) (collectively, the “Term Loan Advances”). The Tranche 1 Advance under the Hercules Term Loan Agreement was funded on September 30, 2021. The Tranche 2 Advance was to be available at the Company’ s election until August 15, 2022, subject to the Company’ s achievement of certain milestone events relating to data from the clinical trials. The Company did not meet the requirements for the Tranche 2 Advance and such funding will, therefore, not be available to the Company. The Tranche 3 Advance is available subject to approval by the Lenders’ investment committee in its sole discretion. The Tranche 3 Advance may be available for funding until, initially, April 1, 2023, and (i) upon the occurrence of certain milestone events relating to the Company’ s receipt of net cash proceeds from unrestricted equity investments in the Company, October 1, 2023, and (ii) upon the occurrence of certain milestone events relating to the Company’ s receipt of net cash proceeds and certain milestone events relating to data from the clinical trials, April 1, 2024.

As security for its obligations, the Company granted Hercules a continuing security interest in substantially all of the assets of the Company, subject to certain customary exceptions, including for intellectual property.

Any outstanding principal on the Term Loan Advances will accrue interest at a floating rate equal to the greater of (i) 9.50% per annum and (ii) the sum of 6.25% plus the prime rate, as published in *The Wall Street Journal*. As of December 31, 2022 and 2021, the interest rate was 13.75% and 9.5%, respectively. Interest payments are payable monthly following the funding of a Term Loan Advance. The Company will be required to make principal payments on the outstanding balance of the Term Loan Advances commencing on April 1, 2023 (the “Term Loan Amortization Date”) in 36 equal monthly installments, plus interest; provided that if the Company has achieved the milestones described above, then the Term Loan Amortization Date will be automatically extended to October 1, 2023 or April 1, 2024, as applicable. Any amounts outstanding under the Term Loan Advances, if not repaid sooner, are due and payable on April 1, 2025 (the “Maturity Date”). On any date that the Company partially repays the outstanding obligations, the Company shall pay the Lenders a charge equal to 6.55% of the original principal amount.

The Company may prepay the outstanding principal amount of the Term Loan Advances at any time (in whole, but not in part), plus accrued and unpaid interest and a prepayment premium equal to (i) 3% of the principal amount outstanding if prepaid on or prior to the first anniversary of the date of Loan Agreement, (ii) 2% of the principal amount outstanding if prepaid after the first anniversary the date of Hercules Loan Agreement but on or prior to the second anniversary of the date of Hercules Loan Agreement, and (iii) 1% of the principal amount outstanding if prepaid after the second anniversary of the date of Hercules Loan Agreement but on or prior to the Maturity Date.

The Hercules Loan Agreement contains customary affirmative and negative covenants which, among other things, requires the Company to maintain at all times a minimum qualified cash balance equaling amounts ranging from \$6.3 million to \$10.0 million (\$10.0 million effective as of August 15, 2022 and December 31, 2022) plus qualified accounts payable (as defined) and limits the Company’ s ability to (i) incur additional indebtedness, (ii) pay dividends or make certain distributions, (iii) dispose of its assets, grant liens or encumber its assets or (iv) fundamentally alter the nature of its business. These covenants are subject to a number of exceptions and qualifications. The Company was in compliance with all debt covenants at December 31, 2022.

The Hercules Loan Agreement also contains customary events of default, including the Company’ s failure to make any principal or interest payments when due, the occurrence of certain bankruptcy or insolvency events or a breach of the covenants. Upon the occurrence of an event of default, Hercules may, among other things, accelerate the Company’ s obligations under the Hercules Loan Agreement.

As of December 31, 2022, the carrying value of the outstanding loan consists of \$12.5 million in principal less an unamortized debt discount of \$0.8 million. The debt issuance costs and the final maturity payment of \$0.8 million, have been recorded as a debt discount which are being accreted to interest expense through the maturity date of the loan. Interest expense relating to the loan for the years ended December 31, 2022 and 2021 was \$1.9 million and \$0.4 million, respectively. Interest expense is calculated using the effective interest method and is

inclusive of non-cash amortization of the debt discount. As of December 31, 2022, the effective interest rate was 19.5%.

On March 7, 2023, the Company entered into an amendment to repay \$7.5 million of the outstanding principal of the Hercules Term Loan, extend the interest only period until September 1, 2023, and reduce the qualified cash balance to \$2.25 million as of March 7, 2023. The Company will be required to make principal payments on the remaining \$5.0 million outstanding principal balance of the Term Loan Advances commencing on September 1, 2023, plus interest, with a final maturity date of April 1, 2025. See Note 19, Subsequent Events.

