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, 2020

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	**84-1368850**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**

950 Winter Street
Waltham, Massachusetts 02451
(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 Global 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 and 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" or "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

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

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

The aggregate market value of the voting stock held by non-affiliates of the registrant on June 30, 2020, the last business day of the registrant's most recently completed second quarter, was $82,832,622, based on the closing price for such stock as reported on the NASDAQ Capital Market on that date.

As of March 8, 2021, there were 40,214,867 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 2021 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.

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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, or this Report, and the other documents we have filed with the U.S. Securities and Exchange Commission that are incorporated herein by reference, contain forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. In particular, you should consider the numerous risks described in the "Risk Factors" section in this Report.

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. 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.

This 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.

The following are some risks and uncertainties, among others, that could cause actual results to differ materially from those expressed or implied by forward looking statements in this Report:

- risks related to our ability to progress any product candidates in preclinical or clinical trials;
- 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 our ability to obtain the capital necessary to fund our operations;
- risks relating to the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- risks related to our ability to obtain adequate financing in the future through product licensing, public or private equity or debt financing or otherwise;
- general business conditions, regulatory environment, competition and market for our products; and
- business abilities and judgment of personnel, and the availability of qualified personnel.

PART I

ITEM 1. BUSINESS

Company Overview

We are a clinical-stage biopharmaceutical company developing novel ribonucleic acid (RNA)-modulating drug candidates, each designed to be a eukaryotic ribosomal selective glycoside (ERSG), formulated to treat rare and ultra-rare premature stop codon diseases. Premature stop codons are point mutations that disrupt the stability of the impacted messenger RNA (mRNA) and the protein synthesis from that mRNA. As a consequence, patients with premature stop codon diseases have reduced levels of, or no, protein from a gene whose product performs an essential function. This type of mutation accounts for some of the most severe phenotypes across genetic diseases. Nonsense mutations have been identified in over 1,800 rare and ultra-rare diseases. Read-through therapeutic development is focused on increasing functional protein synthesis by enabling the cytoplasmic ribosome to read through premature stop codons to produce full-length proteins. As opposed to a typical gene therapy approach of targeting a single, unique mutation in a target disease, this small molecule strategy enables targeting an entire class of mutations across the rare disease landscape. Our small molecule approach has the potential to address a range of different premature stop codons in a single gene since our ERSG compounds are targeted to the ribosomes. ELX-02, our lead investigational drug product candidate, is a small molecule designed to restore production of full-length functional proteins. ELX-02 is in clinical development for systemic administration for cystic fibrosis. ELX-02 is an investigational drug that has not been approved by any global regulatory body. We are also conducting IND-enabling preclinical studies of ERSG compounds for autosomal dominant polycystic kidney disease (ADPKD) and in rare inherited retinal disorders (IRDs) by intravitreal administration with an initial focus on Usher Syndrome. Our preclinical candidate pool consists of a library of novel ERSG drug candidates identified based on read-through potential and cytoplasmic ribosomal selectivity. We hold worldwide development and commercialization rights to ELX-02 and other novel compounds in our read-through library, for all indications, in all territories, under a license from the Technion Research and Development Foundation Ltd. (“TRDF”).

In 2019, we advanced our clinical program for ELX-02 into Phase 2 studies in cystic fibrosis and nephropathic cystinosis following completion of our MAD (multiple ascending dose) study in healthy volunteers and renal impairment study in healthy volunteers as well as volunteers with mild, moderate, and severe renal impairment. The results from the MAD study were presented in 2019 at both the European Cystic Fibrosis Society clinical meeting and the North American Cystic Fibrosis Conference (NACFC). The results have also been published in the *Journal of Clinical Pharmacology in Drug Development* in January of 2021. The results from the renal impairment study, were presented at the 2019 American Society of Nephrology (ASN) Kidney Week and published in December 2020 in the *Journal of Clinical Pharmacology*. The results from the renal impairment study, provided support for both continuing our clinical development programs and evaluating the suitability of our ERSG library for development in additional renal diseases, including ADPKD.

Our research and development strategy targets rare or ultra-rare diseases where a high unmet medical need exists, a nonsense mutation-bearing patient population is established, preclinical read-through can be established in predictive personalized medicine models, and a defined path through Orphan Drug development, regulatory approval, patient access and commercialization is identified. We believe patient advocacy is an important element of patient focused drug development, and we seek opportunities to collaborate with patient advocacy groups throughout the discovery and development process. Our current clinical program for our lead investigational drug product candidate, ELX-02, consists of Phase 2 studies in cystic fibrosis.

We intend to be the global leader in the application of the science of translational read-through and the associated pathway of nonsense mediated decay (NMD). We believe that expanding our expertise across these basic science areas of mRNA regulation, ribosomal function, and protein translation forms a solid foundation to support our discovery and development activities. Our ERSG compounds modulate the activity of the ribosome, a ribonucleoprotein complex of RNAs and proteins responsible for protein production (a process also known as translation). These novel small molecule ERSG compounds are designed to allow the ribosome to read-through a nonsense mutation in mRNA (which is transcribed from the DNA sequence), to restore the translation process to produce full-length, functional proteins and increase the amount of mRNA that would otherwise be degraded as part of a phenomenon called nonsense mediated mRNA decay. As our ERSG compounds target the general mechanism for protein production in the cell, we believe they have the potential to treat numerous genetic diseases where nonsense mutations have impaired gene function. Since nonsense mutations may occur at different positions within a given gene, a potential advantage of the small molecule ERSG approach is being able to use one molecule to address a range of mutations within a given disease state. Our subcutaneously injected ERSG molecules have the potential to be self-administered for systemic disease and to be active across many of the body’s tissues.

We believe that our library of related novel small molecules holds the potential to be disease-modifying therapies that may change the course of numerous genetic diseases and improve the lives of patients. Our early

preclinical data in animal models of nonsense mutations suggests that drug product candidates from our read-through compound ERSG library may have potential beneficial effects for each of the following diseases: cystic fibrosis, nephropathic cystinosis, ADPKD, a variety of IRDs (including Usher Syndrome), primary ciliary dyskinesia, mucopolysaccharidosis type 1, Duchenne muscular dystrophy and Rett syndrome, and have demonstrated the potential for beneficial effects in multiple organs such as the brain, eye, kidney, lungs, muscles and others. Of the novel compounds in our ERSG library, approximately 30 compounds have been selected, based on read-through activity, for continued preclinical research and we anticipate additional compounds advancing toward Investigational New Drug (IND) filings.

Our scientific manuscript titled “ELX-02 generates protein via premature stop codon read-through without inducing native stop codon read-through protein” was published in the August 2020 issue of the *Journal of Pharmacology and Experimental Therapeutics* (JPET). This manuscript demonstrates that while ELX-02 mediates read-through of premature stop codons, the fidelity of native stop codons found at the end of healthy transcripts is maintained. This indicates that translation integrity is preserved with target-therapeutic exposure of ELX-02, consistent with the favorable tolerability profile across our preclinical and clinical data sets.

Currently, the clinical program for our lead investigational drug candidate, ELX-02, is focused on development for cystic fibrosis patients with diagnosed nonsense mutations. We have completed a Phase 1 single ascending dose (SAD) trial, a multiple ascending dose (MAD) trial, and a renal impairment study with healthy volunteers as well as volunteers having mild, moderate and severe renal impairment. The results of the SAD study were published in *Clinical Pharmacology in Drug Development* in January 2019. The results from the MAD study were presented in 2019 at both the European Cystic Fibrosis Society clinical meeting and the North American Cystic Fibrosis Conference (NACFC). The results have also been published in the *Journal of Clinical Pharmacology in Drug Development* in January of 2021. The results from the renal impairment study were presented at the 2019 American Society of Nephrology (ASN) Kidney Week and published in December 2020 in the *Journal of Clinical Pharmacology*.

Our scientific review written by Professor Eitan Kerem, M.D., Senior Attending Physician at the Hadassah CF Center in Jerusalem, Israel and Senior Medical Consultant to Eloxx, titled “ELX-02: an investigational read-through agent for the treatment of nonsense mutation-related genetic disease” was published in October 2020 by the Journal *Expert Opinion on Investigational Drugs*. This manuscript details the development of ELX-02 for the restoration of functional protein in nonsense-mediated disease in support of our ongoing Phase 2 trials.

Our scientific manuscript titled “Targeting *G542X CFTR* Nonsense Alleles With ELX-02 Restores CFTR Function in Human-Derived Intestinal Organoids” was published in the *Journal of Cystic Fibrosis* in February 2021**.** This manuscript reviews the results of our evaluation of ELX-02 mediated read-though, using the CFTR-dependent Forskolin-induced swelling (FIS) assay across a selection of *G542X* homozygous and heterozygous patient-derived organoids, ELX-02 increased CFTR activity in a dose-dependent fashion across a variety of forskolin induction concentrations. The functional increases are similar to those obtained with tezacaftor/ivacaftor in an *F508del* homozygous organoid. Additionally, ELX-02 treatment of these patient-derived organoids results in a 5-fold increase in *CFTR* mRNA when compared with vehicle treated, resulting in normalization of *CFTR* mRNA as measured using Nanostring.

Our Phase 2 cystinosis trial involved two sequential cohorts with three escalating doses in three patients per cohort. The first cohort enrolled three homozygous W138X patients ages 23 to 38, with prior kidney transplants and varying degrees of renal insufficiency. In January 2020, we announced positive data from the first cohort of the Phase 2 study of ELX-02 in the treatment of patients with nonsense mutation-mediated nephropathic cystinosis. The results of the first cohort met the primary safety endpoint and the reductions in white blood cell (WBC) cystine provided a clear indication of biologic activity in these patients at nominal doses > 0.5 mg/kg/day. Following review of the safety and pharmacokinetic data by an independent Safety Review Committee (SRC), the SRC approved progressing to the second cohort that would enable enrolling patients ages 12 and older. Due to study design limitations, patients across all dose groups had elevated and uncontrolled pretreatment WBC cystine levels which made it difficult to fully evaluate ELX-02-mediated WBC cystine reductions. Therefore, we have discontinued this study and will not proceed with the second cohort as contemplated in the original protocol. We plan to continue to review these data with a panel of scientific and clinical experts to determine appropriate modifications for a possible new study design.

The clear indications of biologic activity in this study provide human clinical proof of concept for ELX-02 and de-risk other clinical applications of our ERSG library using this dosage range. These encouraging results also

provide a basis for expansion to studies of additional kidney diseases caused by nonsense mutations, such as ADPKD.

Our Phase 2 cystic fibrosis clinical trial program for ELX-02 is being conducted at leading global investigator sites in Europe, Israel and the United States. On March 25, 2020, we announced that enrollment in these trials had been paused temporarily in response to the global 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 had been resumed in Israel and Europe, and on August 12, 2020, we announced that enrollment had been resumed in the U.S. The COVID-19 pandemic continues to evolve, and we continue to work closely with our clinical sites and investigators. We are also evaluating additional clinical sites in other countries where patient enrollment may be feasible. We remain committed to completing enrollment in these Phase 2 proof of concept clinical trials and reporting top line data in the first half of 2021, which is contingent on no further disruptions due to the COVID-19 pandemic. Several planned Safety Review Committee meetings have occurred and allowed dose escalation up to the top dose level with no drug-related serious adverse events reported to date. Multiple patients have progressed through the four-dose escalation range. The Cystic Fibrosis Foundation ("CF Foundation") is providing funding for a portion of the U.S. program and in December of 2020, expanded its support to include our global clinical trial program. We have since formed a joint program advisory group with the CF Foundation focused on the development of ELX-02 for cystic fibrosis. The Cystic Fibrosis Therapeutics Development Network ("TDN") has sanctioned the Phase 2 study protocol, which is being conducted at TDN member sites. Additional information about our clinical trials can be found at www.ClinicalTrials.gov (Identifiers: NCT04126473 and NCT04135495).

Professor Eitan Kerem, M.D., former Head of the Division of Pediatrics, Children's Hospital, Hadassah Medical Center in Israel, has joined Eloxx as a Senior Medical Consultant. For the U.S. trial, Dr. Ahmet Uluer, Director of the Adult Cystic Fibrosis Program at the Boston Children's Hospital/Brigham and Women's Hospital CF Center, is the lead study investigator. The protocols have been sanctioned by the TDN in the U.S. and the European Cystic Fibrosis Society Clinical Trial Network (which has given our Europe/Israel trial a "high priority" ranking). During October 2019, we completed an interim CMC review meeting with the U.S. Food and Drug Administration (the "FDA") and we have gained alignment with the agency on our manufacturing formulation and process, which we believe will be suitable for our expected drug supply needs through completion of our pivotal trials. The in-person ECFS conference in Lyon, France scheduled for June 2020 was cancelled, and we withdrew our abstract. We presented data from two scientific abstracts at the North American Cystic Fibrosis Virtual Conference (NACFC). The two abstracts were also showcased in the NACFC virtual poster gallery and electronically published as a supplement to *Pediatric Pulmonology*. The live sessions and discussions took place through October 23, 2020. These virtual posters are available to registered attendees on the NACFC online conference platform. The preclinical study results demonstrate ELX-02's selectivity for read-through of premature stop codons versus native stop codons and its ability to restore production of functional *CFTR* in patient-derived organoids.

We believe there is a significant unmet medical need in the treatment of cystic fibrosis patients carrying nonsense mutations on one or both alleles of the CFTR gene. Cystic fibrosis is the most prevalent genetic disease in the western world and there are no currently approved therapies that target the impairment associated with Class 1 CFTR mutations. We believe that nonsense mutations may impact a similar proportion of patients diagnosed with cystinosis. Given the high proportion of pediatric patients in many rare orphan diseases, we intend to apply for relevant Orphan Drug incentives in the U.S. and Europe, including the Rare Pediatric Disease Priority Review Voucher in the U.S. Currently, the European Medicines Agency (the "EMA") has designated ELX-02 as an orphan medicine for the treatment of cystic fibrosis and mucopolysaccharidosis type I (MPS I). The FDA had previously granted orphan drug designation to ELX-02 for the treatment of nephropathic cystinosis, MPS I, and Rett syndrome, and on August 4, 2020, we announced that the FDA had granted orphan drug designation for ELX-02 for the treatment of cystic fibrosis. The FDA's Office of Orphan Drug Products grants orphan status to support the development of medicines for underserved patient populations, or rare disorders, that affect fewer than 200,000 people in the U.S. Orphan drug designation provides certain benefits, including seven years of market exclusivity upon regulatory approval (if received), exemption from FDA application fees, tax credits on qualified U.S. clinical trials and eligibility for grant funding opportunities that can be used for clinical trial costs.

We are also evaluating the suitability of our ERSG library for development in renal diseases associated with nonsense mutations, such as ADPKD. ADPKD is a relatively common inherited genetic kidney disease occurring in between one in 400 and one in 1,000 patients and is the fourth leading cause of end-stage renal disease in the U.S. Over 25% of the primary genetic changes that cause ADPKD are nonsense mutations, where a premature stop codon in the gene leads to a truncated, often unstable, protein. We have evaluated the three most relevant ADPKD nonsense mutations in an *in vitro* read-through assay and have demonstrated significant levels of read-through for ELX-02 and several library compounds, which is the first step in our preclinical development toward an IND.

We continue to progress our ERSG pipeline in IRDs, another area of high unmet medical need, that are associated with vision loss and blindness. There are over 300 IRDs associated with nonsense mutations. In 2020, we reported on a critical milestone demonstrating that several of our library compounds successfully reach retinal disorder-relevant tissue layers and can restore protein production in an animal model. These data support the suitability of our ERSG compounds for reaching and promoting read-through in target cells within the retina. We presented data at the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting in May 2020, which was held virtually. Our IRD research also includes exploring multiple sustained release formulation technologies, and *in vitro* release rates achieved to date have been consistent with our target release profile of one to three months. Our scientific manuscript titled "Intravitreal administration of small molecule read-through agents demonstrate functional activity in a nonsense mutation mouse model" was published in October 2020 by the *Journal of Experimental Eye Research*. This manuscript demonstrates that multiple small molecules in our ERSG library mediate dose-dependent read-through at the back of the eye after a single intravitreal injection. Collectively, our manuscripts demonstrate the wide-ranging potential of our small molecule read-through approach to rare genetic disorders mediated by nonsense mutations; from targeted delivery for inherited retinal disorders to systemic delivery for multi-system disorders like cystic fibrosis.

On February 24, 2020, our Board of Directors approved a leadership and organizational realignment aimed at supporting our efforts to improve operating performance and concentrate development efforts on our core programs. The organizational realignment reduced managerial layers and consolidated roles across the organization, resulting in the elimination of 13 full-time positions during the first quarter of 2020. We incurred a resulting one-time pre-tax charge of $4.0 million during the first quarter of 2020.

Our Technology

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. Nonsense mutations are involved in a large number of genetic diseases such as cystic fibrosis, nephropathic cystinosis, ADPKD, primary ciliary dyskinesia, and an estimated 300 IRDs, including Usher Syndrome. According to the Human Gene Mutation Database (http://www.hgmd.cf.ac.uk/ac/index.php), nonsense mutations account for approximately twelve percent (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.

In eukaryotic cells, the cytoplasmic ribosome is responsible for the production of proteins by a process called translation. As part of the translation process, the genetic information stored in DNA is transcribed to mRNA to specify the sequence of amino acids, the building blocks of protein, required to produce a functional product. The mRNA is decoded by a complex known as the ribosome in the cytoplasm of the cell. The ribosome ratchets along the mRNA and matches three nucleotide stretches, referred to as a codon, with a corresponding aminoacyl transfer RNA (a-tRNA) which carry the correct amino acid to add onto the growing protein chain.

Normal translation termination in eukaryotic cells occurs when a native (canonical) termination codon enters the ribosomal decoding region. The ribosome pauses at these special termination sequences, since there are no complementary a-tRNA for these codons. A complex of termination factors, including eRF1 and eRF3, will next bind to the ribosome and initiate the release of the newly synthesized protein.

When a nonsense mutation occurs, a single DNA nucleotide is substituted for the typical nucleotide, changing a codon for an amino acid into a stop codon. For example, a tryptophan "TGG" codon may be changed to read "TGA" or "TAG", either of which would result in a premature termination signal for the protein. While non-functional, truncated proteins can result from this type of mutation, more often the protein product is unstable and degraded. Since most genes have two copies (referred to as alleles) within the genome, a nonsense mutation on a single copy may be compensated if the other copy still codes for a functional protein. However, when mutations occur on both alleles, disease may occur. The two mutations can be the same mutation (homozygous) or two different disease-causing mutations (heterozygous).

Cells have a system to detect nonsense mutation bearing mRNA copies and remove them from the cell. This process is called nonsense mediated mRNA decay. During the first round of translation, the ribosome removes proteins that are found along the newly made mRNA at regions called exon-exon borders. These regions are remnants of a splicing process that occurs in the nucleus while the RNA is being transcribed. If a stop codon is found by the ribosome during this first round of translation in a location before the last of these exon-exon junction protein complexes, the mRNA is targeted for degradation. Therefore, nonsense mutations result in a “double hit” for the gene, unstable mRNA and reduced functional protein (shown in Figure 1 below).