The Company's scheduled future principal payments for the long-term debt are as follows (in thousands):

	December 31, 2022
2023	\$ 4,204
2024	6,101
2025	2,195
Total future principal payments	12,500
Less: unamortized discount	(782)
Carrying value of long-term debt	11,718
Less: current portion	(3,980)
Add: final Term Loan fee due at maturity in 2023	819
Long-term portion	<u>\$ 8,557</u>

SVB Term Loan

On January 30, 2019, the Company entered into a Loan and Security Agreement (the "Loan Agreement") in the amount of \$15.0 million with Silicon Valley Bank ("SVB") and WestRiver Innovation Lending Fund VIII, L.P. ("WestRiver"), and together with SVB, the "SVB Lenders").

Outstanding principal on the loan accrues interest at a floating rate equal to the greater of (i) 5.25% per annum and (ii) the sum of 2.5% plus the prime rate, as published in The Wall Street Journal. Interest payments are payable monthly. On September 30, 2021, the interest rate was 5.75%. The Company commenced making payments on the outstanding principal balance of the loan on February 1, 2020, which was payable in 36 equal monthly installments and scheduled to fully mature on January 1, 2023.

In conjunction with the initial loan advance, the Company issued warrants to the SVB Lenders to purchase 1,021 shares of common stock at a price of \$440.80 per share (subject to certain adjustments).

The Company may prepay the outstanding principal balance of the loans advanced in whole but not in part, subject to a prepayment fee ranging from 1% to 3% of any amount prepaid, depending upon when the prepayment occurs. The Company will also pay a final payment fee equal to 6% of the total loans advanced, due upon the earlier of maturity or termination of the Loan Agreement.

On September 30, 2021, in connection with the funding of the Hercules Term Loan Tranche 1 Advance and pursuant to a Payoff Letter dated September 30, 2021, the Company voluntarily repaid in full the carrying value of the outstanding loan consisting of \$6.7 million of principal, a final maturity payment of \$0.9 million, and early termination fees of \$0.1 million from funds received under the Hercules Loan Agreement. The debt issuance costs, the valuation of the warrants, and the final maturity payment of \$0.9 million, had been recorded as a debt discount which were being accreted to interest expense through the maturity date of the loan. The remaining unamortized debt discount of \$0.2 million and early termination fees were accounted for as a loss on debt extinguishment and included in other income and expense in the statement of operations for the year ended December 31, 2021. Interest expense relating to the loan for the years ended December 31, 2022 and 2021 was \$0 and \$0.9 million, respectively. Interest expense is calculated using the effective interest method and is inclusive of non-cash amortization of the debt discount.

PPP Loan

In April 2020, the Company entered into a loan agreement with SVB under the U.S. Small Business Administration (the "SBA") Paycheck Protection Program (the "PPP") pursuant to the Coronavirus Aid, Relief and Economic Security Act of 2020 (the "CARES Act") and received loan proceeds of \$0.8 million (the "PPP Loan"). The Company used the loan proceeds for payroll and other covered costs in accordance with the relevant terms and conditions of the CARES Act. The PPP Loan had a maturity date of April 21, 2022 and an interest rate of 1.0% per

annum. Under the terms of the PPP, on September 3, 2021, the PPP Loan was forgiven in full, and the Company recognized a gain on extinguishment of debt of \$0.8 million during the year ended December 31, 2021. The SBA reserves the right to audit any PPP loan, regardless of size. These audits may occur after forgiveness has been granted. In accordance with the CARES Act, all borrowers are required to maintain their PPP loan documentation for six years after the PPP loan was forgiven or repaid in full and to provide that documentation to the SBA upon request.

8. Related Parties

On August 29, 2013, the Company entered into the Technion Agreement with TRDF, with respect to certain technology relating to aminoglycosides and the redesign of aminoglycosides for the treatment of human genetic diseases caused by premature stop mutations and further results of the research of the technology, in order to develop and commercialize products based on such technology. Under the Technion Agreement, TRDF is obligated to provide the Company with research services for an estimated annual payment of \$0.1 million, the precise amount to be agreed by the parties prior to the beginning of each year of the research period. During the years ended December 31, 2022 and 2021 no expenses were incurred. As of December 31, 2022 and 2021 no amounts were recorded in accrued expenses.

In addition, TRDF granted the Company a license to use, market, sell or sub-license the rights of the product developed under the TRDF research results (the "Licensed Product"), as fully defined in the Technion Agreement, for the following considerations: (i) milestone payments up to total consideration of \$6.1 million, to be transferred upon meeting certain milestones as defined in the Technion Agreement; (ii) certain royalties in the low- to mid-single-digit percentage of net sales (subject to change in the case of (a) sublicensing to a big pharmaceutical or biotechnology company, or (b) payment of royalties to third parties, or (c) commercialization by a third party of an authorized generic to a licensed product), for a period until the later of (i) the expiration of a valid claim on the Licensed Product in each country the Licensed Product is sold to, or (ii) a certain amount of years from the date of the first commercial sale of the Licensed Product in such country; and (iii) a low- to mid-double-digit percentage of any non-royalty sub-license income received by the Company from a sub-licensed entity. The Company made no milestone or royalty payments to the TRDF during the years ended December 31, 2022 or 2021.

9. Advances From Collaboration Partners, Legal, and Other Contingencies

Cystic Fibrosis Foundation

During 2019, the Company received a funding award (the "2019 CFF Award") from the Cystic Fibrosis Foundation ("CFF") for up to \$3.6 million and entered into an agreement relating to the award, which agreement was amended in December 2020 and March 2022. Payment of award amounts are subject to the achievement of certain milestones in connection with the Company's global cystic fibrosis development program. The Company will be required to repay amounts received from the CFF (or specified multiples of such amounts) in certain circumstances, including as royalties on net sales, and, in the event of a disposition of the underlying asset (as defined in the agreement), in which case the Company would be obliged to use up to 5% of the amounts received from the disposition to repay up to three times the award amount. The funding provided to the Company is accounted for as an advance from a collaboration partner within the scope of ASC Topic 730, "Research and Development." As of December 31, 2021, the Company had received payments of \$3.4 million, which are recorded as Advances from collaboration partners in the accompanying consolidated financial statements. In March 2022, the Company entered into an agreement with the CFF to amend the 2019 CFF Award to provide for up to an additional \$15.9 million to fund the ongoing global Phase 2 clinical development of ELX-02 in cystic fibrosis (the "2022 CFF Amendment"). The Company received an upfront payment of \$7.0 million in March 2022 and a milestone payment of \$1.5 million in September 2022, which were recorded as Advances from collaboration partners in the accompanying consolidated financial statements. In September 2022, the CFF determined not to continue funding this program and the remaining \$7.4 million of the award under the 2022 CFF Amendment will not be available to the Company under the current development program. Upon successful commercialization of ELX-02 or any derivative products thereof, the Company will pay the CFF royalties up to 6% of net sales based on the on the actual amount of funding from the CFF and potential sales milestones. In addition, the 2022 CFF Agreement includes an embedded derivative arising from a provision that upon the occurrence of a change of control or sale or license of funded assets (each a disposition event), the Company would be required to pay the CFF 10% of the consideration received for the disposition event up to three times the amount of funds received from the CFF under the 2022 CFF Agreement.

In May 2021, the Company received an additional award from the CFF (the "2021 CFF Award") for up to \$2.6 million to help identify optimized oral RMAs for further development in the treatment of cystic fibrosis patients with nonsense mutations. Payment of award amounts are subject to the achievement of certain milestones in

connection with the Company's oral RMA cystic fibrosis development program. The Company will be required to repay amounts received from the CFF (or specified multiples of such amounts) in certain circumstances, including as royalties on net sales (with royalties capped at eight times the award amount received, the "Royalty Cap"), and, in the event of a disposition of the underlying asset. The funding provided to the Company is accounted for as an advance from a collaboration partner within the scope of ASC Topic 730, "Research and Development." As of December 31, 2022 and 2021, the Company had received payments of \$0.6 million and \$0.3 million, respectively, under this award, which are recorded as Advances from collaboration partners in the accompanying consolidated financial statements. The 2021 CFF Award includes an embedded derivative arising from a provision that upon the occurrence of a change of control or sale or license of funded assets (each a disposition event) the Company would be required to pay the CFF 20% of the consideration received for the disposition event, and 10% for a sale or license event, up to eight times the amount of funds received from the CFF under the 2021 CFF Agreement.

The fair value of the embedded derivatives related to the 2019 CFF Award and the 2021 CFF Award as described above were concluded to be de minimis as of December 31, 2021. In conjunction with the 2022 CFF Agreement, the Company estimated the fair value of the embedded derivatives to be \$45 thousand as of December 31, 2022 and has recognized this amount on the consolidated balance sheet as derivative liabilities with the corresponding change in value of \$45 thousand expense recognized as the change in fair value of derivative liabilities in other expense (income), net, in the consolidated statements of operations for the year ended December 31, 2022.

Royalty Commitments to the IIA

To date, the Company has received research and development grants from the Israel Innovation Authority (the "IIA") totaling \$2.6 million. No grants were received for the years ended December 31, 2022 and 2021.

Under the research and development agreements with the IIA and pursuant to applicable law, the Company is required to pay royalties at the rate of 3% on sales to end customers of products candidates developed with funds provided by the IIA, up to an amount equal to 100% of the IIA research and development grants received, plus interest based on the 12-month LIBOR rate. If the Company does not generate sales of products developed with funds provided by the IIA, the Company is not obligated to pay royalties or repay the grants.

As of December 31, 2022, the Company has not commenced the payment obligation of the royalties and has a contingent obligation with respect to royalty-bearing participation received or accrued, amounting to \$2.8 million, including accrued LIBOR interest.