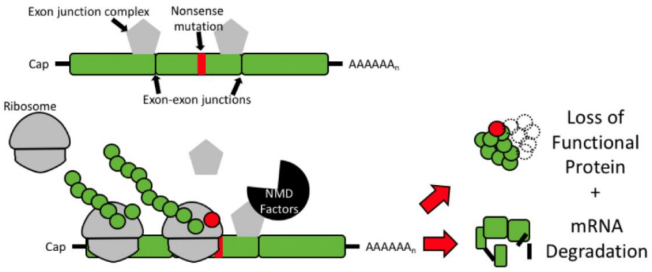

Figure 1: Nonsense Mutations Cause Unstable mRNA and Reduced Functional Protein

Read-through of nonsense mutations is a naturally occurring process that can be attributed to the redundancy “wobble” in the three-nucleotide codon structure. Native read-through occurs in up to 1% of instances in which a ribosome pauses at a stop codon. During read-through, either the typical healthy or a near-cognate substitute tRNA out-competes the termination factor complex to enable the insertion of an amino acid and continuation of translation. By directly binding to the ribosome decoding region, ELX-02 enhances the likelihood of this process by increasing the probability of a tRNA to out-compete the termination complex. As read-through allows the ribosome to proceed with translation through the premature stop, a reduction in nonsense mediated decay and stabilization of the mRNA pool is an additional expected outcome of this process (shown in Figure 2 below). Indeed, ELX-02 is found to increase both the mRNA and functional protein across multiple nonsense mutations. Beyond ELX-02, multiple compounds within our ERSG library demonstrate results consistent with this mechanism of action.

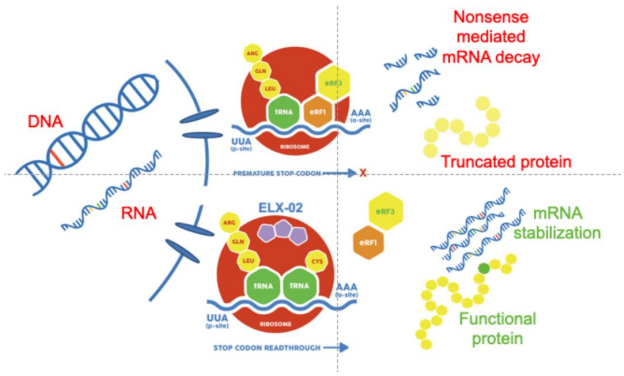

Figure 2: Read-through Allows the Ribosome to Proceed with Translation through the Premature Stop, Reducing mRNA Decay and Increasing the Translation of Functional Protein

We believe that the segment of cystic fibrosis, nephropathic cystinosis, ADPKD, and IRD 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. There are existing *in vitro* assays, animal models and/or biomarker screens that have been demonstrated to be useful in assessing the potential therapeutic benefit of development compounds for these disease states. The design of clinical trials and the endpoints for measuring clinical benefit have been established for the currently approved therapeutics for these disorders. We believe these to be attractive development targets based on the potential use of these precedents to de-risk the program.

Current Data Indicating the Mechanism of Action of ELX-02

ELX-02 is a novel ERSG with increased selectivity for the eukaryotic ribosome. In contrast, aminoglycoside antibiotics, such as gentamicin, are potent antibiotics that bind with high affinity to the decoding site in the prokaryotic ribosome and inhibit protein translation in bacteria as well as the eukaryotic ribosomes. The early observations of eukaryotic read-through activity were made in patients treated with aminoglycosides due to bacterial infections. In eukaryotic cells, aminoglycosides may induce a conformational change that reduces the codon-anticodon recognition, enhancing the ability of an a-tRNA to compete with the release factor complex for binding to the premature termination codon and increasing the probability that translational read-through of premature termination codons occurs. However, despite the promising clinical observations of read-through activity, aminoglycoside antibiotics use 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 has shown a 100-fold lower antibacterial activity and nine-fold higher read-through activity for nonsense mutations; this has been attributed 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, ERSGs are anticipated 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.

ERSGs with improved selectivity for the eukaryotic cytoplasmic ribosome are expected to demonstrate improved rates of full-length protein translation and a reduction in triggered nonsense mediated decay. By binding to the cytoplasmic ribosome and reducing ribosomal stalling, ERSGs are expected to demonstrate increases in mRNA and full-length protein production. Therefore, our read-through activity screening program has used these endpoints to evaluate our compound library portfolio.

Using a well-characterized cell line bearing a nonsense mutation, we are evaluating our compound library for both read-through mediated protein restoration and stabilization of mRNA. While plasmid-based evaluations offer a convenient methodology to evaluate across disease related mutations, this approach is limited to demonstrating the potential for protein restoration alone. Therefore, we have focused on using our molecules to detect read-through of a native mutation, which is subject to nonsense mediated decay, in order to better model an actual disease setting. In this cell line, the protein of interest and its mRNA are significantly reduced. 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.

Our mechanism of action is further supported within disease-relevant model systems, further detailed below. *In vitro* models of nephropathic cystinosis and cystic fibrosis demonstrate dose-dependent increases in target mRNA as well as significant increases in functional protein. Unlike previous read-through programs reported by other groups, our compounds have consistently demonstrated activity against both of these hallmark consequences of nonsense mutations. This understanding of our compounds' activity has enabled our clinical development programs to move forward with confidence.

Scope of Activities

We intend to be the global leader in the application of the science of translational read-through and the associated pathway of NMD.

Cystic Fibrosis

Cystic fibrosis (CF) is the most prevalent genetic disease in the western world and affects an estimated 70,000 to 100,000 patients worldwide, with the vast majority of affected individuals in the U.S., Canada, Europe, and Australia. CF is the most common fatal inherited disease in Caucasians. The incidence of CF varies across the globe ranging between one in 3,500 births in the U.S. and one in 2,000 to 3,000 births in Europe and Australia.

Approximately 12% of CF patients carry a nonsense mutation on the *CFTR* gene. CF is a progressive disease caused by a deficiency in CFTR activity with insufficient ionic transconductance in the cell membrane, which, in turn, leads to the accumulation of thick mucus in vital organs, particularly the lungs, pancreas and gastrointestinal tract. As a result, CF patients experience respiratory infections, chronic lung inflammation, and poor absorption of nutrients as well as many other conditions, and, in most cases, progressive respiratory failure. The life expectancy of CF patients has improved, and the CF Foundation has reported that a person born with cystic fibrosis (CF) between 2014 and 2018 can expect to live an average of 44 years.

CF occurs at a rate of one in 2,500 to 6,000 births, depending on the region and ethnic origin. Patients with CF caused by nonsense mutations have some of the most severe forms of the disease and, other than palliative therapies, no treatment currently exists for them. Mutations in the gene that encodes CFTR protein, which plays a critical role in regulating the viscosity of the mucus layer that lines human organs, cause CF. The CFTR protein forms an ion channel that regulates the flow of ions in and out of the cells of vital organs such as the lungs, pancreas and gastrointestinal tract. We refer to this as ion flow. In tissues like these, CFTR protein conducts ions leading to osmosis as water is drawn out of the cell hydrating the cell surface. Through regulation of the location of the ions across the cell membrane, the amount of salts in the fluid both inside and outside the cell remains balanced.

In CF patients, the *CFTR* gene is defective, and as a result, CF patients lack the functional CFTR protein ion channel necessary to regulate ion flow. An altered ion concentration gradient between the inside and the outside of the cell reduces the amount of water molecules outside the cell, causing the accumulation of thick mucus on the epithelial surface as shown below in Figure 3.

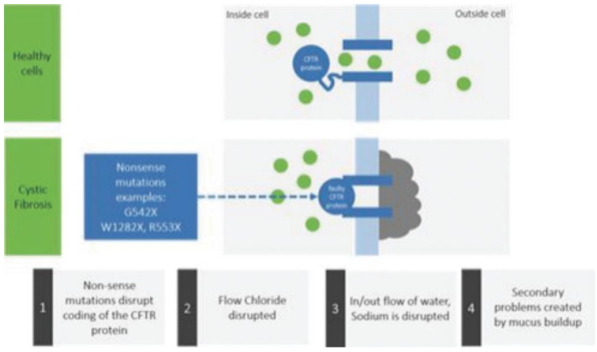

Figure 3: Ion Flow in Normal CFTR Protein Compared to Mutant CFTR Protein

The deficiency in CFTR protein activity in CF patients is particularly problematic in the lungs, where the build-up of thick mucus obstructs airflow and impairs proper immune response, which leads to chronic infection and persistent inflammation. In the pancreas and the gastrointestinal tract, the build-up of mucus prevents the release of digestive enzymes that help the body break down food and impairs the absorption of nutrients, resulting in poor growth and development.

Cystinosis

Cystinosis is an ultra-rare autosomal recessive lysosomal storage disease. Mutations in the *CTNS* gene (cystinosin), on the short arm of chromosome 17 (17p13), cause the primary defect in the disease. Cystinosin is a ubiquitous cystine-selective transport channel in the lysosomal membrane. Loss-of-function mutations prevent cystine efflux from the lysosome, causing massive accumulation of intra-lysosomal cystine in tissues throughout the body, and lead to apoptotic cell death, impaired physiology and end organ damage.

Affected children may appear fairly well until the age of 4 to 6 months, when progressive dysfunction and atrophy of the proximal renal tubule cause Fanconi syndrome and failure to thrive. By 10 to 12 years of age, dialysis or kidney transplantation is required to treat end-stage renal disease. Although the renal allograft is spared, lifespan is diminished by the inexorable dysfunction of other organs.

The most common nonsense mutation in the *CTNS* gene is *W138X*, which has an overall incidence rate of one in every 62,500 live births in Quebec, Canada.

Current treatment includes cysteamine bitartrate (Cystagon® or Procysbi®). Cystagon was approved in the U.S. and Europe in 1994 and Procysbi was approved in the U.S. and Europe in 2013. Both therapies delay but do not cure the condition and despite treatment, patients eventually require dialysis and renal transplantation and experience significant morbidity in other organ systems. See above for information about our Phase 2 clinical trial in nephropathic cystinosis.

Autosomal Dominant Polycystic Kidney Disease

Polycystic Kidney Disease (PKD) is a progressive genetic disorder causing the growth of cysts in the kidneys, reducing kidney function and ultimately leading to kidney failure or end stage renal disease. It is found in all races and occurs equally in men and women. The autosomal dominant form of polycystic kidney disease (ADPKD) is the most common genetic nephropathology, accounting for 5 to 8% of end stage renal disease. Worldwide, ADPKD affects approximately 4 to 7 million individuals and accounts for 7 to 15% of patients on renal replacement therapy. In North America and Europe, ADPKD is responsible for 6 to 10% of end stage renal disease cases. It is estimated that one per 800 to 1,000 in the population carries a mutation for this condition.

Approximately 85 to 90% of patients with ADPKD have the mutations in the *PKD1* gene; most of the remaining patients have the *PKD2* gene. Estimates suggest over 30% of ADPKD mutations are nonsense variants and therefore represent a favorable target for read-through therapeutics given the large patient population, substantial subset of nonsense mutations, disease severity and limited treatment options. We have evaluated the three most relevant ADPKD nonsense mutations in an *in vitro* read-through assay and have demonstrated significant levels of read-through for ELX-02 and several library compounds which is the first step in our preclinical development toward IND.

Inherited Retinal Disorders

Inherited retinal disorders (also called inherited retinal dystrophies, or IRDs) are a group of rare eye disorders caused by inherited gene mutations which can result in vision loss or blindness. Some IRDs, such as Retinitis Pigmentosa (RP), Usher Syndrome, or Choroideremia (CHM) are associated with a gradual loss of vision, eventually leading to complete blindness. In other conditions such as Leber's Congenital Amaurosis (LCA), patients may be born with or experience vision loss in infancy or early childhood.

Usher Syndrome is the most common genetic disorder involving hearing and vision abnormalities and is the most common cause of deafness-blindness with visual impairment due to photoreceptor degeneration. Three types of Usher Syndrome have been identified based on genetic causes, severity of hearing loss and age of onset. USH1 patients are typically born with severe hearing loss and are diagnosed early in life with vision problems beginning at or before age 10. USH2 patients are characterized by progressive hearing loss from birth, with onset of vision loss at adolescence. USH3 has the slowest progression, with vision loss developing in the second decade of life. In most countries, USH1 accounts for one-third of all patients with USH2 accounting for about two-thirds of all USH patients. U.S. prevalence is estimated at approximately 6,200 Type 1 and approximately 8,900 Type 2 patients. It is estimated that there are over 4,000 patients in North America with nonsense forms of Usher Syndrome. Effective read-through has been demonstrated in vitro for *USH2A* (USH2), *PCDH15* (USH1) and *USH1C* (USH1) nonsense mutations. *USH2A* nonsense variants are estimated to affect more than 2,500 patients in the U.S. alone. There are four *USH2A* splice site variants, with the largest having over 70 exons, potentially limiting gene therapy development due to vector size limitations.

RP causes night blindness in adolescence and gradual visual field loss in adulthood (most patients are legally blind by age 40). RP can occur as a localized disorder with visual impairment only, or as part of a broader syndrome (e.g., Usher Syndrome). More than 50 different causative genes have been identified and the U.S. incidence is estimated at approximately 67,000 patients. Given this high genetic heterogeneity even in nonsense mediated disease (no single gene comprises more than 10% of RP cases), there is a significant need to identify broader cross-gene therapies. Read-through proof of principle has been shown via *in vitro* models of *USH2A*, *RHO*, *MERTK*, and *RP2* nonsense mutation variants, with 5 to 20% rescue of protein function demonstrated.

In December 2017, the FDA approved Spark Therapeutics' LuxturnaÒ as the first gene therapy for retinal dystrophy caused by mutations in the RPE65 gene and targeting approximately 1,000 to 2,000 patients with confirmed biallelic *RPE65* mutation-associated retinal dystrophy. While many gene therapies focus on specific IRDs, many target genes share related ocular disease pathways, suggesting a broader gene-agnostic approach may provide greater treatment opportunities. IRDs such as Usher Syndrome and RP represent favorable targets for read-through therapeutics given the high unmet need and the opportunity to target multiple nonsense mutations across a variety of genes. Read-through therapeutics offer potential treatment for patient subsets not addressed by gene therapy due to gene size or small patient subsets.

Primary Ciliary Dyskinesia

Primary Ciliary Dyskinesia (PCD) is a genetically heterogeneous disease which is predominantly inherited as an autosomal recessive disorder. PCD is associated with abnormal ciliary function resulting in impaired mucociliary clearance, recurrent/chronic upper and lower respiratory tract infection and male infertility. PCD prevalence is estimated to involve one in 20,000 individuals; however, disease symptom variability and low familiarity with PCD likely leads to substantial patient under-diagnosis. PCD patient treatment largely focuses on airway clearance (devices and aerosolized therapies), infection control (anti-microbial therapy), and inflammation control (antibiotic therapy). There have been few randomized trials of PCD treatment to date.

More than 30 different genes have been identified to be causative for PCD with approximately 25% of identified gene mutations having nonsense mutations. *In vitro* studies of aminoglycoside-mediated read-through in PCD nonsense mutations found positive read-through efficacy in several UGA-associated stop codons. PCD is an attractive disease target given the high unmet medical need, positive preclinical read-through data, potential for treatment across multiple genes, high prevalence of nonsense mutations, and lack of disease modifying treatments.

Other Nonsense Mediated Genetic Disorders

Muscular dystrophies are genetic disorders involving progressive muscle wasting and weakness. Duchenne muscular dystrophy (DMD) is the most common and one of the most severe types of muscular dystrophy with the average age of death for DMD patients in the mid-twenties. DMD occurs when a mutation in the dystrophin gene prevents the cell from making a functional dystrophin protein. Because the dystrophin gene is located on the X chromosome, DMD occurs almost exclusively in young boys. Genetic tests are available to determine if a patient's DMD is caused by a nonsense mutation. Based on a publication from Prior, et al. (1995) in the *American Journal of Human Genetics*, it is estimated that a nonsense mutation is the cause of DMD in approximately 13% of patients. Treatments for DMD include Translarna™ (ataluren), approved in the European Union ("EU") for the treatment of the underlying cause of DMD. EXONDYS 51® (eteplirsen) injection is also approved in the U.S. for the treatment of DMD patients with exon 51 skipping mutations.

Mucopolysaccharidosis type I (MPS I) is a chronic, progressive genetic disorder caused by a deficiency of the enzyme alpha-L-iduronidase (IDUA). Children with severe MPS I often die in the first decade of life due to respiratory failure, cardiac valvulopathy, and cardiorespiratory problems. The deficiency of the IDUA enzyme leads to the accumulation of a class of molecules called glycosaminoglycans (GAGs). The accumulation of GAGs causes disruption in the movement of molecules inside the cell and leads to the subsequent dysfunction of cells, tissues and organs. Globally, MPS I occurs in about one in every 100,000 births for the severe form and one in 500,000 for the attenuated form. About 70% of MPS I patients carry one of two nonsense mutations: *Q70X* and *W402X*. Estimates suggest that 50 to 80% of all MPS I patients present with the severe versus attenuated form of the disease. MPS I disease-specific treatments include enzyme replacement therapy and hematopoietic stem cell transplantation.

Rett syndrome is a X-linked neurodevelopmental disorder that predominantly affects girls and has a worldwide incidence of one in every 10,000 to 15,000 female births. The condition generally follows normal development in the first 6 to 18 months of age, followed by a period of regression in language and motor skills including repetitive stereotyped hand movements. Rett syndrome patients also have numerous comorbidities that are thought to contribute to a shortened lifespan. There is a high unmet medical need in Rett syndrome given no current treatment exists for the underlying cause of the disease. Loss-of-function mutations in the gene encoding the transcriptional regulator *methyl-CpG binding protein 2* ("*M*ECP*2*") account for most cases of Rett syndrome. Nonsense mutations in the *M*ECP*2* gene account for approximately 30% of Rett syndrome cases. The most prominent nonsense mutations found in Rett syndrome, *R168X*, *R255X*, *R270X* and *R294X*, are all caused by a change of arginine to the stop codon, UGA.

Status of Clinical Programs

We have completed our Phase 1a and Phase 1b studies of ELX-02. In support of our Phase 2 studies currently underway, we have advanced our global health authority interactions and manufacturing activities.

Phase 1 Clinical Studies

We completed a Phase 1 program in healthy volunteers designed to support studies of ELX-02 in patient populations in any indication caused by nonsense mutations and assess the safety of ELX-02. This phase of testing included a small number of healthy volunteers. The studies assessed the effects of ELX-02 on humans and measured bioavailability, excretion, safety and side effects, as well as the pharmacokinetics (what the body does to the drug) with increasing doses. Our Phase 1 studies included SAD and MAD studies.