Commitments to TRDF

Since August 29, 2013, the Company has had an ongoing agreement with TRDF. Refer to Note 8, "Related Parties", for further information.

License Agreement between Zikani and President and Fellows of Harvard College

On February 10, 2015, Zikani entered into an agreement with the President and Fellows of Harvard College ("Harvard") to license certain patent rights owned by Harvard. This license agreement was subsequently amended and restated on March 31, 2020. Harvard is entitled to receive clinical and regulatory milestone payments totaling up to \$3.6 million in the aggregate per licensed product approved in the United States, European Union, and Japan. The Company is also obligated to make additional royalty payments to Harvard upon the occurrence of certain sales milestones per licensed product up to a mid-single digit royalty percentage. The royalty percentage depends on the product and whether such licensed product is covered by a valid claim within the certain patent rights that the Company licenses from Harvard. Further, the Company may sub license the patent rights and any income, with the Company obligated to remit to Harvard fees ranging from 20% to 30% of such sublicense income up to the achievement of certain milestone events. There were no royalties recorded in 2022 or 2021.

Under this agreement, the Company has an exclusive, worldwide, royalty-bearing license under Harvard's interest in the Patent Rights, and a non-exclusive, worldwide, royalty-bearing license under Harvard's interest in the Harvard Know-How, solely to develop, make, have made, use, offer for sale, sell, have sold and import and export licensed products solely within the field.

Harvard retains the right, for itself and for other not-for-profit research organizations, to practice the patent rights within the scope of the license granted above, solely for non-commercial research, educational and scholarly purposes; provided, that, nothing herein shall be construed as permitting Harvard or any such not-for-profit research organization to grant any rights to any third party, including any for-profit sponsor, to practice or exploit any of the patent rights for any commercial purpose that would be inconsistent with the terms of the exclusive license of the patent rights, including any right to develop, manufacture, market or sell licensed products for use in the field; and the United States federal government retains rights in the patent rights pursuant to 35 U.S.C. § 200-212 and 37

C.F.R. § 401 et seq., and any right granted in this agreement greater than that permitted under 35 U.S.C. §§ 200-212 or 37 C.F.R. § 401 et seq. will be deemed modified.

In addition to the license agreement, the Company also reimburses Harvard for certain costs related to the maintenance and further development of patents developed through the founding stockholder's research. For the year ended December 31, 2022, the Company incurred \$0.2 million of patent expenses due to Harvard. For the year ended December 31, 2021, the Company incurred immaterial patent expenses due to Harvard.

Contingencies

From time to time, the Company may become involved in various lawsuits and legal proceedings, which arise in the ordinary course of business. The Company is currently unaware of any material pending legal proceedings to which it is a party or of which its property is the subject. However, the Company may at times in the future become involved in litigation in the ordinary course of business, which may include actions related to or based on its intellectual property and its use, customer claims, employment practices and employee complaints and other events arising out of its operations. When appropriate in management's estimation, the Company will record adequate reserves in its financial statements for pending litigation. Litigation is subject to inherent uncertainties, and an adverse result in any such matters could adversely impact its reputation, operations, and its financial operating results or overall financial condition.

The Company accounts for contingent liabilities in accordance with ASC Topic 450, "Contingencies". A provision is recorded when it is both probable that a liability has been incurred and the amount of the loss can be reasonably estimated. With respect to legal matters, provisions are reviewed and adjusted to reflect the impact of negotiations, estimated settlements, legal rulings, advice of legal counsel and other information and events pertaining to a particular matter. As of December 31, 2022 and 2021, the Company was not a party to any litigation that is reasonably possible to have a material adverse effect on the Company's business, financial position, results of operations or cash flows. Legal costs incurred in connection with loss contingencies are expensed as incurred.

10. Stockholders' Deficit

As of December 31, 2022, the Company had 500,000,000 shares authorized of common stock, \$0.01 par value, of which 2,166,356 shares were outstanding and 5,000,000 shares authorized of preferred stock, \$0.01 par value, of which no shares were issued or outstanding.

Common Stock

Public Offerings

On May 13, 2021, the Company closed an underwritten public offering of 958,333 shares of its common stock at a price of \$54.00 per share and received gross proceeds of approximately \$51.8 million, before deducting underwriting discounts and commissions of \$3.1 million and offering expenses of \$0.8 million.

At the Market Offering Program

On September 30, 2021, the Company entered into a Sales Agreement with SVB Leerink, LLC ("SVB Leerink") pursuant to which the Company may offer and sell up to \$50.0 million of shares of its common stock (the "ATM Shares") from time to time, through an "at the market offering" program (the "ATM Program"), under which SVB Leerink will act as sales agent. Pursuant to the Sales Agreement, the Company will set the parameters for the sale of ATM Shares, including the number of ATM Shares to be issued, the time period during which sales are requested to be made, limitations on the number of ATM Shares that may be sold in any one trading day and any minimum price below which sales may not be made. The Company is not obligated to make any sales of Shares under the ATM Program. The Company had not sold any shares under the ATM Program as of December 31, 2022.

Warrants

Eloxx Limited issued warrants to purchase shares of common stock in conjunction with the Share Purchase Agreements prior to the December 2017 reverse merger between Eloxx Limited and Sevion Therapeutics, Inc. The

Company also issued warrants to purchase shares of common stock in connection with the SVB Loan Agreement. During the year ended December 31, 2022, transactions related to warrants were as follows:

	Shares	Weighted average exercise price	Weighted average remaining contractual life (years)
Warrants outstanding at December 31, 2021	8,097	\$ 172.40	1.74
Granted	-		
Exercised	-		
Forfeited	(7,076)	133.91	
Warrants outstanding at December 31, 2022	<u>1,021</u>	<u>\$ 440.80</u>	<u>6.08</u>
Warrants exercisable at December 31, 2022	<u>1,021</u>	<u>\$ 440.80</u>	<u>6.08</u>

11. Stock-Based Compensation

Stock Incentive Plans

On March 12, 2018, the Company's Board of Directors (the "Board") adopted the 2018 Equity Incentive Plan (the "2018 Plan"). The 2018 Plan became effective on April 20, 2018 upon approval by the stockholders of the Company with the outstanding options and shares available for future grant under any prior plans being assumed by the 2018 Plan. The initial total number of shares available under the 2018 Plan for awards to employees, non-employee directors and other key personnel was 125,000 shares.

Stock options granted have a ten-year contractual life and, upon termination of service, vested options are generally exercisable between one and three months following the termination date, while unvested options are forfeited immediately.

Summary of Stock Option Activity

Transactions during the year ended December 31, 2022 related to stock options granted to employees and directors were as follows:

	Shares	Weighted average exercise price per Share	Weighted average remaining contractual life (years)	Aggregate intrinsic value (in thousands)
Options outstanding as of December 31, 2021	222,611	\$ 209.60	7.23	\$ 254
Granted	86,112	17.88		
Exercised	-	-		
Forfeited	(59,320)	367.39		
Options outstanding as of December 31, 2022	<u>249,403</u>	<u>\$ 105.87</u>	<u>8.12</u>	<u>\$ 3</u>
Options exercisable at December 31, 2022	<u>81,809</u>	<u>\$ 214.06</u>	<u>6.39</u>	<u>\$ 3</u>

As of December 31, 2022, the unrecognized compensation cost related to the outstanding options was \$5.3 million and is expected to be recognized over a weighted-average period of 2.43 years.

The weighted average grant date fair values of stock options granted during the years ended December 31, 2022 and 2021 were \$12.20 and \$62.40, respectively.

The following table presents the assumptions used to estimate the fair values of stock options granted in the periods presented:

	Year ended December 31,	
	2022	2021
Dividend yield	0%	0%
Volatility	78%-82%	76%-77%
Risk-free interest rate	1.84%-3.96%	0.87%-1.33%
Expected term (years)	5.5-6.0	6.0
Contractual term (years)	10	10

Summary of Restricted Stock Unit Activity

Transactions during the year ended December 31, 2022 related to RSUs granted to employees were as follows:

	Shares	Weighted average grant date fair value per share
Unvested at December 31, 2021	157	\$ 600.80
Vested	(157)	600.80
Unvested at December 31, 2022	-	\$ -

As of December 31, 2022, there was no remaining unrecognized compensation costs related to the RSUs.

Stock-based Compensation Expense

Stock-based compensation expense relates to stock options granted to employees, non-employee directors and consultants, time-based restricted stock units granted to employees and performance-based stock options and restricted stock units granted to an employee. The total equity-based compensation expense related to all of the Company's equity-based awards was recognized as follows (in thousands):

	Year ended December 31,	
	2022	2021
Research and development	\$ 1,319	\$ 1,336
General and administrative	1,702	7,831
Total stock-based compensation expense	\$ 3,021	\$ 9,167

12. Income Taxes

The components of income (loss) before taxes on income are as follows (in thousands):

	Year ended December 31,	
	2022	2021
U.S.	\$ (22,991)	\$ (47,849)
Israel	(13,074)	(18,895)
Australia	-	17
Loss before taxes on income	\$ (36,065)	\$ (66,727)

There were no taxes on income during the years ended December 31, 2022 or 2021.