The Phase 1a SAD study was completed in 2018 and the results were published in *Clinical Pharmacology in Drug Development* in January 2019. The SAD study included five doses of ELX-02 ranging from 0.3 mg/kg to 7.5 mg/kg in order to determine the pharmacokinetic profile and safety from single administration. ELX-02 was shown to be generally well tolerated over the dose range with no observations of renal toxicity. During the study, observations of transient adverse events resulting from ELX-02 administration were mild with the exception of a single moderate auditory adverse effect of interest but of unclear physiological significance and without clinical impact. Overall the results were supportive of continued clinical development.

In 2019, we completed a Phase 1b MAD study for ELX-02. The study was designed as a randomized, double-blinded, placebo-controlled, multiple dose escalating study in healthy subjects. The study was expanded to include additional cohorts to evaluate lower drug concentrations and/or administration schedule. In addition, we completed a renal study with ELX-02 in subjects with mild, moderate, and severe renal impairment. The results from the renal impairment study provided support for both continuing our clinical development programs and evaluating the suitability of our ERSG library for development in additional renal disorders, including ADPKD and cystinuria.

The results from the MAD study were presented in 2019 at both the European Cystic Fibrosis clinical meeting and the North American Cystic Fibrosis Conference (NACFC). The results have also been published in the *Journal of Clinical Pharmacology in Drug Development* in January of 2021. The results from the renal impairment study were presented at the 2019 American Society of Nephrology (ASN) Kidney Week and published in December 2020 in the *Journal of Clinical Pharmacology*.

Phase 2 Clinical Studies

Currently, our Phase 2 clinical trial program for our lead investigational drug candidate, ELX-02, is focused on development for cystic fibrosis patients with diagnosed nonsense mutations.

Our Phase 2 program for ELX-02 is actively dosing patients and continuing to enroll patients at leading global investigator sites in the U.S., Europe and Israel. We expect to achieve full enrollment and report top line results during the first half of 2021. The CF Foundation is providing funding for a portion of the US program and in December of 2020, expanded its support to include our global clinical trial program. We have since formed a joint program advisory group with the CF Foundation focused on the development of ELX-02 for cystic fibrosis.

For the U.S. trial, Dr. Ahmet Uluer, Director of the Adult Cystic Fibrosis Program at the Boston Children’s Hospital/Brigham and Women’s Hospital CF Center, is the lead study investigator. The protocols have been sanctioned by the TDN in the U.S. and the European Cystic Fibrosis Society Clinical Trial Network (which has given our Europe/Israel trial a “high priority” ranking). In October 2019, we completed an interim CMC review meeting with the FDA, and we have gained alignment with the agency on our manufacturing formulation and process, which we believe will be suitable for our expected drug supply needs through completion of our pivotal trials.

Status of Preclinical Programs

We have completed a comprehensive series of preclinical studies to assess the safety, pharmacokinetics and pharmacology of ELX-02. In addition, we have verified read-through activity of additional library molecules and identified a set of promising candidate molecules to evaluate across new indications such as ADPKD. We have also continued our preclinical assessment of activity of our ELX compounds in IRDs, validating read-though activity against several Usher Syndrome mutations and initiating ocular tolerability and IND-enabling studies. We are also progressing preclinical development of our compounds in ADPKD.

Safety and Pharmacokinetic Studies of ELX-02

A comprehensive toxicology program in accordance with the ICH guideline M3 (R2) was completed for ELX-02 to support clinical studies.

In definitive, 28-day, repeat-dose toxicity studies in rats and dogs, ELX-02 had little or no effect on body weight, food consumption, clinical signs of toxicity, ophthalmology, cardiovascular parameters, hematology or coagulation parameters. At dose levels higher than those intended for humans, ELX-02 has no cochlear toxicity as evidenced in anatomic and functional hearing studies in 28-day rat studies. We completed 3-month toxicology studies in juvenile rats and in young dogs, as well as chronic toxicology studies in these two species for 6 and 9months, respectively. These studies showed no mortality and no significant in-life toxicity. ELX-02 was not genotoxic in the core battery of in vitro and in vivo genotoxicity assays. Collectively, these results support the human lifetime use of ELX-02. ELX-02 is 98% bioavailable following sub-cutaneous administration. Additionally, ELX-02 does not undergo metabolization and is excreted unchanged almost exclusively via the urine.

Pharmacology Studies of ELX-02

We have conducted a series of preclinical studies to demonstrate the primary pharmacodynamics of ELX-02 in several genetic disease indications. We have tested the translational read-through capabilities of ELX-02 *in vitro* and *in vivo*, in cells and in animal models of nonsense mutations.

We have shown the *in vitro* read-through activity of ELX-02 in an array of plasmids engineered to contain nonsense mutations of genetic diseases and in cell-based models of CF, cystinosis, DMD, MPS I, and Rett syndrome.

In CF, ELX-02 induced about 30% of wild-type CFTR levels after 48 hours in heterozygous *G542/F508del* human bronchial epithelial cells. In the *G542X* transgenic mouse, ELX-02 showed an approximate 5-fold increase in CFTR activity compared to control after twice weekly treatment for four weeks with 60 mg/kg.

In order to evaluate read-through across a series of CF genotypes, we initiated a program to evaluate restoration of CFTR activity in patient-derived organoids. An organoid is a three-dimensional, multi-cellular *in vitro* system derived from stem cells isolated from rectal biopsies. When grown suspended in an extracellular matrix substrate, the cells adopt a polarized endothelial spheroid structure. CFTR protein localizes to the apical surface (the inner surface of the sphere) and is capable of driving chloride ions into the inner lumen. When an ion imbalance, relative to the ion concentration surrounding the organoid is present, water is driven into the inner lumen of the organoid as a means to equilibrate the concentration. This action results in the swelling of the organoid, a function measurable by high-content imaging. Similar to measuring CFTR conductivity in other systems, such as human bronchial epithelial cells, CFTR activity is stimulated in the organoid system with forskolin to produce cyclic adenosine monophosphate, a signaling molecule that stimulates CFTR channel activity. Organoids derived from nonsense mutation CF patients lack apparent swelling in this system due to their lack of functional CFTR. As a stem cell derived system, organoids are a renewable model permitting repeat testing from a single patient's biopsy. We partner with Hubrecht Organoid Technology (HUB), a not-for-profit organization founded out of the Hubrecht Institute, KNAW and University Medical Center Utrecht in the Netherlands to evaluate the nonsense-bearing CF patient organoids in its biobank. These studies demonstrate that across the most common CF causing nonsense alleles (*G542X*, *W1282X*, *R553X*, *R1162X*, *R1066C* and *E60X*) accounting for greater than 75% of the CF nonsense allele population, ELX-02 significantly increases CFTR function and *CFTR* mRNA in a dose dependent fashion. ELX-02 mediated CFTR function is observed in both homozygous and complex heterozygous nonsense bearing patient-derived organoids. ELX-02 is the first clinical development candidate molecule to demonstrate activity against these nonsense mutations in the organoid model system. Activity in the organoid swelling assay is dependent on both proper production and localization of functional CFTR protein; therefore, the activity observed with ELX-02 supports that the CFTR protein resulting from read-through of these mutations is both functional and localized to the correct cellular location. *CFTR* mRNA levels were monitored by NanoString, which demonstrated that *G542X* and *W1282X* CF organoids have the expected reduction in *CFTR* mRNA resulting from nonsense mediated decay. ELX-02 increased *CFTR* mRNA dose-dependently to the range observed in healthy organoids. While approved CF therapies lack efficacy against this type of CF mutation, organoids with responsive mutations (e.g. *G551D*, *F508del*) demonstrate activity in the organoid swelling assay in a manner that correlates with clinical responsiveness in informative endpoints such as FEV1 and sweat chloride change. When considering the ELX-02 results with the correlation reports of other approved molecules in this assay, the response mediated by ELX-02 read-through meets or exceeds the activity necessary to significantly improve FEV1 and sweat chloride concentration. We continue to evaluate new organoid genotypes in an effort to prioritize additional nonsense alleles for inclusion in future clinical trials.

Eloxx is a member of the European HIT-CF project consortium, a European Union-funded preclinical and clinical research program evaluating the efficacy and safety of disease modifying drug candidates, including ELX-02, in CF patients with rare genetic mutations. The goal of the project is to investigate whether a positive response to therapies in a patient derived organoid can be predictive of clinical response in a controlled trial.

HIT-CF represents a new era in CF treatment and personalized medicine, as it has the potential to shift therapeutic trials from patients to the laboratory. HIT-CF has informed Eloxx that over 100 organoids from unique individuals with rare nonsense mutations have already been enrolled in the program and preclinical drug response screening is ongoing. The HIT-CF consortium plans to complete the preclinical stage and initiate the clinical phase in 2021.

In cystinosis, ELX-02 increased read-through of the *CTNS W138X* mutation by 30-fold in a cell-free plasmid assay system. In primary homozygous *W138X* fibroblasts, ELX-02 led to a dose-dependent increase in normalized *CTNS* mRNA levels, consistent with a decrease in nonsense mediated mRNA decay. Functional protein restoration was supported in primary fibroblasts by demonstrating an ELX-02 mediated reduction in cellular cystine levels to wild-type levels. When combined with the standard of care, cysteamine, ELX-02 reduction in cellular cystine levels was additive. These data support that ELX-02 has the potential to impact the primary etiology of this ultra-rare disease.

In IRDs, a series of academic collaborations have shown that our candidate compounds demonstrate dose-dependent increases in read-through of Usher Syndrome 2A and 1F mutations in a cellular plasmid-based reporter assay; they also show restoration of Usher 1C protein and harmonin. Upcoming studies will confirm these findings. We are also evaluating multiple compounds for ocular tolerability, as measured by preservation of the electroretinogram and retinal histology, when delivered by intravitreal injection in rabbits. These studies demonstrate that our compounds have a favorable tolerability profile in comparison to the reference aminoglycoside, gentamicin. These findings are consistent with our hypothesis that the improved specificity for the eukaryotic cytosolic ribosome over the mitochondrial ribosome will reduce off-target associated toxicities.

Ongoing Screening and IND-Enabling Studies of Eloxx ERSG Library Compounds

Screening of our ERSG library in new indications has provided a foundation for expansion into additional therapeutic efforts. In new indications, compounds are evaluated for read-through potential against prevalent gene-specific nonsense mutations, tissue exposure and functional evidence of the target protein's production. This data-centric approach enables selection of the ideal ERSG and establishes the preclinical assays required for our genetics-based personalized medicine strategy in new indications. We believe that one or more of these preclinical ERSG drug candidates are potentially suitable for clinical development and we are continuing to conduct pre-IND studies to evaluate their potential.

Manufacturing Status

We have completed the manufacture of the clinical drug product to support our full Phase 2 clinical trial program. We have further identified a commercial manufacturer and are engaged in process development and scale-up activities required to support Phase 3 clinical development. In October 2019, we completed an interim CMC review meeting with the FDA, and we have gained alignment with the agency on our manufacturing formulation and process, which we believe will be suitable for our expected drug supply needs through completion of our pivotal trials.

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 these 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 with TRDF dated August 29, 2013. As of December 31, 2020, this family included issued patents in the U.S., Europe, Canada, Hong Kong, Israel and Japan, and pending applications in the U.S., India, and Israel. Issued patents in this family includes 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, 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 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 current 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, 2020, this family included pending applications in the U.S., Europe, Australia, Brazil, Canada, China, Hong Kong, Israel, India, and Japan. Any patents issuing 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, 2020, this family includes a pending Patent Cooperation Treaty (“PCT”) application. 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 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, 2020, this family included issued patents in the U.S., Europe, Canada, India, Israel and Japan, and pending applications in the U.S. 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 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, 2020, this family included an issued patent in the U.S. and pending applications in the U.S., Europe, Australia, Brazil, Canada, China, Hong Kong, India, Israel and Japan. The other family includes pending applications in the U.S., Europe, Australia, Brazil, Canada, China, Hong Kong, Israel, India, and Japan. Patents that have issued or which ay 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 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, 2020, this family included pending applications in the U.S., Europe, Australia, Brazil, Canada, China, EAPO, 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 that we may be granted.

We own one additional patent family directed to the use of various Eloxx read-through inducing compounds to treat polycystic kidney disease (PKD). As of December 31, 2020, this family included one pending PCT application. Any patents that may issue in the future from this family are currently expected to expire in 2040, not including any extensions of term for which we may be eligible that we may be granted.

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 U.S., patent term may be extended in certain instances by patent term adjustment, or 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 Europe, 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.

On August 29, 2013, we entered into a license agreement with TRDF (the "Technion Agreement"), which was further amended and addended to reflect, inter alia, 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.

Manufacturing

ELX-02 is 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 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

Drug Development and Approval in the United States

The preclinical studies and clinical testing, manufacture, labeling, storage, record keeping, advertising, promotion, export, and marketing, among other things, of our product candidates are subject to extensive regulation by governmental authorities in the U.S., the EU and other territories. In the U.S., pharmaceutical products are regulated by the FDA under the Federal Food, Drug, and Cosmetic Act (the "FDCA") and other laws, including, in the case of biologics, the Public Health Service Act. Failure to comply with FDA requirements, both before and after product approval, may subject us and/or our partners, contract manufacturers, and suppliers to administrative or judicial sanctions, including FDA refusal to approve applications, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, fines and/or criminal prosecution.

The process for obtaining regulatory approval to market a medicine is expensive, often takes many years, and can vary substantially based on the type, complexity, and novelty of the product candidate involved. The steps required before a drug may be approved for marketing of an indication in the U.S. generally include:

(a) preclinical laboratory tests and animal tests;

(b) submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials may commence;

(c) adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate for its intended use;

(d) submission to the FDA of an NDA;

(e) FDA pre-approval inspection of the manufacturing and clinical study sites identified in the NDA; and

(f) FDA review and approval of the NDA.

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as toxicological and pharmacological animal studies to assess the potential safety and efficacy of the product candidate. Preclinical safety tests intended for submission to FDA must be conducted in compliance with FDA's current Good Laboratory Practice ("cGLP") regulations and the U.S. Department of Agriculture's Animal Welfare Act. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND application that must become effective before human clinical trials may be commenced. The IND will automatically become effective 30 days after receipt by the FDA, unless the FDA before that time raises concerns about the drug candidate or the conduct of the trials as outlined in the IND. The IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can proceed. We cannot assure you that submission of an IND will result in FDA authorization to commence clinical trials or that once commenced, other concerns will not arise. The FDA may stop the clinical trials at any time by placing them on "clinical hold" because of concerns about the safety of the product being tested, or for other reasons.

Clinical trials involve the administration of the investigational product to healthy volunteers or to patients, under the supervision of qualified principal investigators. The conduct of clinical trials is subject to extensive regulation, including compliance with the FDA's bioresearch monitoring regulations and current Good Clinical Practice ("cGCP") requirements, which establish standards for conducting, recording data from, and reporting the results of clinical trials, and are intended to assure that the data and reported results are credible and accurate, and that the rights, safety, and well-being of study participants are protected.

Clinical trials must be conducted in accordance with protocols that detail the objectives of the study, the criteria for determining subject eligibility and ineligibility, the dosing plan, patient monitoring requirements, timely reporting of adverse events, and other elements necessary to ensure patient safety, and any efficacy criteria to be evaluated. Each protocol must be submitted to FDA as part of the IND; further, each clinical study at each clinical site must be reviewed and approved by an independent institutional review board, or IRB, prior to the recruitment of subjects. The IRB's role is to protect the rights and welfare of human subjects involved in clinical studies by evaluating, among other things, the potential risks and benefits to subjects, processes for recruiting subjects and obtaining informed consent, monitoring of data to ensure subject safety, and provisions to protect the subjects' privacy. Foreign studies conducted under an IND application must meet the same requirements that apply to studies being conducted in the U.S. Data from a foreign study not conducted under an IND may be submitted in support of an NDA if the study was conducted in accordance with cGCP and FDA is able to validate the data.

Clinical trials are typically conducted in three sequential phases, but the phases may overlap, and different trials may be initiated with the same drug candidate within the same phase of development in similar or differing patient populations. Phase 1 studies may be conducted in a limited number of patients but are usually conducted in healthy volunteer subjects. The drug is usually tested for safety and, as appropriate, for absorption, metabolism, distribution, excretion, pharmacokinetics and pharmacodynamics. Phase 2 usually involves studies in a larger, but still limited patient population to preliminarily evaluate the efficacy of the drug candidate for specific, targeted indications; to determine dosage tolerance and optimal dosage; and to identify possible short-term adverse effects and safety risks. Phase 3 trials are undertaken to gather additional information to evaluate the product's overall risk-benefit profile, and to provide a basis for physician labeling. Phase 3 trials evaluate clinical efficacy of a specific endpoint and test further for safety within an expanded patient population at geographically dispersed clinical study sites. Phase 1, 2 or 3 testing might not be completed successfully within any specific time period, if at all, with respect to any of our product candidates. Results from one trial are not necessarily predictive of results from later trials. Furthermore, the FDA, sponsor, IRB or the Data Safety Monitoring Board ("DSMB") for a trial may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

We must register each controlled clinical trial, other than Phase 1 trials, on a website administered by the NIH (http://clinicaltrials.gov). Registration must occur not later than 21 days after the first patient is enrolled, and the submission must include descriptive information (e.g., a summary in lay terms of the study design, type and desired outcome), recruitment information (e.g., target number of participants and whether healthy volunteers are accepted), location and contact information, and other administrative data (e.g., FDA identification numbers). Within one year of a trial's completion, information about the trial including characteristics of the patient sample, primary and secondary outcomes, trial results written in lay and technical terms, and the full trial protocol must be submitted to the ClinicalTrials.gov databank. The results information is posted to the website unless the drug has not yet been approved, in which case the NIH posts the information shortly after approval. An NDA, and certain other submissions to the FDA, require certification of compliance with these clinical trials database requirements. There are proposals to expand the applicability of these registration requirements to additional studies.

The results of the preclinical studies and clinical trials, together with other detailed information, including information on the manufacture and composition of the product and proposed labeling for the product, are submitted to the FDA as part of an NDA requesting approval to market the product candidate for a proposed indication. Under the Prescription Drug User Fee Act, as amended, the fees payable to the FDA for reviewing an NDA, as well as annual fees for commercial manufacturing establishments and for approved products, can be substantial. The NDA review fee alone can exceed $2.87 million subject to certain limited deferrals, waivers and reductions that may be available to a qualifying NDA sponsor for a specific NDA. Each NDA submitted to the FDA for approval is typically reviewed for administrative completeness and reviewability within sixty days following submission of the application. If the FDA finds the NDA sufficiently complete, the FDA will "file" the NDA, thus triggering a full review of the application. The FDA may refuse to file any NDA that it deems incomplete or not properly reviewable at the time of submission. Current FDA performance goals provide for action on 90% of standard applications for a new molecular entity within 10 months of the 60-day filing date. However, the FDA may not approve a drug within these established timeline goals and its review clock for a particular NDA is subject to change from time to time because the review process is often significantly extended by FDA requests for additional information or clarification. We may encounter difficulties or unanticipated costs in our efforts to secure necessary FDA approvals, which could delay or preclude us from marketing our product candidates. As part of its review, the FDA may refer applications for novel drug products or drug products that present difficult questions of safety or efficacy to an advisory committee composed of outside experts, for evaluation and a recommendation as to whether the application should be approved and under what conditions. The advisory committee process may cause delays in the approval timeline. The FDA is not bound by the recommendation of an advisory committee, but it considers such recommendations carefully, particularly after negative recommendations or limitations, when making drug approval decisions.

Further, the outcome of the FDA review process, even if generally favorable, may not be an actual approval but instead a "complete response letter" communicating the FDA's decision not to approve the application at that time, outlining the deficiencies in the NDA that need to be addressed in order to be eligible for approval, and identifying what information and/or data (including any additional preclinical or clinical data or manufacturing information) is required before the application can be approved. Even if such additional information and data are submitted, the FDA may decide that the NDA still does not meet the standards for approval. Data from clinical trials are not always conclusive, and the FDA may interpret data differently than we do.

The development testing and approval processes require substantial time, effort and financial resources, and each may take years to complete. Data obtained from clinical trials are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all.

The FDA typically will inspect one or more clinical sites to assure compliance with cGCP before approving an NDA. The FDA also will inspect the facility or the facilities at which the product is manufactured before the NDA is approved to assure compliance with cGMP. The FDA will not approve the product unless cGCP and cGMP compliance is satisfactory. The FDA may also take into account results of inspections performed by certain counterpart foreign regulatory agencies in assessing compliance with cGCP or cGMP. The FDA has entered into international agreements with foreign agencies, including the EMA, in order to facilitate this type of information sharing. If the FDA determines the application, clinical sites, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the NDA submission and often will request additional testing or information.

The FDA may deny approval of an NDA if applicable statutory or regulatory criteria are not satisfied, or may require additional testing or information, which can delay the approval process. FDA approval of any application may include many delays or may never be granted. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that an NDA does not satisfy the regulatory criteria for approval. If a product is approved, the approval will impose limitations on the indicated use or uses for which the product may be marketed, may require that warning statements be included in the product labeling, and may require that additional studies be conducted following approval as a condition of the approval. The FDA may limit the indications for use, approve narrow labeling relegating a drug to second-line or later-line use, add limitations of use to the labeling or place other conditions on approvals, which could restrict the marketing of an approved product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. FDA also may impose restrictions and conditions on product distribution, prescribing or dispensing in the form of a Risk Evaluation Mitigation Strategy ("REMS") to ensure the safe use of the drug, or otherwise limit the scope of any approval. In determining whether a REMS is necessary, the FDA must consider the size of the population likely to use the drug, the seriousness of the disease or condition to be treated, the expected benefit of the drug, the duration of treatment, the seriousness of known or potential adverse events, and whether the drug is a new molecular entity. A REMS may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate health care providers of the drug's risks, limitations on who may prescribe or dispense the drug, or other measures that the FDA deems necessary to assure the safe use of the drug. To market an approved product for other indicated uses, or to make certain manufacturing or other changes, FDA review and approval of an NDA Supplement or new NDA are required, which may themselves necessitate further clinical testing, and the payment of applicable review fees. Additional post-marketing testing and surveillance to monitor the safety and/or efficacy of a product may be required. In addition, new government requirements may be established that could delay or prevent regulatory approval of our product candidates under development.

Under the Pediatric Research Equity Act of 2003 ("PREA"), NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is determined by the FDA to be safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers, to a qualifying NDA sponsor. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted. As the FDA has not issued regulations applying PREA to orphan-designated indications, submission of a pediatric assessment is not presently required for an application to market a product for an orphan-designated indication. However, PREA compliance may be required if approval is sought for other indications for which the drug has not received orphan designation.

Post-approval Requirements

After FDA approval of a product is obtained, we will be required to comply with a number of post-approval requirements, including, among other things, establishment registration and product listing, prescription drug program fees, record-keeping requirements, reporting certain adverse reactions and production problems to the FDA, providing updated safety and efficacy information, and complying with requirements concerning advertising and promotional labeling. As a condition of approval of an NDA, the FDA may require the applicant to conduct additional clinical trials or other post-marketing testing and surveillance to further monitor and assess the drug's safety and efficacy.

The FDA regulates strictly the marketing, labeling, advertising and promotion of drug products that are placed on the market. Although physicians may prescribe a drug for off-label uses, manufacturers may only promote for the approved indication(s) and in accordance with the approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses and any other false or misleading promotion. Failure to comply with the laws and regulations governing advertising and promotion can have negative consequences, including adverse publicity, warning and untitled letters from the FDA, requests for corrective advertising or communications with doctors, and civil penalties or criminal prosecution.

In addition, the distribution of approved prescription pharmaceutical products is subject to the Prescription Drug Marketing Act ("PDMA"), which regulates the distribution of drugs and drug samples at the federal level and sets minimum standards for the registration and regulation of drug distributors by the states. Similarly, the Drug Supply Chain Security Act ("DSCSA") regulates the distribution of prescription pharmaceutical drugs, requiring implementation of an electronic interoperable system to identify and trace each prescription drug at the saleable unit level through the distribution system. The DSCSA also imposes obligations on drug manufacturers related to suspect product identification and removal, verification, dealing only with authorized trading partners, and other elements. The DSCSA is planned to be incrementally implemented over a 10-year period, with serialization of prescription drug products distributed in the U.S. effective November 27, 2017 for drug manufacturers. The PDMA, DSCSA, and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Also, quality control and manufacturing procedures must continue to conform to cGMP after approval. The FDA periodically inspects manufacturing facilities post-approval to assess continued compliance with cGMP, which imposes certain procedural and recordkeeping requirements. Accordingly, manufacturers must continue to expend time, money and effort in the area of process and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

We rely, and expect to continue to rely, on third parties for the production of clinical and any future commercial quantities of our product candidates. Future FDA inspections may identify compliance issues at our facilities or at the facilities of our contract manufacturers that may disrupt production or distribution or require substantial resources to correct. In addition, discovery of problems with a product or the failure to comply with applicable requirements may result in restrictions on a product, manufacturer or holder of an approved NDA, including withdrawal or recall of the product from the market or other voluntary, FDA-initiated or judicial action that could delay or prohibit further marketing.

Once approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if issues bearing on the product's safety or efficacy are discovered. Newly discovered or developed safety or effectiveness data or other information may also necessitate changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. New government requirements, including those resulting from new legislation, may be established that could delay or prevent FDA approval of our products under development or negatively impact the marketing of any future approved products.

Orphan Drug Designation

We have received orphan drug designation from the FDA for ELX-02 for the treatment of cystic fibrosis, MPS I, Rett syndrome, and nephropathic cystinosis. The FDA may grant orphan drug designation to drugs intended to treat a "rare disease or condition," which is defined as a disease or condition that affects fewer than 200,000 individuals in the U.S., or more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making available in the U.S. a drug for this type of disease or condition will be recovered from sales in the U.S. for that drug. Orphan drug designation must be requested before applying for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. Orphan drug designation can provide opportunities for grant funding towards clinical trial costs, tax advantages and FDA user-fee benefits. In addition, if a product which has an orphan drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. Competitors may receive approval of different drugs or biologics for the indication(s) for which the orphan product has exclusivity.

Rare Pediatric Disease Designation and Priority Review Voucher

Some orphan drugs may also qualify for designation as a "rare pediatric disease" under Section 529 of the FDCA. Section 529 is similar to the Orphan Drug Act, as both require that the "rare disease or condition" affect fewer than 200,000 persons in the U.S. In the Advancing Hope Act of 2016, Section 529 was changed so that the "rare pediatric disease" must also meet the additional criteria of being a serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents. Under Section 529 of the FDCA, the FDA will award priority review vouchers to sponsors of rare pediatric disease product applications that meet these criteria. Under this program, a sponsor who receives an approval for a drug or biologic for a "rare pediatric disease" may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product.

Hatch-Waxman Regulatory Exclusivity

Market and data exclusivity provisions under the FDCA can delay the submission or the approval of certain applications for competing products. The FDCA provides a five-year period of non-patent data exclusivity within the U.S. to the first applicant to gain 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. During the exclusivity period, the FDA generally may not accept for review an abbreviated new drug application ("ANDA") or a 505(b)(2) NDA submitted by another company that references the previously approved drug. An ANDA or 505(b)(2) NDA may be submitted after four years if it contains a certification of patent invalidity or non-infringement.

For some applications that do not qualify for five-year exclusivity, the FDCA provides a shorter three-year period of market exclusivity. Three-year exclusivity applies to an NDA, 505(b)(2) NDA, or supplement to an existing NDA or 505(b)(2) 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, for new indications, dosages, strengths or dosage forms of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and, as a general matter, does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for generic versions of the original, unmodified drug product. 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 all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent market exclusivity in the U.S. and, if granted, provides for the attachment of an additional six months of market protection to the term of any existing Orange Book-listed patents or regulatory exclusivity, including the non-patent exclusivity periods described above. This six-month exclusivity may be granted based on the voluntary completion of a pediatric study or studies in accordance with an FDA-issued "Written Request" for such a study or studies.

Regulation Outside the United States

In order to market any product outside of the U.S., we would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, preclinical studies, clinical trials, marketing authorization, commercial sales and distribution of any future approved products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others.

Regulation in the European Union

We have obtained an orphan medicinal product designation from the European Commission, following an evaluation by the EMA's Committee for Orphan Medicinal Products, for ELX-02 for the treatment of cystic fibrosis and MPS I. The European Commission can grant orphan medicinal product designation to products for which the sponsor can establish that it is intended for the diagnosis, prevention, or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in 10,000 people in the EU, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives it is unlikely that sales of the drug in the EU would generate a sufficient return to justify the necessary investment. In addition, the sponsor must establish that there is no other satisfactory method approved in the EU of diagnosing, preventing or treating the condition, or if such a method exists, the proposed orphan drug will be of significant benefit to patients. Orphan medicinal product designation is not a marketing authorization. It is a designation that provides a number of benefits, including fee reductions, regulatory assistance, and the opportunity to apply for a centralized EU marketing authorization, as well as 10 years of market exclusivity following a marketing authorization. During this market exclusivity period, neither the EMA, nor the European Commission nor the Member States can accept an application or grant a marketing authorization for a "similar medicinal product." A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The market exclusivity period for the authorized therapeutic indication may be reduced to six years if, at the end of the fifth year, it is established that the orphan designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. In addition, a competing similar medicinal product may in limited circumstances be authorized prior to the expiration of the market exclusivity period, including if it is shown to be safer, more effective or otherwise clinically superior to our product. Our product can lose orphan designation, and the related benefits, prior to us obtaining a marketing authorization if it is demonstrated that the orphan designation criteria are no longer met.

Overview of Application Process

To obtain regulatory approval of a drug under the EU's regulatory systems and authorization procedures, an applicant may submit a Marketing Authorization Application ("MAA") under a centralized, decentralized, or national procedure. The centralized procedure is compulsory for certain medicinal products, including orphan medicinal products, like ELX-02 and medicinal products produced by certain biotechnological processes, and optional for certain other innovative products. The centralized procedure enables applicants to obtain a marketing authorization that is valid in all EU member states based on a single application. Under the centralized procedure, the EMA's Committee for Human Medicinal Products ("CHMP") is required to adopt an opinion on a valid application within 210 days, excluding clock stops, during which additional written or oral information is to be provided by the applicant in response to questions. More specifically, on day 120 of the procedure, once the CHMP has received the preliminary assessment reports and opinions from the rapporteur and co-rapporteur, the CHMP prepares a list of potential outstanding issues, referred to as "other concerns" or "major objections." These are sent to the applicant together with CHMP's recommendation. The CHMP can make one of two recommendations: (1) the marketing authorization could be granted provided that satisfactory answers are given to the "other concerns" and/or "major objections" identified and that all conditions outlined in the list of outstanding issues are implemented and complied with; or (2) the product is not approvable since there are "major objections."

Applicants have three months from the date of receiving the potential outstanding issues to respond to the CHMP and can request a three-month extension if necessary. The granting of a marketing authorization will depend on the recommendations and potential major objections identified by the CHMP as well as the ability of the applicant to adequately respond to these findings. An accelerated assessment can be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of major public health interest, in particular from the viewpoint of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days. After the adoption of the CHMP opinion, a decision on the MAA must be adopted by the European Commission, after consulting the EU member states, which in total should be completed in 67 days.

An applicant for an MAA may request a re-examination in the event of a negative opinion, in connection with which CHMP appoints new rapporteurs. Within 60 days of receipt of the negative opinion, the applicant must submit a document explaining the basis for its request for re-examination. The CHMP has 60 days to consider the applicant's request for re-examination. The applicant may request an oral explanation before the CHMP, which is routinely granted, following which CHMP will adopt a final opinion. The final opinion, whether positive or negative, is published by the CHMP shortly following the CHMP meeting at which the oral explanation takes place.

Conditional Marketing Authorizations

In specific circumstances, EU legislation enables applicants to obtain a marketing authorization on a conditional basis prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional approvals may be granted for products designated as orphan medicinal products, if (1) the risk-benefit balance of the product is positive, (2) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (3) the product fulfills unmet medical needs, and (4) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions and/or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization. The granting of a conditional marketing authorization will depend on the applicant's ability to fulfill the conditions imposed within the agreed upon deadline.

Variations to Conditional Marketing Authorizations

After the granting of a conditional marketing authorization, the marketing authorization holder may apply to vary the conditional marketing authorization under a variation procedure. In the case of the introduction of an additional therapeutic indication, the timeframe for the variation procedure for the initial assessment of the dossier is generally 90 days (plus up to 20 days for validation).

In the framework of a variation application assessment procedure, however, the EMA may send one or more requests for supplementary information to the marketing authorization holder, requiring that additional information be provided by the marketing authorization holder to support its variation application. Such supplementary requests will be sent together with a timetable stating the date by when the marketing authorization holder must submit the requested data and, where appropriate, the extended evaluation period to be applied to such variation procedure. The 90-day variation procedure may be suspended for up to three months for the marketing authorization holder to submit its responses to such supplementary requests. The marketing authorization holder will be notified of the outcome of the CHMP's assessment of the variation procedure within 15 days from the adoption of the CHMP opinion. If unfavorable, the CHMP opinion may be subject to a re-examination procedure upon the marketing authorization holder's request. This may imply an additional minimum two-month procedure. If the CHMP opinion is favorable, the European Commission will vary the marketing authorization to introduce the additional therapeutic indication within approximately two months from the receipt of the final CHMP opinion.

Additional Requirements and Considerations

Prior to obtaining a marketing authorization in the EU, applicants have to demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan ("PIP"), covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver, or (3) a deferral for one or more of the measures included in the PIP. In the case of orphan medicinal products, completion of an approved PIP can result in an extension of the aforementioned market exclusivity period from ten to twelve years.

In the EU, independently generated data submitted as part of a full marketing authorization application dossier are protected by regulatory data protection (‘data exclusivity’) for a period of eight years from the granting of a marketing authorization for a ‘reference product’. This means that for a period of eight years, competent authorities may not accept marketing authorization applications that rely on the independently generated data in the marketing authorization dossier of the reference product. Generic medicinal products that rely on the independently generated data of the reference product may not be placed on the market for 10 years from the granting of the initial marketing authorization for the reference medicinal product. These periods of data exclusivity and market exclusivity do not prevent other companies from obtaining a marketing authorization based on their own independently generated data.

If we are able to obtain a marketing authorization for ELX-02 for any indication in the EU, we will be required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. We must, for example, comply with the EU’s stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed. Other requirements relate to, for example, the manufacturing of products and active pharmaceutical ingredients in accordance with good manufacturing practice standards. Competent authorities of EU member states may conduct inspections to verify our compliance with applicable requirements, and we will have to continue to expend time, money and effort to remain compliant. Non-compliance with EU requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties in the EU. Similarly, failure to comply with the EU’s requirements regarding the protection of individual personal data can also lead to significant penalties and sanctions. Individual EU member states may also impose various sanctions and penalties in case we do not comply with locally applicable requirements.

Off-label promotion of medicinal products is prohibited in the EU. The applicable laws at the EU level and in the individual EU member states also prohibit the direct-to-consumer advertising of prescription-only medicinal products. Violations of the rules governing the promotion of medicinal products in the EU could be penalized by administrative measures, fines and imprisonment. These laws may further limit or restrict our promotional activities with health care professionals. In addition, legislation adopted at the EU level and by individual EU member states require that promotional materials and advertising in relation to medicinal products comply with the product’s Summary of Product Characteristics (“SmPC”), as approved by the competent authorities. The SmPC is the document that provides information to physicians concerning the safe and effective use of the medicinal product. Promotion of indications not covered by the SmPC is specifically prohibited.

The EMA is responsible for coordinating inspections to verify compliance with the principles of GCP, cGMP, GLP, and good pharmacovigilance practices (“GVP”). These inspections are also intended to verify compliance with other aspects of the supervision of authorized medicinal products in use in the EU. The EMA coordinates any inspection requested by the CHMP in connection with the assessment of an MAA. Inspections may be routine or triggered by issues arising during the assessment of the dossier or by other information, such as previous inspection experience. Inspections usually are requested during the initial review of an MAA but could also arise post-authorization.

Inspectors are drawn from member states of the EU and the European Economic Area. Following an inspection, the inspectors provide a written inspection report to the inspected site or applicant and provide an opportunity for response. Some inspection reports require follow-up and may result in additional adverse consequences due to critical or major findings. The inspectors and the CHMP will comment on any response from an inspected site or applicant and may monitor future compliance with any proposed corrective action plan.

Possible consequences of critical and major findings resulting from GCP inspections include rejection of clinical trial data, causing significant delays in obtaining final marketing authorization, or other direct action by national regulatory authorities.

Early Access Programs

Many jurisdictions around the world allow the supply of unauthorized medicinal products in the context of strictly regulated and exceptional early access programs, and some countries may provide reimbursement for drugs provided in the context of such programs. In the EU, the legal basis for early access programs, also referred to as named-patient and compassionate use programs, is set out in the EU legislation regulating the authorization, manufacture, distribution and marketing of medicinal products. Detailed regulatory requirements applicable to early access programs have been adopted and implemented by EU member states in their national laws. The promotion, advertising and marketing of unauthorized medicinal products is generally prohibited, and authorization for early access programs must generally be obtained from national competent authorities, which might not grant such

authorization. Obtaining authorization for an early access program in one country does not ensure that authorization will be obtained in another country. U.S. law permits "expanded access" (also known as compassionate use and treatment use) for certain patients with serious diseases who have no comparable alternative treatment options. To provide expanded access in the U.S., sponsors must submit detailed regulatory information to the FDA. FDA authorization depends on several different factors, including whether expanded access will interfere with related clinical trials or drug development. In addition, the Right to Try Act was signed into law in the U.S. on May 30, 2018 and allows certain eligible patients to have access to certain eligible investigational drugs outside of clinical trials if the patient's licensed treating physician certifies that the patient has exhausted FDA-approved treatment options and cannot participate in a clinical trial of the investigational drug. Sponsors may not promote products as safe or effective for expanded access or right to try uses.