The significant components of the Company's deferred tax assets were comprised of the following (in thousands):

	December 31,	
	2022	2021
Deferred tax assets:		
Net operating loss carryforwards	\$ 58,334	\$ 57,716
Stock-based compensation	1,831	3,143
Reserves and allowances	170	337
U.S. tax credits and other credits	8,226	6,009
Capitalized research and development expenditures	11,184	3,988
Operating lease right-of-use assets	(197)	(338)
Operating lease liabilities	203	363
Other	226	371
Total deferred tax assets	79,977	71,589
Valuation allowance	(79,977)	(71,589)
Net deferred tax assets	<u>\$ —</u>	<u>\$ —</u>

Deferred taxes are recognized for temporary differences between the basis of assets and liabilities for financial statements and income tax purposes. The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. As of December 31, 2022 and 2021, based on the Company's history of operating losses, the Company has concluded that it is more likely than not that the benefit of the deferred tax assets will not be realized. Accordingly, the Company has provided a full valuation allowance for deferred tax assets as of December 31, 2022 and 2021.

As of December 31, 2022 and 2021, the Company provided valuation allowances of approximately \$80.0 million and \$71.6 million, respectively, on U.S. federal, U.S. state and Israeli tax jurisdiction deferred tax assets to reduce the carrying amounts of these assets to zero. The net changes in the Company's valuation allowances were increases of \$8.4 million and \$19.0 million during the years ended December 31, 2022 and 2021, respectively. For both the years ended December 31, 2022, the increase in the valuation allowance was primarily related to losses generated during the period and increases in research and development credits and other tax credits, partially offset by a reduction in the stock-based compensation deferred tax asset associated with cancelled awards.

For the years ended December 31, 2022 and 2021 the expected tax expense based on the federal statutory rate is reconciled with the actual tax expense as follows:

	Year ended December 31,	
	2022	2021
U.S. federal statutory rate	21.0%	21.0%
State tax rate, net of federal benefit	2.2	1.0
Permanent differences	(7.4)	(7.3)
Tax credits	6.6	3.5
Effect of rate differences from statutory	1.0	0.6
Change in valuation allowance	(23.4)	(18.8)
Income tax provision	0.0%	0.0%

The main reconciling item between the statutory tax rate and the Company's effective tax rate is the recognition of valuation allowances in respect to deferred taxes related to accumulated net operating losses carried forward and temporary differences due to the uncertainty of the realization of such deferred taxes.

As of December 31, 2022 and 2021, the Company had U.S. federal net operating loss ("NOL") carryforwards of \$159.2 million and \$158.8 million, respectively. U.S. federal NOL carryforwards will begin to expire, if not utilized, beginning in 2023 through 2037. Included in the U.S. federal NOL carryforward as of December 31, 2022 are \$84.1 million of NOLs generated after the effective date of the Tax Cuts and Jobs Act of 2017 (the "Tax Act"), which are not subject to expiration but may not be carried back and are only eligible to offset up to a maximum of 80% of taxable income generated in a given year. It is uncertain if and to what extent various U.S. states will conform their net operating loss rules to the Tax Act.

As of December 31, 2022 and 2021, the Company had U.S. state NOL carryforwards of \$25.9 million and \$24.2 million, respectively, which may be available to offset future income tax liabilities.

As of December 31, 2022 and 2021, the Company had federal research tax credit carryforwards of \$8.1 million and \$5.9 million, respectively, available to reduce future tax liabilities and which expire at dates beginning in 2026 through 2041.

As of December 31, 2022 and 2021, the Company had Israeli NOL carryforwards of \$101.2 million and \$99.3 million, respectively, which carry forward indefinitely.

Under the provisions of the Internal Revenue Code ("IRC"), the net operating loss and tax credit carryforwards are subject to review and potential adjustments by the Internal Revenue Service and state tax authorities. Under Section 382 of the Internal Revenue Code and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50 percent change, by value, in its equity ownership over a three-year period, the corporation's ability to use its pre-change NOL carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. The Company may have experienced ownership changes in the past, including the reverse merger of Sevion Therapeutics, Inc. on December 19, 2017 at which time the Company's pre-change U.S. federal NOL carryforward was \$77.2 million, and its research tax credit was \$0.7 million. The Company may have experienced ownership change in the Zikani Merger on April 2, 2021. The Company has done a high-level evaluation on the Zikani U.S. federal NOL carryforwards and credits and have written them down accordingly. The Company may experience additional ownership changes in the future as a result of subsequent shifts in its stock ownership, some of which may be outside of its control. Although the Company has not completed its analysis, it is reasonably possible that its federal NOLs available to offset future taxable income could materially decrease. This reduction would be offset by an adjustment to the existing valuation allowance for an equal and offsetting amount. Additionally, the state NOLs available to offset future state income could similarly decrease, which would also be offset by an equal and offsetting adjustment to the existing valuation allowance. Given the offsetting adjustments to the existing valuation allowance, any ownership change is not expected to have an adverse material effect on the Company's Consolidated Financial Statements.