Pharmaceutical Pricing and Reimbursement

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of pharmaceuticals have been a focus of this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. For example, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 expanded Medicare coverage for drug purchases by the elderly and changed the way Medicare covers and pays for pharmaceutical products. Cost reduction initiatives and other provisions of this law may decrease the coverage and reimbursement rate that we may receive for any products approved in the U.S. Likewise, healthcare reform measures under the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, referred to together as the Affordable Care Act, contain provisions that may reduce the profitability of drug products by increasing the minimum level of Medicaid rebates payable by manufacturers of brand-name drugs from 15.1% to 23.1%, effective 2011, extending the Medicaid rebate to Medicaid managed care plans, changing the Medicaid rebate rates for line extensions or new formulations of oral solid dosage forms, mandating discounts for certain Medicare Part D beneficiaries, and imposing a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs," effective 2011, expanding the types of entities eligible for the "Section 340B discounts" for outpatient drugs, requiring manufacturers to participate in a coverage gap discount program, under which they must agree to offer point-of-sale discounts (75% effective as of 2019) off negotiated prices of applicable branded drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D and creating a process for approval of biologic therapies that are similar to or interchangeable with approved biologics. There are numerous steps required to implement the Affordable Care Act, and implementation remains ongoing. Congress also has enacted, and may continue to seek, legislative changes that alter, delay, or eliminate some of its provisions. On February 1, 2016, the Centers for Medicare and Medicaid Services released a long-awaited new rule, the Medicaid Program Covered Outpatient Drug Final Rule, effective April 1, 2016, implementing various provisions of the Affordable Care Act related to "covered outpatient drugs," including revising the calculation of "average manufacturer price" and addressing other issues relating to Medicaid price reporting and reimbursement. These and other changes contribute to the uncertainty of the ongoing implementation and impact of the Affordable Care Act; they also underscore the potential for additional reform going forward. Certain provisions of enacted or proposed legislative changes may negatively impact coverage and reimbursement of healthcare products and services.

Increasing pricing pressure continues from managed care organizations, government agencies and programs, particularly for new and innovative therapies, that could negatively affect sales and profit margins for any product candidate for which we receive regulatory approval for commercial sale. In the U.S., these include practices of managed care groups, federal and state exchanges, and institutional and governmental purchasers. Changes to the health care system enacted as part of health care reform in the U.S., as well as increased purchasing power of entities that negotiate on behalf of Medicare, Medicaid, and private sector beneficiaries, could negatively impact our sales and profit margins. Such pressures may also increase the risk of litigation or investigations by the government regarding pricing calculations. There has also been recent negative publicity and Congressional scrutiny around pharmaceutical drug pricing in the U.S. These dynamics may give rise to negative reactions to pricing decisions for products for which we may receive regulatory approval in the future, possibly limiting our ability to generate revenue and attain profitability. Moreover, the pharmaceutical industry will likely face greater regulation and political and legal action in the future. In this healthcare regulatory climate, there may be significant delays in and impediments to obtaining coverage and reimbursement for newly approved drugs. Any regulatory approval of our products is limited to specific diseases and indications for which our products have been deemed safe and effective by the FDA. Coverage by federal healthcare programs may be more limited than the purposes for which the drug is approved by the FDA or comparable foreign regulatory authorities' coverage of the same products. In the U.S. and

markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the extent to which the costs of the products will be covered and reimbursed by third-party payors, including government healthcare programs such as Medicare and Medicaid, private health insurers and other organizations. Obtaining reimbursement for orphan drugs may be particularly difficult because of the higher prices typically associated with drugs directed at smaller populations of patients. In addition, third-party payors are likely to impose strict requirements for reimbursement in connection with the use of a higher priced drug. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of products from countries where they may be sold at lower prices than in the U.S.

The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. Third-party payors are increasingly challenging the price and examining the cost-effectiveness of medical products and services. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. Our product candidates may not be considered cost-effective. In the future, we may need to conduct direct head-to-head studies to demonstrate clinical superiority and cost-effectiveness. Our product candidates may not be considered clinically superior and cost-effective to competitor products.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and other third-party payors fail to provide adequate coverage and reimbursement. In addition, there is an increasing emphasis on managed care in the U.S. that may negatively impact pharmaceutical pricing.

In some countries, particularly in the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing and reimbursement negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. In some countries, governments can set conditions that must be satisfied for prices to be set at a certain value. Political, economic and regulatory developments may further complicate pricing and reimbursement negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states, and parallel distribution (arbitrage between low-priced and high-priced member states), can further reduce prices. In some countries, we may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidate to other available therapies in order to obtain reimbursement or pricing approval.

Freedom of Information Requests

We are also subject, in the U.S. and many other countries, to various regulatory schemes that require disclosure of clinical trial data or allow access to our data via freedom of information requests. We have been and may, from time to time, be notified by regulators, such as the EMA or the competent authorities of EU member states or the FDA that they have received a freedom of information request for documents that they hold relating to our company, including information related to our product candidates.

Fraud and Abuse Laws

Any present or future arrangements with third-party payors, healthcare providers and professionals and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may restrict certain marketing and contracting practices. These laws include, and are not limited to, anti-kickback and false claims statutes.

Both the federal Foreign Corrupt Practices Act (“FCPA”), and the UK Bribery Act of 2010 (“Bribery Act”), are broad in scope and require companies to make and keep books and records that accurately and fairly reflect the transactions of the company and to devise and maintain an adequate system of internal accounting controls. The FCPA prohibits the offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to improperly influence any act or decision, secure any other improper advantage, or obtain or retain business. Under the Bribery Act, companies which carry on a business or part of a business in the United Kingdom may be held liable for bribes given, offered or promised to any person, including non-UK government officials and private persons, by employees and persons associated with the company in order to obtain or retain business or a business advantage for the company.

The federal Anti-Kickback Statute in the U.S. prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, in cash or kind, to induce or reward either the referral of an individual for, or the purchase, or order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid. This statute has been broadly interpreted to apply to manufacturer arrangements with prescribers, purchasers and formulary managers, among others. Although a number of statutory exemptions and regulatory safe harbors exist to protect certain common activities from prosecution, the exemptions and safe harbors for this statute are narrow, and practices that involve compensation intended to induce prescriptions, purchases, or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Our practices may not always meet all of the criteria for safe harbor protection. Further, the Affordable Care Act amended the intent requirement of the federal anti-kickback and criminal health care fraud statutes. This amendment provides that a person or entity no longer needs to have knowledge of these statutes or specific intent to violate them. In addition, the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act. Several other countries, including the United Kingdom, have enacted similar anti-kickback, fraud and abuse laws and regulations.

The federal False Claims Act imposes civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. Several pharmaceutical and health care companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the free product. Other companies have been prosecuted for causing false claims to be submitted because of these companies' marketing of a product for unapproved, and thus non-reimbursable, uses. Potential liability under the federal False Claims Act includes mandatory treble damages and significant per claim penalties, currently set at $11,665 to $23,331 per false claim. The majority of states also have statutes or regulations similar to the federal anti-kickback statute and False Claims Act, which apply to items and services reimbursed under Medicaid and other state programs; furthermore, in several states, these statutes and regulations apply regardless of the payor. Sanctions under these federal and state laws may include civil monetary penalties, exclusion of a manufacturer's product from reimbursement under government programs, debarment, criminal fines, and imprisonment.

The Affordable Care Act included a provision requiring certain providers and suppliers of items and services to Federal Health Care Programs to report and return overpayments within sixty days after they are "identified," or the Overpayment Statute. In February 2016, the Centers for Medicare and Medicaid Services ("CMS") released long-awaited regulatory guidance (in the form of a final rule) to Medicare Part A and Part B providers and suppliers regarding how to comply with the Overpayment Statute. CMS had previously released a final rule addressing overpayments involving Medicare Part C and Part D providers in May 2014. Although Medicare Part A/B/C/D providers and suppliers have faced federal False Claims Act liability since 2010 for failures to comply with the Overpayment Statute, these final rules interpreting the Overpayment Statute provide guidance to providers and suppliers regarding how to comply appropriately with applicable obligations, and guidance to government regulators and enforcement authorities regarding monitoring and prosecuting suspected violations. This final rule is not directly applicable to manufacturers but may impact their customers and potential customers who are Medicare providers and suppliers.

The federal Physician Payments Sunshine Act, enacted as part of the Affordable Care Act, and its implementing regulations, require manufacturers of drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to payments and other transfers of value made to covered recipients, such as physicians and teaching hospitals, as well as physician ownership and investment interests. Payments made to physicians and certain research institutions for clinical trials are included within the scope of this law. Pharmaceutical manufacturers are required to report and disclose payments and ownership and investment interests held by physicians and their immediate family members during the preceding calendar year. Manufacturers were required to make these first reports for information collected in 2013 by March 31, 2014. Such information is publicly available from the Secretary of Health and Human Services in a searchable format, with data collected in each calendar year published the following June. Failure to submit required information may result in civil monetary penalties of up to $150,000 per year (and up to $1.0 million per year for "knowing failures") for all payments, transfers of value or ownership or investment interests not reported in an annual submission. If not preempted by this federal law, several states currently require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products and to report gifts and payments to individual physicians in those states. Depending on the state, legislation may prohibit various other marketing related activities, or require the posting of information relating to clinical studies and their outcomes. In addition, certain states, such as California, Nevada, Connecticut and Massachusetts, require pharmaceutical companies to implement compliance programs or marketing codes and several other states are considering similar proposals. Manufacturers that fail to comply with these state laws can face civil penalties.

Statutory requirements to disclose publicly payments made to healthcare professionals and healthcare organizations have also been enacted in certain EU member states. In addition, self-regulatory bodies of the pharmaceuticals industry, such as the European Federation of Pharmaceutical Industries and Associations have published codes of conduct to which its members have agreed to abide by, that require the public disclosure of payments made to healthcare professionals and healthcare organizations.

The Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal liability for executing a scheme to defraud any healthcare benefit program and for knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services. HIPAA also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information, and imposes criminal and civil liability for violations of these obligations. Recently, the U.S. federal government criminally prosecuted an employee of a pharmaceutical company for an alleged violation of the privacy requirements under HIPAA. Furthermore, certain privacy laws and genetic testing laws may apply directly to our operations and/or those of our collaborators and may impose restrictions on our use and dissemination of individuals' health information.

The foregoing discussion should be read in conjunction with the information appearing under "Risk Factors" and the subheading which begins "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." This risk factor contains important information regarding some of the risks to our business arising as a result of fraud and abuse laws.

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 (our lead indication) and cystinosis. Additional competition to ELX-02 may arise from other programs that do not target a specific *CFTR* mutation class but work via other mechanisms.

COVID-19

The outbreak of COVID-19 and the preventive or protective actions that we, our employees, consultants, suppliers, contract research organizations (CROs), and other partners or governments may take may significantly disrupt our business operations. We are diligently working to ensure that we can continue to operate with minimal disruption, and to mitigate the impact of the pandemic on our employees' health and safety and that of the patients and healthcare professionals in our clinical trials. However, given the significant uncertainty regarding the ongoing impact of the COVID-19 outbreak, there remains a risk that we or our employees, contractors, suppliers, and other partners may be prevented from conducting business activities for indefinite periods of time, including due to a substantial percentage of personnel contracting the virus or due to shutdowns that may be requested or mandated by governmental authorities. Given the interconnectivity of the global economy and the possible rate of future global transmission of the virus, the full extent to which the pandemic could affect the global economy is unknown and its impact may extend beyond the areas which are currently known by us to be affected.

Our management and Board of Directors are focused on the operational challenges resulting from the COVID-19 pandemic. To date, the pandemic has not had a material adverse impact on our financial condition, and we have not had to lay off or furlough any employees. Operations have continued even though our clinical trials were temporarily paused. Both Phase 2 clinical trials have now resumed. We are evaluating various alternatives to remain flexible and adapt to changing circumstances that may arise in the near and long term. We continue to monitor our operations, states of affairs in the regions in which we and our business partners operate and conduct research and clinical trial activities, and applicable government recommendations. As a result, we have made modifications to our normal operations, including restrictions on business travel and meetings, permitting employees to work remotely and the implementation of COVID-19 workplace safety guidelines to screen employees and office visitors for COVID-19 symptoms upon entering our offices. We have also implemented one-way traffic flows, social-distanced workspaces, additional cleaning requirements and mandatory face coverings for common spaces and provided components of Personal Protective Equipment (PPE) for all employees working out of our various office locations. Notwithstanding these measures, the COVID-19 pandemic could affect the health and availability of our workforce as well as those of the third parties we rely on. If members of our management and other key personnel in critical functions across our organization are unable to perform their duties or have limited availability due to COVID-19, we may not be able to execute on our business strategy and our operations may be adversely impacted. We may also experience limitations in employee resources, including due to illness of employees or their families or the desire of employees to avoid contact with individuals or large groups of people. In addition, we have experienced and will continue to experience disruptions to our business operations resulting from quarantines, self-isolations and travel and other restrictions on our employees which may impact their ability to perform their job responsibilities.

The extent and severity of the impact of the current global health crisis on our business and clinical trials will be determined largely by the ability of patients and prospective patients in our clinical trials to access trial sites, the ability of personnel from our CROs to oversee the administration of our drug in accordance with trial protocols and our ability to monitor and communicate effectively with our CROs, staff at clinical trial sites and principal investigators. In addition, the impact of the COVID-19 pandemic on the operations of the FDA and other health authorities may delay potential advancement of our product candidates.

Human Capital

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.

As of December 31, 2020, we had 20 employees in the United States and 5 employees in Israel. We believe that we have a good relationship with our employees.

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, 2020, 40% of our employees were female and 60% 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.

The success of our business is fundamentally connected to the well-being of our employees. In response to the COVID-19 pandemic, we implemented modifications to our normal operations, including restrictions on business travel and meetings, permitting employees to work remotely and the implementation of COVID-19 workplace safety guidelines. Our COVID-19 workplace safety guidelines require screening of employees and office visitors for COVID-19 symptoms upon entering our offices, social-distanced workspaces, additional cleaning requirements and mandatory face coverings for common spaces. We also provide components of PPE for all employees working out of our various office locations.

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.

Additional Information

Our principal executive offices are located at 950 Winter Street, Waltham, Massachusetts 02451, and our phone number is (781) 577-5300.

Our corporate website is *http://www.eloxxpharma.com*. The public can access, through a link on the “Investors” section of our website, free of charge, all reports and other information on file with the United States Securities and Exchange Commission (“SEC”), immediately after we electronically submit such material to the SEC. In addition, we will provide electronic or paper copies of our filings free of charge upon request. Information contained on our corporate website or any other website is not incorporated into this Report and does not constitute a part of this Report.

In addition, the public may read and copy any materials filed by the Company with the SEC at the SEC’s Public Reference Room located 100 F Street, NE, Washington, DC 20549. Interested parties may call 1-800-SEC-0330 for further information. The SEC also maintains a website containing publicly available information, at *https://www.sec.gov*.

We post our code of business conduct and ethics, which applies to all employees, including all executive officers, senior financial officers and directors, in the “Corporate Governance” sub-section of the “Investors” section of our corporate website. Our code of business conduct and ethics complies with Item 406 of SEC Regulations S-K and the Rules of the NASDAQ Stock Market. We intend to disclose any changes to the code that affect the provisions required by Item 406 of Regulation S-K and any waivers of the code of ethics for our executive officers, senior financial officers or directors, on our corporate website.

ITEM 1A. RISK FACTORS

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 follow directly under the heading "Risk Factors" and should be carefully considered, together with other information in this Form 10-K and our other filings with the SEC before making an investment decision regarding our common stock.

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

- The success of our lead product candidate, ELX-02, is critical to our business. If ELX-02 fails during development, it may adversely impact the commercial viability of ELX-02 and our business.
- Positive results from preclinical or in vitro and in vivo testing of ELX-02 are not necessarily predictive of the results of future clinical trials of ELX-02. If we cannot achieve positive results in our clinical trials for ELX-02, we may be unable to successfully develop, obtain regulatory approval for and commercialize ELX-02.
- Our product candidates, including ELX-02, 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.
- Our clinical trials are costly, lengthy, time-consuming and difficult to design and implement, may result in unforeseen costs and could be delayed or terminated, which may have a material adverse effect on our business, results of operations and financial condition.
- 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.
- Because our clinical trials depend upon third-party researchers, scientists and consultants, the results of our clinical trials and such research activities are subject to delays and other risks that are beyond our control, which could impair our clinical development programs.
- We are subject to extensive governmental regulation including the requirements of the FDA and comparable foreign regulatory authorities for development and approval of our product candidates before they can be marketed.
- We may not obtain the necessary FDA, EMA or other worldwide regulatory approvals to commercialize our product candidates in a timely manner, if at all, which would have a material adverse effect on our business, results of operations and financial condition.
- 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.
- 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 obtain orphan drug marketing exclusivity for ELX-02 or any of our other potential product candidates for other indications.
- 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.

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

Risks Related to Our Business and Operations

- We are seeking 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.
- Changes in healthcare laws and implementing regulations, as well as changes in healthcare policy, may affect coverage and reimbursement of our product candidates in ways that we cannot currently predict, and these changes could adversely affect our business and financial condition.
- Our business could be adversely affected by the effects of widespread public health epidemics and other factors beyond our control.
- Security breaches, cyber-attacks, or other disruptions could expose us to liability and affect our business and reputation.
- We rely on third parties to conduct some or all aspects of our product manufacturing, protocol development, research and preclinical and clinical testing, and these third parties may not perform satisfactorily.
- Our future success depends on our ability to retain key employees, consultants and advisors and to attract, retain and motivate qualified personnel.

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.
- 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 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.
- 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.

Risks Related to Our Regional Operations

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

Risks Related to Our Common Stock

- Our stock price may be volatile and may or may not reflect our operations or value, and therefore purchasers of our common stock could incur substantial losses.
- Our directors, executive officers and principal stockholders own a significant percentage of our capital stock, and they may exert significant influence over the direction of the Company and make decisions that an investor may consider to be adverse to such investor’s interest.
- Future sales and issuances of our securities or rights to purchase securities, whether in connection with a financing transaction or otherwise, could result in dilution of the percentage ownership of our stockholders and could cause the prices of our securities to decrease.

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 other information in this Report, 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 depend heavily on the success of our lead product candidate, ELX-02. If ELX-02 fails during development or suffers any material delays, it may adversely impact the commercial viability of ELX-02 and our business.

We currently have no products approved for sale. To date, we have invested substantial efforts and financial resources 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.

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. 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 in humans of our product candidates. The clinical trials, manufacturing and marketing of ELX-02, and any future product candidates, will be subject to extensive and rigorous review and regulation by numerous governmental authorities in the U.S., the EU and other jurisdictions where we intend to test and, if approved, market our current and future product candidates. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through preclinical studies and clinical trials that the product candidate is safe and effective for use in each target indication, and potentially in specific patient populations, including the pediatric population. This process can take many years and may include post-marketing studies and surveillance, which would require the expenditure of substantial additional resources. Of the large number of drugs in development for approval in the U.S. and the EU, only a small percentage successfully complete the FDA or EMA regulatory approval processes 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 or any of our future product candidates will be successfully developed or commercialized.

Preclinical studies and clinical trials are expensive, difficult to design and implement, can take many years to complete and are uncertain as to outcome. The start or end of a clinical trial is often delayed or halted due to changing regulatory requirements, manufacturing challenges, required clinical trial administrative actions, slower than anticipated patient enrollment, changing standards of care, availability or prevalence of use of a comparative therapeutic or required prior or combination therapy, clinical outcomes or financial constraints. For instance, delays or difficulties in patient enrollment or difficulties in retaining trial participants can result in increased costs, longer development times or termination of a clinical trial. Clinical trials of a new product candidate require the enrollment of a sufficient number of patients, including patients who are suffering from the disease the product candidate is intended to treat and who meet other eligibility criteria. Rates of patient enrollment are affected by many factors, including the size of the patient population, the eligibility criteria for the clinical trial, the age and condition of the patients, the stage and severity of disease, the nature of the protocol, the proximity of patients to clinical sites and the availability of effective treatments for the relevant disease.

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. Clinical trials can be delayed for a variety of reasons, including delays related to:

- obtaining regulatory approval to commence a trial;
- reaching agreement on acceptable terms with prospective contract research organizations, or 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, or IRB, approval at each clinical trial site;
- recruiting suitable patients to participate in a trial;
- having patients complete a trial or return for post-treatment follow-up;
- clinical trial sites deviating from trial protocol or dropping out of a trial;
- adding new clinical trial sites;
- unforeseen factors beyond our control, including public health concerns such as the COVID-19 pandemic; or
- manufacturing sufficient quantities of product candidate for use in clinical trials.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. Furthermore, we rely on third parties, such as CROs and clinical trial sites, to ensure the proper and timely conduct of our clinical trials and while we have agreements governing their committed activities, we may have limited influence over their actual performance.

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, we announced that enrollment in our Phase 2 clinical trial in cystic fibrosis had resumed in the U.S. COVID-19 is continuing to evolve and we continue to work closely with our clinical trial sites and investigators to ensure that patient enrollment will continue as quickly as is feasible in a safe environment for our patients. While we remain committed to completing enrollment in these Phase 2 proof of concept clinical trials and reporting top line data in the first half of 2021 contingent on no further disruptions due to the COVID-19 pandemic, we cannot provide assurances as to when this will be accomplished or 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.

We could encounter delays if prescribing physicians encounter unresolved ethical issues associated with enrolling patients in clinical trials of our product candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles. Further, a clinical trial may be suspended or terminated by us, our collaborators, the IRB of the institutions in which such trials are being conducted, the Data Safety Monitoring Board (“DSMB”) for such trial, or by the FDA or other regulatory authorities due to a number of factors, including:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;
- unforeseen safety issues or adverse side effects;
- failure to demonstrate a benefit from using a drug;

- changes in governmental regulations or administrative actions; or
- lack of adequate funding to continue the clinical trial.

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 investigational new drug application ("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.

If we experience delays in the completion of any clinical trial of our product candidates, the commercial prospects of our product candidates may be impaired and our ability to generate product revenues from such product candidates may be delayed. 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.

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.

All marketing activities associated with product candidates that are approved for sale in the U.S., if any, will be, directly or indirectly through our customers, subject to numerous federal and state laws governing the marketing and promotion of pharmaceutical products in the U.S., including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act and the Health Insurance Portability and Accountability Act ("HIPAA"). These laws may adversely impact, among other things, our proposed sales, marketing and education programs.

The federal Anti-Kickback Statute prohibits persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce either the referral of an individual, or the furnishing, recommending, or arranging for a good or service, for which payment may be made under a federal healthcare program, such as the Medicare and Medicaid programs. The term "remuneration" has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of co-payments and deductibles, ownership interests and providing anything at less than its fair market value. The reach of the Anti-Kickback Statute was also broadened by the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or the PPACA, which, among other things, amends the intent requirement of the federal Anti-Kickback Statute and the applicable criminal healthcare fraud statutes. Pursuant to the amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act (discussed below) or the civil monetary penalties statute, which imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. Penalties for violations of the federal Anti-Kickback Statute include criminal penalties and civil sanctions such as fines, imprisonment and possible exclusion from Medicare, Medicaid and other state or federal healthcare programs. Many states have also adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs.

The federal False Claims Act imposes liability on any person who, among other things, knowingly presents, or causes to be presented, a false or fraudulent claim for payment by a federal healthcare program. The "qui tam" provisions of the False Claims Act allow a private individual to bring civil actions on behalf of the federal government alleging that the defendant has submitted a false claim to the federal government, and to share in any monetary recovery. In addition, various states have enacted false claims laws analogous to the False Claims Act. Many of these state laws apply where a claim is submitted to any third-party payer and not merely a federal healthcare program. When an entity is determined to have violated the False Claims Act, it may be required to pay up to three times the actual damages sustained by the government, plus civil penalties up to approximately $22,000 for each separate false claim.

The HIPAA created several new federal crimes, including health care fraud, and false statements relating to health care matters. The health care fraud statute prohibits knowingly and willfully executing a scheme to defraud any health care benefit program, including private third-party payors. The false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services.

We are unable to predict whether we could be subject to actions under any of these or other fraud and abuse laws, or the impact of such actions. Moreover, to the extent that any of our product candidates will be sold in a foreign country, if approved for marketing, we and our current or future collaborators may be subject to similar foreign laws and regulations. If we or any of our current or future collaborators are found to be in violation of any of the laws described above and other applicable state and federal fraud and abuse laws, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from government healthcare reimbursement programs and the curtailment or restructuring of our operations, any of which could have a material adverse effect on our business, results of operations and financial condition.

Positive results from preclinical or in vitro and in vivo testing of ELX-02 are not necessarily predictive of the results of future clinical trials of ELX-02. If we cannot achieve positive results in our clinical trials for ELX-02, we may be unable to successfully develop, obtain regulatory approval for and commercialize ELX-02.

Positive results from our preclinical testing of ELX-02 in vitro and in vivo may not necessarily be predictive of the results from our ongoing and planned clinical trials in humans. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical trials after achieving positive results in preclinical and in vitro and in vivo studies, and we, or the third parties whose product candidates we expect to be co-administered with ELX-02, may face similar setbacks. Preclinical and clinical data are often susceptible to varying interpretations and analyses, and the FDA or EMA or other regulatory agencies may require changes to our protocols or other aspects of our clinical trials or require additional studies. Additionally, many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA or EMA approval. If we fail to secure positive results from our clinical trials of ELX-02 or regulatory agencies require us to undertake significant additional studies as a result of our data, the development timeline, regulatory approval and commercialization prospects for our lead product candidate, and, correspondingly, our business and financial prospects, would be materially adversely affected, which may result in termination of development activities, the inability to raise additional needed capital and/or a precipitous decline in our stock price, as well as impair our ability to enter into collaboration arrangements or damage existing strategic partnerships.

Our product candidates, including ELX-02, 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, 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. It is possible that, during the course of the clinical development of ELX-02 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.

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;
- we may be required to change the way the product is administered or to conduct additional clinical studies;
- 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.

Our clinical trials may be costly, lengthy, time-consuming and difficult to design and implement, may result in unforeseen costs and could be delayed or terminated, which may have a material adverse effect on our business, results of operations and financial condition.

For human trials, patients must be recruited, and each product candidate must be tested at various doses and formulations for each clinical indication. In addition, to ensure safety and effectiveness, the effect of drugs often must be studied over a long period of time, especially for the chronic genetic diseases that we will be studying. Many of our programs focus on diseases with small patient populations, making patient recruitment and enrollment difficult. Insufficient patient enrollment in our clinical trials could delay or cause us to abandon a product development program. We may decide to abandon development of a product candidate or a study at any time due to unfavorable results, or we may have to spend considerable resources repeating clinical trials or conducting additional trials, either of which would increase costs and delay any revenue from those product candidates, if any.

Failure or delay in the commencement or completion of our clinical trials may be caused by several factors, including:

- slower than expected rates of patient recruitment, particularly with respect to trials of rare diseases such as nonsense mutation cystic fibrosis;
- determination of dosing levels and corresponding effect analysis;
- unforeseen safety issues;
- lack of effectiveness during clinical trials;
- inability to monitor patients adequately during or after treatment;
- inability or unwillingness of medical investigators and IRBs to follow our clinical protocols;
- unforeseen factors beyond our control, including public health concerns such as the COVID-19 pandemic; and
- lack of sufficient funding to finance the clinical trials.

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.

Some of the diseases that our product candidates are intended 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 targets small populations and patient numbers have not been determined definitively, we must be able to identify patients in order to complete our development programs, secure regulatory approval and commercialize ELX-02 successfully.

In addition, the protocols for our clinical trials generally mandate that a patient cannot be involved in more than one clinical trial for the same indication. Therefore, subjects that participate in ongoing clinical trials for products that are competitive with our product candidates are not eligible to participate in our clinical trials. 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. 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, we announced that enrollment in our Phase 2 clinical trial in cystic fibrosis had resumed in the U.S. COVID-19 is continuing to evolve and we continue to work closely with our clinical trial sites and investigators to ensure that patient enrollment will continue as quickly as is feasible in a safe environment for our patients. We are also evaluating additional clinical sites in other countries where patient enrollment may be feasible. Additionally, significant additional costs as a result of this delay in enrollment or failure to complete enrollment in accordance with our objectives may have a material adverse impact on our financial condition and results of operations.

Because our clinical trials depend upon third-party researchers, scientists and consultants, the results of our clinical trials and such research activities are subject to delays and other risks that are, to a certain extent, beyond our control, which could impair our clinical development programs and our competitive position.

We depend on independent investigators, consultants, researchers, medical experts, collaborators, chemists, toxicologists and a small number of medical institutions and third-party contract research organizations to assist with our research efforts and conduct our preclinical and clinical trials and related activities. These collaborators, scientists, consultants and other third parties have provided, and we expect that they will continue to provide, valuable advice and services regarding our clinical development programs and product candidates. These collaborators, scientists, consultants and other third parties are not our employees, may have other commitments that would limit their future availability to us and typically will not enter into non-compete agreements with us. We cannot control the amount or timing of resources that they devote to our preclinical and or clinical development programs and they may not assign as great a priority to our preclinical or clinical development programs or pursue them as diligently as we would if we were undertaking such programs directly. If outside collaborators fail to devote sufficient time and resources to our preclinical and clinical development programs, or if their performance is substandard, the authorization of INDs and clinical trial applications ("CTAs") and the approval of anticipated new drug applications ("NDAs") and other marketing applications, and our introduction of new drugs, if any, may be delayed or impeded, which could impair our clinical development programs and would have a material adverse effect on our business and results of operations. These collaborators may also have relationships with other commercial entities, some of whom may compete with us and we may be unable to prevent them from establishing competing businesses or developing competing products. The extent to which the COVID-19 pandemic and municipalities' efforts to combat it through temporary quarantines, containment zones and limitations on travel, as well as other restrictions, may create business disruptions within the organizations of our third-party researchers, scientists and consultants, as well as CROs, clinical trial sites and patient assistance groups, that result in the unavailability of personnel needed to successfully conduct and complete our clinical trials, may have a material adverse impact on our business and financial condition.

We are subject to extensive governmental regulation including the requirements of the FDA and comparable foreign regulatory authorities for development and approval of our product candidates before they can be marketed.

We, our product candidates, our suppliers, our contract manufacturers, our contract testing laboratories and our clinical trial sites and clinical trial researchers are subject to extensive regulation by the FDA and comparable foreign regulatory authorities. Failure to comply with applicable requirements of the FDA or comparable foreign regulatory authorities could result in, among other things, any of the following actions:

- warning letters;
- fines and other monetary penalties;
- unanticipated expenditures;
- holds on the initiation or continuation of clinical trials;

- delays in the FDA's or other foreign regulatory authorities' approving, or the refusal of any regulatory authority to approve, any product candidate;
- product recall or seizure;
- interruption of manufacturing or clinical trials;
- operating restrictions;
- injunctions; and
- criminal prosecutions.

In addition to the approval requirements, other numerous and pervasive regulatory requirements apply, both before and after approval of our product candidates, to us, our product candidates, and our suppliers, contract manufacturers, and contract laboratories, and our clinical trial sites and clinical trial researchers including requirements related to testing, manufacturing, quality control, labeling, advertising, promotion, distribution, exporting product materials, reporting to the FDA of certain adverse experiences associated with use of the product candidate, and obtaining additional approvals for certain modifications to the product candidate or its labeling or claims following approval, if any.

We also are subject to inspection by the FDA and comparable foreign regulatory authorities, to determine our compliance with regulatory requirements, as are our suppliers, contract manufacturers, contract testing laboratories, and our clinical trial sites and clinical researchers, and there can be no assurance that the FDA or any other comparable foreign regulatory authority will not identify compliance issues that may disrupt production or distribution, or require substantial resources to correct. We may be required to make modifications to our manufacturing operations in response to these inspections, which may require significant resources and may have a material adverse effect upon our business, results of operations and financial condition.

The approval process for any product candidate may also be delayed by changes in government regulation, future legislation or administrative action or changes in policy of the FDA and comparable foreign regulatory authorities that occur prior to or during their respective regulatory reviews of such product candidate. Delays in obtaining regulatory approvals with respect to any product candidate may:

- delay commercialization of, and our ability to derive product revenue from, such product candidate;
- delay any regulatory-related milestone payments payable under outstanding collaboration agreements;
- require us to perform costly procedures with respect to such product candidate; or
- otherwise diminish any competitive advantages that we may have with respect to such product candidate.

We may not obtain the necessary FDA, EMA or other worldwide regulatory approvals to commercialize our product candidates in a timely manner, if at all, which would have a material adverse effect on our business, results of operations and financial condition.

We need FDA approval to commercialize our product candidates in the U.S., EMA approval to commercialize our product candidates in the EU and approvals from other foreign regulatory authorities to commercialize our product candidates elsewhere in the world. In order to obtain FDA approval of any of our product candidates, we must submit to the FDA an NDA demonstrating that the product candidate is safe for humans and effective for its intended use. This demonstration requires significant research and animal tests, which are referred to as preclinical studies, as well as human tests, which are referred to as clinical trials. In the EU, we must submit a Marketing Authorization Application, or MAA, to the EMA. Satisfaction of the regulatory requirements of the FDA, the EMA and other foreign regulatory authorities typically takes many years, depends upon the type, complexity and novelty of the product candidate and requires substantial resources for research, development and testing. Even if we comply with all the requests of regulatory authorities, they may ultimately reject any marketing applications that we file for our product candidates, or we might not obtain regulatory clearance in a timely manner if at all. Companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced or late-stage clinical trials, even after obtaining promising earlier trial results or preliminary findings or other comparable results for such clinical trials. Further, even if favorable testing data is generated during the clinical trials of a product candidate, the applicable regulatory authority may not accept or approve the marketing application filed by a pharmaceutical or biotechnology company for the product candidate. Failure to obtain approval of the FDA, EMA or comparable foreign regulatory authorities of any of our product candidates in a timely manner, if at all, will severely undermine our business, financial condition and results of operation by reducing our potential marketable products and our ability to generate corresponding product revenue.

Our research and clinical efforts may not result in drugs that the FDA, EMA or other foreign regulatory authorities consider safe for humans and effective for indicated uses, which would have a material adverse effect on our business, results of operations and financial condition. After clinical trials are completed for any product candidate, if at all, the FDA, EMA and other foreign regulatory authorities have substantial discretion in the drug approval process of the product candidate in their respective jurisdictions and may require us to conduct additional clinical testing or perform post-marketing studies, which would cause us to incur additional costs. Incurring such costs may have a material adverse effect on our business, results of operations and financial condition.

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 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 obtain orphan drug marketing exclusivity for ELX-02 or any of our other potential product candidates for other indications.

Regulatory authorities in some jurisdictions, including the U.S. and the 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 of 1983, 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 annually in the U.S. Similarly, in Europe, a medicinal product may receive orphan designation under Article 3 of Regulation (EC) 141/2000. This applies to products that are intended for 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 FDA has granted orphan drug designation for ELX-02 for the treatment of cystic fibrosis, MPS I and Rett syndrome. We may seek orphan drug designation for our other product candidates, and with respect to other indications. Generally, 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 indication for that time period. The applicable period is seven years in the U.S. Orphan drug exclusivity may be lost if the FDA determines that the request for designation contained an untrue statement of material fact or omitted material information required by the orphan drug regulations, if FDA subsequently finds that the drug was not in fact eligible for designation at the time of the designation request submission, if the underlying NDA for approval 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 candidate from competition because different drugs can be approved for the same 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. Similarly, if our competitors are able to obtain orphan product exclusivity for their products in the same indications for which we are developing our product candidates, we may not be able to have our products approved by the applicable regulatory authority for a significant period of time.

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 fully integrated biopharmaceutical companies and smaller biopharmaceutical 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.

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, 2020, had an accumulated deficit of $(171.6) million. Historically, 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 will 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. 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 and/or other product candidates further into clinical development;
- continue to experience 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.

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 and other product candidates;
- the costs, timing and outcome of any regulatory review of ELX-02 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 financing, 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.

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 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. 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.

Risks Related to Our Business and Operations

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.

The trading market for our common stock is influenced by the research and reports that securities or industry analysts publish. As a public company, we are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, the Sarbanes-Oxley Act of 2002, or 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 on a timely basis 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 maintain effective internal controls over financial reporting could be more difficult due to the measures imposed by municipalities in efforts to combat the COVID-19 pandemic, such as quarantines, containment zones and limitations on travel, which may limit the availability of employees and other personnel necessary to adequately monitor and oversee the effectiveness of our internal controls.

Various rules and regulations applicable to public companies make it more difficult and more expensive for us to maintain directors' and officers' liability insurance, and we may be required to accept reduced coverage or incur substantially higher costs to maintain coverage. If we are unable to maintain adequate directors' and officers' liability insurance, our ability to recruit and retain qualified officers and directors, especially those directors who may be deemed independent for purposes of the Nasdaq stock market rules, will be significantly curtailed.