The Company is subject to income taxes in the United States and Israel and Australia. The Company files income tax returns in the U.S. and in several states. The federal and state tax returns are generally subject to tax examination by taxing authorities for tax years December 31, 2019 to present. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service or state tax authorities to the extent utilized in a future period. The Israeli income tax returns remain open to examination beginning in 2013 to present. The Australia income tax returns remain open to examination beginning in 2021 to present. If and when the Company claims NOL carryforwards from any prior years against future taxable income, those losses may be examined by the taxing authorities.

13. Net Loss Per Share

The loss and the weighted average number of shares used in computing basic and diluted net loss per share for the years ended December 31, 2022 and 2021, are as follows (in thousands, except share and per share data):

	Year ended December 31,	
	2022	2021
Numerator:		
Net loss	\$ (36,065)	\$ (66,727)
Denominator:		
Weighted average number of shares of common stock used in computing net loss per share, basic and diluted	2,166,311	1,749,071
Net loss per share, basic and diluted	<u>\$ (16.65)</u>	<u>\$ (38.15)</u>

For the years ended December 31, 2022 and 2021, the totals of outstanding preferred stock, stock options, stock warrants and restricted stock units, as applicable, excluded from the calculation of the diluted net loss per share due to their anti-dilutive effect were 250,424 and 230,865, respectively.

14. Other Expense (Income), net

Other Expense (income) consisted of the following (in thousands):

	Year ended December 31,	
	2022	2021
Interest and other income	\$ (274)	\$ (8)
Interest and other expense	1,949	1,259
Foreign currency exchange losses (gains), net	3	(2)
Research and development tax credit income	(77)	—
Change in fair value of derivative liabilities	45	—
Gain on debt extinguishment	—	(808)
Loss on debt extinguishment	—	268
Total other expense (income), net	<u>\$ 1,646</u>	<u>\$ 709</u>

15. Segment and Geographic Information

Operating segments are defined as components of an enterprise (business activity from which it earns revenue and incurs expenses) about which discrete financial information is available and regularly reviewed by the chief operating decision maker in deciding how to allocate resources and in assessing performance. The Company's chief operating decision maker is its Chief Executive Officer. The chief operating decision maker reviews consolidated operating results to make decisions about allocating resources and assessing performance for the entire company. The Company views its operations and manages its business as one operating segment; however, it operates in three geographic regions: the U.S., Israel, and Australia. Substantially all of the Company's assets are located in the U.S.

16. Merger Accounting

On April 1, 2021, the Company, acquired Zikani (the "Zikani Merger"), pursuant to an Agreement and Plan of Merger (the "Merger Agreement"). Under the terms of the Merger Agreement, the Company issued 189,920 shares of common stock, \$0.01 par value per share ("Eloxx Common Stock"), in exchange for all of the issued and outstanding equity interests of Zikani (the "Merger Consideration"). In addition, the Company issued 11,054 restricted stock units under the Eloxx Pharmaceuticals, Inc. 2018 Equity Incentive Plan (the "Equity Plan") to certain employees of Zikani in respect of each individual's prospective service as an employee, officer, consultant or director of the Company.

The Company has been determined to be the acquiring company for accounting purposes and has concluded the merger represents an asset acquisition by the Company of Zikani. To determine the accounting for this transaction under U.S. GAAP, a company must assess whether an integrated set of assets and activities will be accounted for as an acquisition of a business or an asset acquisition. The guidance requires an initial screen test to determine if substantially all of the relative fair value of the gross assets acquired is concentrated in a single asset or group of similar non-financial assets. If that screen is met, the set is not a business. In connection with the Zikani Merger, substantially all of the consideration paid is allocable to the fair value of acquired in-process research and development ("IPR&D") and, as such, the acquisition is treated as an asset acquisition. Zikani's assets and liabilities have been initially recognized by allocating the accumulated cost of the acquisition based on their relative fair values, as estimated in good faith by management. The net assets acquired as of the transaction date has been combined with the assets, liabilities, and results of operations of the Company on consummation of the Merger. In accordance with ASC 730, Research and Development, the portion of the Merger Consideration allocated to the acquired IPR&D based on its relative fair value is included as an operating expense as there is no alternative future use.

The total consideration for the Merger is as follows (in thousands, except per share data):

Number of shares of Eloxx common stock issued to Zikani stockholders ⁽¹⁾	190
Actual closing price per share of Company common stock as reported on the Nasdaq Global Market on April 1, 2021	\$ 134.40
Adjusted for a discount for lack of marketability ("DLOM") ⁽¹⁾	87.5% \$ 117.60
Fair value of common stock consideration	22,335
Transaction costs	1,003
Total purchase price	<u>\$ 23,338</u>

- (1) The shares of common stock issued as merger consideration are unregistered and subject to trading restriction under Rule 144. The Company estimated the DLOM based on consideration of multiple valuation methods. A DLOM is applied to the Company's quoted common stock price to estimate the value of Eloxx common stock issued on a minority, non-marketable basis. The Eloxx Common Stock issued was offered and sold in transactions exempt from registration under the Securities Act of 1933, as amended (the "Securities Act"), in reliance on Section 4(a)(2) thereof and Regulation D thereunder.