We are seeking 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 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.

Comprehensive tax reform bills could adversely affect our business and financial condition.

On December 22, 2017, and effective January 1, 2018, the U.S. government enacted H.R. 1, "An Act to provide for reconciliation pursuant to titles II and V of the concurrent resolution on the budget for fiscal year 2018" (informally titled the "Tax Cuts and Jobs Act", or TCJA), which includes significant changes to the taxation of business entities. The TCJA, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), implementation of a "base erosion anti-abuse tax" which requires U.S. corporations to make an alternative determination of taxable income without regard to tax deductions for certain payments to affiliates, taxation of certain non-U.S. corporations' earnings considered to be "global intangible low taxed income" (also referred to as "GILTI"), repeal of the alternative minimum tax, or AMT, for corporations and changes to a taxpayer's ability to either utilize or refund the AMT credits previously generated, changes in the attribution rules relating to shareholders of certain "controlled foreign corporations", limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. In response to the COVID-19 pandemic, the CARES Act was signed into law in March 2020. The CARES Act lifts certain deduction limitations originally imposed by the TCJA. Corporate taxpayers may carry back net operating losses (NOLs) originating during 2018 through 2020 for up to five years, which was not previously allowed. The CARES Act also eliminates the 80% of taxable income limitations by allowing corporate entities to fully utilize NOL carryforwards to offset taxable income in 2018, 2019 or 2020. Taxpayers may generally deduct interest up to the sum of 50% of adjusted taxable income plus business interest income (30% limit under the TCJA) for tax years beginning January 1, 2019 and 2020. The CARES Act allows taxpayers with alternative minimum tax credits to claim a refund in 2020 for the entire amount of the credits instead of recovering the credits through refunds over a period of years, as originally enacted by the TCJA.

Notwithstanding the reduction in the corporate income tax rate, the TCJA remains subject to interpretation and further guidance from U.S. taxing authorities and as a result the overall impact of this tax reform is uncertain and may change due to interpretation changes, and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various U.S. states will conform their tax laws to the TCJA. The impact of the TCJA on holders of our common stock is also uncertain and could be adverse. We are unable to predict what tax reform may be proposed or enacted in the future or what effect such changes would have on our business, but such changes, to the extent they are brought into tax legislation, regulations, policies or practices, could affect our effective tax rates in the future in countries where we have operations and have an adverse effect on our overall tax rate in the future, along with increasing the complexity, burden and cost of tax compliance. We urge our stockholders to consult with their legal and tax advisors with respect to the TCJA and the CARES Act and the potential tax consequences of investing in or holding our common stock.

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

As of December 31, 2020, we had U.S. federal and state net operating loss, or "NOL", carryforwards of $108.9 million and $13.7 million, respectively, and federal research tax credit carryforwards of $3.6 million. Certain U.S. NOL carryforwards will begin to expire, if not utilized, beginning in 2021 through 2037, and the research tax credits will expire beginning in 2026 through 2040. Included in these U.S. federal NOL carryforwards are $34.9 million of NOLs generated after the effective date of the 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 United States Internal Revenue Code of 1986, as amended, or 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, including in connection with the reverse merger on December 19, 2017 at which time our pre-change U.S. federal NOL carryforward was $77.2 million and research tax credit was $0.7 million. 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 an adverse material effect on our Consolidated Financial Statements. Finally, as of December 31, 2020, we had Israeli NOL carryforwards of $86.9 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 reflected on our balance sheet, even if we attain profitability.

We could be subject to additional tax liabilities.

We are subject to federal, state and local taxes in the U.S. 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.

Changes in healthcare laws and implementing regulations, as well as changes in healthcare policy, may affect coverage and reimbursement of our product candidates in ways that we cannot currently predict, and these changes could adversely affect our business and financial condition.

In the U.S., a number of legislative and regulatory initiatives have focused on containing the cost of healthcare. The Patient Protection and Affordable Care Act, or PPACA, was enacted in March 2010. This law substantially changed the way healthcare is financed by both governmental and private insurers in the U.S., and significantly impacts the pharmaceutical industry. PPACA contains a number of provisions that are expected to impact our business and operations, in some cases in ways we cannot currently predict. Changes that may affect our business include those governing enrollment in federal healthcare programs, reimbursement changes, rules regarding prescription drug benefits under health insurance exchanges, expansion of the 340B program, expansion of state Medicaid programs, fraud and abuse enforcement and rules governing the approval of biosimilar products. These changes will impact existing government healthcare programs and will result in the development of new programs, including Medicare payment for performance initiatives and improvements to the physician quality reporting system and feedback program. In early 2016, CMS issued final regulations to implement the changes to the Medicaid Drug Rebate Program under PPACA. These regulations became effective on April 1, 2016. Moreover, in the future, Congress could enact legislation that further increases Medicaid drug rebates or other costs and charges associated with participating in the Medicaid Drug Rebate Program. Legislative changes to the PPACA also remain possible. The issuance of regulations and coverage expansion by various governmental agencies relating to the Medicaid Drug Rebate Program has increased and will continue to increase our costs and the complexity of compliance, has been and will be time-consuming, and could have a material adverse effect on our results of operations.

Governments in countries where we operate have adopted or have shown significant interest in pursuing legislative initiatives to reduce costs of healthcare. We expect that the implementation of current laws and policies, the amendment of those laws and policies in the future, as well as the adoption of new laws and policies, could have a material adverse effect on our industry generally and on our ability to generate or increase future product sales, if any, or successfully commercialize our product candidates, or could limit or eliminate our future spending on development projects. In many cases, these government initiatives, even if enacted into law, are subject to future rulemaking by regulatory agencies. Although we have evaluated these government initiatives and the impact on our business, we cannot know with certainty whether any such law, rule or regulation will adversely affect coverage and reimbursement of our product candidates, or to what extent, until such laws, rules and regulations are promulgated, implemented and enforced, which could sometimes take many years. The announcement or adoption of regulatory or legislative proposals could delay or prevent our entry into new markets, affect our reimbursement or sales in the markets where we are already selling our approved products, if any, and materially harm our business, financial condition and results of operations.

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 recent novel strain of coronavirus (COVID-19), initially limited to a region in China and now affecting the global community, 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 productiveness, 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. 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, we announced that enrollment in our Phase 2 clinical trial in cystic fibrosis had resumed in the U.S. COVID-19 is continuing to evolve and we continue to work closely with our clinical sites and investigators. While we remain committed to completing enrollment in these Phase 2 proof of concept clinical trials and reporting top line data in the first half of 2021, we cannot provide assurances as to when this will be accomplished or 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.

We may be subject to numerous and varying privacy and security laws, and our failure to comply could result in penalties and reputational damage.

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. If we fail to comply with applicable laws and regulations, 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.

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 2016, the EU formally adopted the General Data Protection Regulation, or GDPR, which applies to all EU member states as of May 25, 2018 and replaces the former EU Data Protection Directive. The regulation introduces new data protection requirements in the EU and imposes substantial fines for breaches of the data protection rules. The GDPR must be implemented into national laws by the EU member states and imposes strict obligations and restrictions on the ability to collect, analyze, and transfer personal data, including health data from clinical trials and adverse event reporting. Data protection authorities from different EU member states have interpreted the privacy laws differently, which adds to the complexity of processing personal data in the EU, and guidance on implementation and compliance practices are often updated or otherwise revised. Any failure to comply with the rules arising from the GDPR and related national laws of EU member states could lead to government enforcement actions and significant penalties against us, and adversely impact our operating results. The GDPR will increase our responsibility and liability in relation to personal data that we process and we may be required to put in place additional mechanisms ensuring compliance with EU data protection rules.

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 and infrastructure may be vulnerable to such attacks or may be breached, including due to employee error or malfeasance. We have also implemented information security measures to protect patients’ personal information against the risk of inappropriate and unauthorized external use and disclosure. 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 technology systems to operate our business and our ability to effectively manage our business depends on the security, reliability and adequacy of our 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. Like other companies in our industry, we have experienced attacks to our data and systems, including malware and computer viruses. If our systems failed or were breached or disrupted, patient and other data and information may become compromised, 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 would 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.

We rely on third parties to conduct some or all aspects of our product manufacturing, protocol development, research and preclinical and clinical testing, and these third parties may not perform satisfactorily.

We do not expect to independently conduct all aspects of our product manufacturing, protocol development, research and preclinical and clinical testing. We currently rely, and expect to continue to rely, on third parties with respect to these items.

Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it could delay our product development activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all applicable laws and regulations and study protocols. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, we will not be able to complete, or may be delayed in completing, the preclinical studies and clinical trials required to support future NDA submissions and approval of our product candidates.

Reliance on third-party manufacturers, testing sites, and investigators entails risks to which we would not be subject if we developed, researched, tested, and manufactured the product candidates ourselves, including:

- the inability to negotiate manufacturing, testing, and research agreements with third parties under commercially reasonable terms;
- reduced control as a result of using third-party manufacturers, testing laboratories, and research sites and investigators for all aspects of manufacturing, testing, and research activities;
- termination or nonrenewal of manufacturing, testing, or research agreements with third parties in a manner or at a time that is costly or damaging to us; and
- 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.

Any of these events could lead to clinical trial delays, failure to obtain regulatory approval or impact our ability to successfully commercialize future products. Some of these events could be the basis for FDA action, including injunction, recall, seizure or total or partial suspension of production or testing. Any one of these events could cause our business to be materially harmed and our results of operations would be adversely impacted.

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. 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, as all of our employees are “at will” employees. 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. 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 or have limited availability due to COVID-19, 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, 2020, we owned or licensed 27 issued patents and 47 pending patent applications in the U.S. and abroad, not including U.S. provisional applications. However, with regard to the pending provisional 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.

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, and may, in the future, expand operations to other regional locations in Europe and elsewhere as circumstances require. Accordingly, political and economic conditions in Israel and the surrounding region in particular, may directly affect our operations. Regional instability may lead to a deterioration in the political and trade relationships that exist 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 approximately $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 LIBOR interest) up to approximately $2.7 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, or 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 of 3% to 6% 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 LIBOR interest, in the amount of approximately $2.7 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.

Our common stock began trading on The Nasdaq Global Market on April 26, 2018 under the symbol "ELOX." 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 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, 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, 2020, individuals held share awards to purchase or receive an aggregate of 4,476,678 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, 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 950 Winter Street, Waltham, Massachusetts, and consist of 10,674 square feet of office space under lease until September 2021, with an option to extend the lease period for additional three years. We also lease additional office space in Morristown, New Jersey and 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. We are currently assessing the impact of the COVID-19 pandemic and the increase in remote work on our future real estate 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. 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, which may include 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. 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

Since April 26, 2018, our common stock has traded on The NASDAQ Capital Market under the symbol "ELOX." Prior to that date, our common stock traded on the OTCQB market under the symbol "ELOX".

Holders

As of March 8, 2021, there were approximately 65 holders of record of our common stock. The actual number of holders of our common stock is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers or held by other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Recent Sales of Unregistered Securities

None, except as previously disclosed on our Quarterly Reports on Forms 10-Q and Current Reports on Forms 8-K.

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, 2020.

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. SELECTED FINANCIAL DATA

Not applicable to a "smaller reporting company" as defined in Item 10(f)(1) of Regulation S-K.

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

The following information should be read in conjunction with the consolidated financial statements and related notes thereto included in this Annual Report on Form 10-K (this "Report").

Except for the historical information contained in this Report, the matters discussed herein may be deemed to be forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. In this Report, words such as "may," "expect," "anticipate," "estimate," "intend," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements.

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

The following information and any forward-looking statements should be considered in light of factors discussed elsewhere in this Report, including those risks identified under Item 1A., Risk Factors. In many instances, dollar amounts contained in the narrative descriptions in the following section of this Report are stated in approximate values, pursuant to generally accepted rounding conventions. We caution readers not to place undue reliance on any forward-looking statements made by us, which speak only as of the date they are made. We disclaim any obligation, except as specifically required by law and the rules of the U.S. Securities and Exchange Commission (the "SEC"), to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

Company Overview

We are a clinical-stage biopharmaceutical company developing novel ribonucleic acid (RNA)-modulating drug candidates, each designed to be a eukaryotic ribosomal selective glycoside (ERSG), formulated to treat rare and ultra-rare premature stop codon diseases. Premature stop codons are point mutations that disrupt the stability of the impacted messenger RNA (mRNA) and the protein synthesis from that mRNA. As a consequence, patients with premature stop codon diseases have reduced levels of, or no, protein from a gene whose product performs an essential function. This type of mutation accounts for some of the most severe phenotypes across genetic diseases. Nonsense mutations have been identified in over 1,800 rare and ultra-rare diseases. Read-through therapeutic development is focused on increasing functional protein synthesis by enabling the cytoplasmic ribosome to read through premature stop codons to produce full-length proteins. As opposed to a typical gene therapy approach of targeting a single, unique mutation in a target disease, this small molecule strategy enables targeting an entire class of mutations across the rare disease landscape. Our small molecule approach has the potential to address a range of different premature stop codons in a single gene since our ERSG compounds are targeted to the ribosomes. ELX-02, our lead investigational drug product candidate, is a small molecule designed to restore production of full-length functional proteins. ELX-02 is in clinical development for systemic administration for cystic fibrosis. ELX-02 is an investigational drug that has not been approved by any global regulatory body. We are also conducting IND-enabling preclinical studies of ERSG compounds for autosomal dominant polycystic kidney disease (ADPKD) and in rare inherited retinal disorders (IRDs) by intravitreal administration with an initial focus on Usher Syndrome. Our preclinical candidate pool consists of a library of novel ERSG drug candidates identified based on read-through potential and cytoplasmic ribosomal selectivity. We hold worldwide development and commercialization rights to ELX-02 and other novel compounds in our read-through library, for all indications, in all territories, under a license from the Technion Research and Development Foundation Ltd. ("TRDF").

In 2019, we advanced our clinical program for ELX-02 into Phase 2 studies in cystic fibrosis and nephropathic cystinosis following completion of our MAD (multiple ascending dose) study in healthy volunteers and renal impairment study in healthy volunteers as well as volunteers with mild, moderate, and severe renal impairment. The results from the MAD study were presented in 2019 at both the European Cystic Fibrosis Society clinical meeting and the North American Cystic Fibrosis Conference (NACFC). The results have also been published in the *Journal of Clinical Pharmacology in Drug Development* in January of 2021. The results from the renal impairment study were presented at the 2019 American Society of Nephrology (ASN) Kidney Week and published in December 2020 in the *Journal of Clinical Pharmacology*. The results from the renal impairment study provided support for both continuing our clinical development programs and evaluating the suitability of our ERSG library for development in additional renal diseases, including ADPKD.

Our research and development strategy targets rare or ultra-rare diseases where a high unmet medical need exists, a nonsense mutation-bearing patient population is established, preclinical read-through can be established in predictive personalized medicine models, and a defined path through Orphan Drug development, regulatory approval, patient access and commercialization is identified. We believe patient advocacy is an important element of patient focused drug development, and we seek opportunities to collaborate with patient advocacy groups throughout the discovery and development process. Our current clinical program for our lead investigational drug product candidate, ELX-02, consists of Phase 2 studies in cystic fibrosis.

We intend to be the global leader in the application of the science of translational read-through and the associated pathway of nonsense mediated decay (NMD). We believe that expanding our expertise across these basic science areas of mRNA regulation, ribosomal function, and protein translation forms a solid foundation to support our discovery and development activities. Our ERSG compounds modulate the activity of the ribosome, a ribonucleoprotein complex of RNAs and proteins responsible for protein production (a process also known as translation). These novel small molecule ERSG compounds are designed to allow the ribosome to read-through a nonsense mutation in mRNA (which is transcribed from the DNA sequence), to restore the translation process to produce full-length, functional proteins and increase the amount of mRNA that would otherwise be degraded as part of a phenomenon called nonsense mediated mRNA decay. As our ERSG compounds target the general mechanism for protein production in the cell, we believe they have the potential to treat numerous genetic diseases where nonsense mutations have impaired gene function. Since nonsense mutations may occur at different positions within a given gene, a potential advantage of the small molecule ERSG approach is being able to use one molecule to address a range of mutations within a given disease state. Our subcutaneously injected ERSG molecules have the potential to be self-administered for systemic disease and to be active across many of the body’s tissues.

We believe that our library of related novel small molecules holds the potential to be disease-modifying therapies that may change the course of numerous genetic diseases and improve the lives of patients. Our early preclinical data in animal models of nonsense mutations suggests that drug product candidates from our read-through compound ERSG library may have potential beneficial effects for each of the following diseases: cystic fibrosis, nephropathic cystinosis, ADPKD, a variety of IRDs (including Usher Syndrome), primary ciliary dyskinesia, mucopolysaccharidosis type 1, Duchenne muscular dystrophy and Rett syndrome, and have demonstrated the potential for beneficial effects in multiple organs such as the brain, eye, kidney, lungs, muscles and others. Of the novel compounds in our ERSG library, approximately 30 compounds have been selected, based on read-through activity, for continued preclinical research and we anticipate additional compounds advancing toward Investigational New Drug (IND) filings.

Our scientific manuscript titled “ELX-02 generates protein via premature stop codon read-through without inducing native stop codon read-through protein” was published in the August 2020 issue of the *Journal of Pharmacology and Experimental Therapeutics* (JPET). This manuscript demonstrates that while ELX-02 mediates read-through of premature stop codons, the fidelity of native stop codons found at the end of healthy transcripts is maintained. This indicates that translation integrity is preserved with target-therapeutic exposure of ELX-02, consistent with the favorable tolerability profile across our preclinical and clinical data sets.

Currently, the clinical program for our lead investigational drug candidate, ELX-02, is focused on development for cystic fibrosis patients with diagnosed nonsense mutations. We have completed a Phase 1 single ascending dose (SAD) trial, a multiple ascending dose (MAD) trial, and a renal impairment study with healthy volunteers as well as volunteers having mild, moderate and severe renal impairment. The results of the SAD study were published in *Clinical Pharmacology in Drug Development* in January 2019. The results from the MAD study were presented in 2019 at both the European Cystic Fibrosis Society clinical meeting and the North American Cystic Fibrosis Conference (NACFC). The results have also been published in the *Journal of Clinical Pharmacology in Drug Development* in January of 2021. The results from the renal impairment study were presented at the 2019 American Society of Nephrology (ASN) Kidney Week and published in December 2020 in the *Journal of Clinical Pharmacology*.

Our scientific review written by Professor Eitan Kerem, M.D., Senior Attending Physician at the Hadassah CF Center in Jerusalem, Israel and Senior Medical Consultant to Eloxx, titled "ELX-02: an investigational read-through agent for the treatment of nonsense mutation-related genetic disease" was published in October 2020 by the Journal *Expert Opinion on Investigational Drugs*. This manuscript details the development of ELX-02 for the restoration of functional protein in nonsense-mediated disease in support of our ongoing Phase 2 trials.