The following table summarizes the allocation of the cost of the acquisition to the respective assets acquired and liabilities assumed, based on their relative fair values.

Cash and cash equivalents	\$ 1,954
Restricted cash	191
Prepaid expenses and other current assets	296
Operating lease right-of-use asset	1,810
Property and equipment ⁽²⁾	192
Intangible assets ⁽³⁾	467
Total Assets	<u>4,910</u>
Accounts payable	1,219
Accrued expenses	748
Current portion of operating lease liability	588
Operating lease liability	1,222
Total liabilities	<u>3,777</u>
Net assets acquired	1,133
In process research and development acquired ⁽⁴⁾	22,205
Purchase price	<u>23,338</u>

- (2) Zikani's property and equipment consists principally of laboratory and computer equipment, furniture and fixtures and leasehold improvements.
- (3) Employee-related intangible assets relate to Zikani's assembled workforce acquired in the Zikani Merger.
- (4) IPR&D represents the allocated consideration based on the estimated fair value of Zikani's IPR&D. In accordance with ASC 730, Research and Development, the fair value of IPR&D acquired in an asset acquisition with no alternative future use be allocated a portion of the consideration transferred and charged to expense at the acquisition date.

In addition, the Company incurred and expensed costs directly related to the Zikani Merger totaling approximately \$1.0 million during the year ended December 31, 2021, included in general and administrative expenses in the consolidated statement of operations.

Since the closing date of the Zikani Merger, the results of Zikani' s operations have been included in the Company' s consolidated financial statements.

17. Marketable Securities

Below is a summary of cash, cash equivalents and marketable securities at December 31, 2021 (in thousands):

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash and cash equivalents	\$ 42,268	\$ —	\$ —	\$ 42,268
Marketable securities - U.S. treasuries	—	—	—	—
Total cash, cash equivalents and marketable securities	\$ 42,268	\$ —	\$ —	\$ 42,268

As of December 31, 2022 and 2021, no credit losses were identified related to the cash equivalents or marketable securities. As of December 31, 2022, the Company did not have any marketable securities.

18. Fair Value Measurements

Assets and liabilities measured at fair value on a recurring basis as of December 31, 2022 are as follows (in thousands):

	Total	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Assets				
Money market funds included in cash and cash equivalents	\$ 18,737	\$ 18,737	\$ —	\$ —
Liabilities				
Embedded derivatives	\$ 45	\$ —	\$ —	\$ 45

The Company is party to certain funding awards with the Cystic Fibrosis Foundation, which contain embedded derivatives (refer to Note 9). As of the balance sheet date, the Company has determined the fair value of these embedded derivatives using a Monte Carlo simulation of the occurrence of a disposition event. The Company has used observable input assumptions such as the amount of funding, the Royalty Cap, as well as unobservable assumptions such as the time to occurrence of 3 years, as well as the probability of occurrence of a disposition event. The table below provides a rollforward of the fair value of the embedded derivatives, a Level 3 fair value estimate (in thousands), for the year ended December 31, 2022:

Fair value of embedded derivatives, December 31, 2021	\$ —
Change in fair value of embedded derivative liabilities	45
Fair value of embedded derivatives, December 31, 2022	\$ 45

19. Subsequent Events

On March 7, 2023, the Company and Hercules entered into the First Amendment to the Loan and Security Agreement (the "Hercules LSA Amendment") to amend the terms of the Hercules Loan Agreement. The amended terms provided for the Company to repay \$7.5 million of the outstanding principal, which the Company did on March 7, 2023. The Company will be required to make principal payments on the remaining \$5.0 million outstanding principal balance of the Term Loan Advances commencing on September 1, 2023 instead of the original Term Loan Amortization Date of April 1, 2023, plus interest, with a final maturity date of April 1, 2025. Any amounts outstanding under the Term Loan Advances, if not repaid sooner, are due and payable on April 1, 2025 (the "Maturity Date"). Further, the Company may prepay the outstanding amount of the Term Loan Advances at any time, plus accrued and unpaid interest, and with no prepayment premium. Additionally, the debt covenant that required the Company to maintain at all times a minimum qualified cash balance equaling amounts ranging from \$6.3 million to \$10.0 million (\$10.0 million in effect as of December 31, 2022) plus qualified accounts payable, was decreased to \$2.25 million effective as of March 7, 2023 and may be further reduced to \$0 if the Company has raised \$20.0 million in equity investments prior to May 31, 2023.