Our scientific manuscript titled "Targeting *G542X CFTR* Nonsense Alleles With ELX-02 Restores CFTR Function in Human-Derived Intestinal Organoids" was published in the *Journal of Cystic Fibrosis* in February 2021**.** This manuscript reviews the results of our evaluation of ELX-02 mediated read-though, using the CFTR-dependent Forskolin-induced swelling (FIS) assay across a selection of *G542X* homozygous and heterozygous patient-derived organoids, ELX-02 increased CFTR activity in a dose-dependent fashion across a variety of forskolin induction concentrations. The functional increases are similar to those obtained with tezacaftor/ivacaftor in an *F508del* homozygous organoid. Additionally, ELX-02 treatment of these patient-derived organoids results in a 5-fold increase in *CFTR* mRNA when compared with vehicle treated, resulting in normalization of *CFTR* mRNA as measured using Nanostring.

Our Phase 2 cystinosis trial involved two sequential cohorts with three escalating doses in three patients per cohort. The first cohort enrolled three homozygous W138X patients ages 23 to 38, with prior kidney transplants and varying degrees of renal insufficiency. In January 2020, we announced positive data from the first cohort of the Phase 2 study of ELX-02 in the treatment of patients with nonsense mutation-mediated nephropathic cystinosis. The results of the first cohort met the primary safety endpoint and the reductions in white blood cell (WBC) cystine provided a clear indication of biologic activity in these patients at nominal doses > 0.5 mg/kg/day. Following review of the safety and pharmacokinetic data by an independent Safety Review Committee (SRC), the SRC approved progressing to the second cohort that would enable enrolling patients ages 12 and older. Due to study design limitations, patients across all dose groups had elevated and uncontrolled pretreatment WBC cystine levels which made it difficult to fully evaluate ELX-02-mediated WBC cystine reductions. Therefore, we have discontinued this study and will not proceed with the second cohort as contemplated in the original protocol. We plan to continue to review these data with a panel of scientific and clinical experts to determine appropriate modifications for a possible new study design.

The clear indications of biologic activity in this study provide human clinical proof of concept for ELX-02 and de-risk other clinical applications of our ERSG library using this dosage range. These encouraging results also provide a basis for expansion to studies of additional kidney diseases caused by nonsense mutations, such as ADPKD.

Our Phase 2 cystic fibrosis clinical trial program for ELX-02 is being conducted at leading global investigator sites in Europe, Israel and the United States. On March 25, 2020, we announced that enrollment in these trials had been paused temporarily in response to the global 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 had been resumed in Israel and Europe, and on August 12, 2020, we announced that enrollment had been resumed in the U.S. The COVID-19 pandemic continues to evolve, and we continue to work closely with our clinical sites and investigators. We are also evaluating additional clinical sites in other countries where patient enrollment may be feasible. We remain committed to completing enrollment in these Phase 2 proof of concept clinical trials and reporting top line data in the first half of 2021, which is contingent on no further disruptions due to the COVID-19 pandemic. Several planned Safety Review Committee meetings have occurred and allowed dose escalation up to the top dose level with no drug-related serious adverse events reported to date. Multiple patients have progressed through the four-dose escalation range. The Cystic Fibrosis Foundation ("CF Foundation") is providing funding for a portion of the U.S. program and in December of 2020, expanded its support to include our global clinical trial program. We have since formed a joint program advisory group with the CF Foundation focused on the development of ELX-02 for cystic fibrosis. The Cystic Fibrosis Therapeutics Development Network ("TDN") has sanctioned the Phase 2 study protocol, which is being conducted at TDN member sites. Additional information about our clinical trials can be found at www.ClinicalTrials.gov (Identifiers: NCT04126473 and NCT04135495).

Professor Eitan Kerem, M.D., former Head of the Division of Pediatrics, Children's Hospital, Hadassah Medical Center in Israel, has joined Eloxx as a Senior Medical Consultant. For the U.S. trial, Dr. Ahmet Uluer, Director of the Adult Cystic Fibrosis Program at the Boston Children's Hospital/Brigham and Women's Hospital CF Center, is the lead study investigator. The protocols have been sanctioned by the TDN in the U.S. and the European Cystic Fibrosis Society Clinical Trial Network (which has given our Europe/Israel trial a "high priority" ranking). During October 2019, we completed an interim CMC review meeting with the U.S. Food and Drug Administration (the "FDA") and we have gained alignment with the agency on our manufacturing formulation and process, which we believe will be suitable for our expected drug supply needs through completion of our pivotal trials. The in-person ECFS conference in Lyon, France scheduled for June 2020 was cancelled, and we withdrew our abstract. We presented data from two scientific abstracts at the North American Cystic Fibrosis Virtual Conference (NACFC). The two abstracts were also showcased in the NACFC virtual poster gallery and electronically published as a supplement to *Pediatric Pulmonology*. The live sessions and discussions took place through October 23, 2020. These virtual posters are available to registered attendees on the NACFC online conference platform. The preclinical study results demonstrate ELX-02's selectivity for read-through of premature stop codons versus native stop codons and its ability to restore production of functional *CFTR* in patient-derived organoids.

We believe there is a significant unmet medical need in the treatment of cystic fibrosis patients carrying nonsense mutations on one or both alleles of the CFTR gene. Cystic fibrosis is the most prevalent genetic disease in the western world and there are no currently approved therapies that target the impairment associated with Class 1 CFTR mutations. We believe that nonsense mutations may impact a similar proportion of patients diagnosed with cystinosis. Given the high proportion of pediatric patients in many rare orphan diseases, we intend to apply for relevant Orphan Drug incentives in the U.S. and Europe, including the Rare Pediatric Disease Priority Review Voucher in the U.S. Currently, the European Medicines Agency (the "EMA") has designated ELX-02 as an orphan medicine for the treatment of cystic fibrosis and mucopolysaccharidosis type I (MPS I). The FDA had previously granted orphan drug designation to ELX-02 for the treatment of nephropathic cystinosis, MPS I, and Rett syndrome, and on August 4, 2020, we announced that the FDA had granted orphan drug designation for ELX-02 for the treatment of cystic fibrosis. The FDA's Office of Orphan Drug Products grants orphan status to support the development of medicines for underserved patient populations, or rare disorders, that affect fewer than 200,000 people in the U.S. Orphan drug designation provides certain benefits, including seven years of market exclusivity upon regulatory approval (if received), exemption from FDA application fees, tax credits on qualified U.S. clinical trials and eligibility for grant funding opportunities that can be used for clinical trial costs.

We are also evaluating the suitability of our ERSG library for development in renal diseases associated with nonsense mutations, such as ADPKD. ADPKD is a relatively common inherited genetic kidney disease occurring in between one in 400 and one in 1,000 patients and is the fourth leading cause of end-stage renal disease in the U.S. Over 25% of the primary genetic changes that cause ADPKD are nonsense mutations, where a premature stop codon in the gene leads to a truncated, often unstable, protein. We have evaluated the three most relevant ADPKD nonsense mutations in an *in vitro* read-through assay and have demonstrated significant levels of read-through for ELX-02 and several library compounds, which is the first step in our preclinical development toward an IND.

We continue to progress our ERSG pipeline in IRDs, another area of high unmet medical need, that are associated with vision loss and blindness. There are over 300 IRDs associated with nonsense mutations. In 2020, we reported on a critical milestone demonstrating that several of our library compounds successfully reach retinal disorder-relevant tissue layers and can restore protein production in an animal model. These data support the suitability of our ERSG compounds for reaching and promoting read-through in target cells within the retina. We presented data at the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting in May 2020, which was held virtually. Our IRD research also includes exploring multiple sustained release formulation technologies, and *in vitro* release rates achieved to date have been consistent with our target release profile of one to three months. Our scientific manuscript titled "Intravitreal administration of small molecule read-through agents demonstrate functional activity in a nonsense mutation mouse model" was published in October 2020 by the *Journal of Experimental Eye Research*. This manuscript demonstrates that multiple small molecules in our ERSG library mediate dose-dependent read-through at the back of the eye after a single intravitreal injection. Collectively, our manuscripts demonstrate the wide-ranging potential of our small molecule read-through approach to rare genetic disorders mediated by nonsense mutations; from targeted delivery for inherited retinal disorders to systemic delivery for multi-system disorders like cystic fibrosis.

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 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 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, 2020 and 2019, 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 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.

Results of Operations

For discussion of 2019 results and comparison with 2018 results, refer to Part II, Item 7, “Management's Discussion and Analysis of Financial Condition and Results of Operations” in our Annual Report on Form 10-K for the fiscal year ended December 31, 2019.

Comparison of the Years Ended December 31, 2020 and 2019

Dollar amounts in the following table are in thousands:

	Year ended December 31,			
	2020	2019	2020 / 2019	
Operating expenses:				
Research and development	$ 14,590	$ 26,349	$ (11,759)	(45) %
General and administrative	14,847	24,206	(9,359)	(39) %
Restructuring charges	4,018	—	4,018	— %
Total operating expenses	33,455	50,555	(17,100)	(34) %
Loss from operations	(33,455)	(50,555)	17,100	(34) %
Other (income) expense, net	1,122	319	803	252 %
Loss before income taxes	(34,577)	(50,874)	16,297	(32) %
Provision for income taxes	—	—	—	— %
Net loss	$ (34,577)	$ (50,874)	$ 16,297	(32) %

Research and development expenses

Research and development expenses were $14.6 million for the year ended December 31, 2020 compared to $26.3 million for the year ended December 31, 2019, a decrease of $11.8 million. The decrease was primarily related to a decrease in salaries and other personnel related costs of $1.2 million, a $1.5 million decrease in stock-based compensation expense, and a $9.1 million decrease in expenses related to subcontractors, consultants and advisors in connection with continued development of ELX-02 due to the impact of the COVID-19 pandemic. These decreases were all primarily related to the realignment actions taken by our Board of Directors in February 2020, including reductions in research and development headcount and in external spending.

General and administrative expenses

General and administrative expenses were $14.8 million for the year ended December 31, 2020 compared to $24.2 million for the year ended December 31, 2019, a decrease of $9.4 million. The decrease was primarily related to a $3.3 million decrease in stock-based compensation expense, a $4.1 million decrease in expenses attributable principally to infrastructure related costs including legal, accounting and other professional fees and a $1.9 million decrease in salaries and other personnel related costs. These decreases were all primarily related to the realignment actions taken by our Board of Directors in February 2020, including reductions in general and administrative headcount and in external spending.

Restructuring charges

Restructuring charges of $4.0 million for the year ended December 31, 2020 resulted from the leadership and organizational realignment during the first quarter of 2020. The total included $1.9 million related to contract termination and employee separation costs (primarily severance and benefits) and $2.1 million of non-cash stock compensation, relating to accelerated vesting of executive stock awards. There were no similar charges during the year ended December 31, 2020.

Other expense (income), net

We recorded $1.1 million in other expense, net for the year ended December 31, 2020 compared to $0.3 million for the year ended December 31, 2019, an increase of $0.8 million. The increase was primarily due a decrease in interest income of $0.7 million and investment income of $0.3 million, offset by a $0.2 million decrease in debt issuance costs and interest expense related to the commencement of principal repayments on the term loan in February 2020.

Provision for income taxes and net operating loss carryforwards

There were no provisions for or benefits from income taxes recorded in the years ended December 31, 2020 and 2019. As of December 31, 2020, we had U.S. federal and state net operating loss ("NOL") carryforwards of $108.9 million and $13.7 million, respectively, and federal research tax credit carryforwards of $3.6 million. Certain U.S. net operating loss carryforwards will begin to expire, if not utilized, beginning in 2021 through 2037, and the research tax credits will expire beginning in 2027 through 2037. These NOL carryforwards could expire unused and be unavailable to offset future income tax liabilities. Included in these U.S. federal NOL carryforwards are $34.9 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. Under the Tax Act, federal net operating losses incurred beginning in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited. It is uncertain if and to what extent various U.S. states will conform to the newly enacted federal tax law. Also, as of December 31, 2020, we had Israeli NOL carryforwards of $86.9 million, which carry forward indefinitely.

Liquidity, Capital Resources and Going Concern

Liquidity is the ability of a company to generate funds to support its current and future operations, satisfy its obligations, and otherwise operate on an ongoing basis. Significant factors in the management of liquidity are funds generated by operations, levels of accounts receivable and accounts payable and capital expenditures. To date, we have not generated revenue from sales of any product or service.

Since our inception, we have incurred significant operating losses. Our net losses were $(34.6) million and $(50.9) million for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, we had an accumulated deficit of $(171.6) 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. 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.

We may never achieve profitability, and unless and until we do, we will continue to need to raise additional cash to fund our operations. On February 24, 2020, our Board of Directors approved a leadership and organizational re-alignment, which is expected to achieve annual cost savings of approximately $4.9 million primarily related to salaries and benefits, with fiscal year 2020 savings of approximately $2.3 million, net of severance costs. Our cash, and cash equivalents are highly liquid investments with original maturities of one year or less at the date of purchase and consist of cash in operating accounts and secured investments, primarily money market funds.

Although the impact of the COVID-19 pandemic on clinical operations and trial enrollment cannot fully be determined, we believe that our cash and cash equivalents of $24.7 million at December 31, 2020, will enable us to meet the anticipated cash needs required to reach top line Phase 2 data in cystic fibrosis; however, this amount 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. Beyond that point, 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 without additional funding through 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 we are unable to obtain adequate financing, we will evaluate alternatives which may include reducing or deferring operating expenses, which may have a material adverse effect on our operations and future prospects.

Principal Financing Activities

On April 30, 2018, we completed an underwritten public offering of 5,899,500 shares of our common stock, including the exercise in full by the underwriter of its overallotment option to purchase an additional 769,500 shares, at the public offering price of $9.75 per share for gross proceeds of approximately $57.5 million, before deducing the underwriting discounts and commissions and offering expenses of approximately $3.9 million.

In November 2018, we entered into an Equity Distribution Agreement with Citigroup Global Markets Inc. and Cantor Fitzgerald & Co., pursuant to which we sold 236,462 shares of common stock and received proceeds of $2.9 million, net of issuance costs of $0.1 million through December 31, 2019, of which 35,362 shares of common stock, with received net proceeds of $0.7 million were sold in January of 2019. The shares sold were pursuant to an effective registration statement as described below.

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.

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 following the funding of the loan. On December 31, 2020, the interest rate was 5.75%. We commenced making payments on the outstanding principal balance of the loan on February 1, 2020, which is payable in 36 equal monthly installments. Amounts outstanding under the loan are due and payable on January 1, 2023.

In conjunction with the initial loan advance, we issued warrants (the "Warrants") to the Lenders to purchase an aggregate of 40,834 shares of our common stock at a warrant exercise price of $11.02 (subject to certain adjustments), which price was calculated using the 10-day average bid price of our common stock prior to the date of the Loan Agreement.

We may prepay the outstanding principal balance of the loans advanced by the Lenders 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. We 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.

Under the terms of the Loan Agreement, we granted first priority liens and security interests in substantially all of our assets (excluding all of its intellectual property, which is subject to a negative pledge) and a pledge by us of the shares of one of our wholly-owned subsidiaries as collateral for the obligations thereunder. The Loan Agreement also contains representations and warranties by us and the Lenders and indemnification provisions in favor of the Lenders and customary covenants (including limitations on other indebtedness, liens, acquisitions, investments and dividends, but no financial covenants), and events of default (including payment defaults, breaches of covenants following any applicable cure period, a material impairment in the perfection or priority of the Lenders' security interest in the collateral, and events relating to bankruptcy or insolvency).

On June 24, 2019, we completed an underwritten public offering of 3,833,334 shares of common stock at the public offering price of $9.00 per share and received gross proceeds of approximately $34.5 million, before deducting underwriting discounts and commissions of $2.1 million and offering expenses of $0.2 million.

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 expect to use the loan proceeds for payroll and other covered costs in accordance with the relevant terms and conditions of the CARES Act. We issued a promissory note for the PPP Loan with a maturity date of April 21, 2022 and an interest rate of 1.0% per annum. Monthly payments of principal and interest will be due beginning on September 21, 2021, although interest accrues from the issuance date. We may prepay the PPP Loan without penalty or premium, and the promissory note provides for customary events of default. A PPP loan may be partially or entirely forgiven based on employee retention for the 24-week period starting on the loan date through October 2020, and the use of loan proceeds for payroll or other specified costs during the same period. Forgiveness is also based on the employer maintaining or restoring headcount and maintaining salary levels. Forgiveness is reduced if headcount declines or if salaries decrease. Any loan forgiveness will be made subject to SVB approval in accordance with SBA requirements.

Cash Flows

The following table presents the major components of net cash flows provided by (used in) operating, investing and financing activities for the periods presented (in thousands):

	Year ended December 31,	
	2020	2019
Net cash used in operating activities	$ (28,166)	$ (39,391)
Net cash provided by (used in) investing activities	$ 33,792	$ (33,524)
Net cash (used in) provided by financing activities	$ (3,438)	$ 46,800

Our operating activities used cash of $28.2 million and $39.4 million for the years ended December 31, 2020 and 2019, 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, 2020, our net loss was $34.6 million, partially offset by non-cash charges of $8.7 million related to stock-based compensation expense and $0.1 million of depreciation expense. Changes in working capital for the period were $3.4 million, related primarily to decreases in accounts payable and accrued expenses. During the year ended December 31, 2019, our net loss was $50.9 million, partially offset by non-cash charges of $11.4 million related to stock-based compensation expense and $0.1 million of depreciation expense. Changes in working capital for the period were $0.6 million, related primarily to changes in accounts payable and accrued expenses.

Our investing activities provided cash of $33.8 million and used cash of $33.5 million for the years ended December 31, 2020 and 2019, respectively. Cash provided by investing activities during the year ended December 31, 2020 was primarily related to $33.8 million of proceeds from maturities of marketable securities. Cash used in investing activities during the year ended December 31, 2019 consisted primarily of purchases of marketable securities of $67.2 million, offset by proceeds of $33.8 million received upon maturities of marketable securities.

Our financing activities used cash of $3.4 million and provided cash of $46.8 million for the years ended December 31, 2020 and 2019, respectively. During the year ended December 31, 2020, net cash used in financing activities resulted primarily from $4.6 million in term loan principal repayments, offset by $0.8 million received from the PPP Loan and $0.4 million in advances received from collaboration partners. During the year ended December 31, 2019, net cash provided by financing activities resulted primarily from net proceeds of $32.2 million from our public offering of common stock in June 2019, the issuance of debt of $14.7 million (net of issuance costs) in January 2019, and proceeds of $0.7 million from the sale of common stock, offset by $1.4 million of taxes paid upon the vesting of restricted stock units.

Form S-3 and Equity Sales

On April 10, 2018, we filed a shelf registration statement (the "April 2018 Shelf") on Form S-3 with the U.S. Securities and Exchange Commission (the "SEC"). The April 2018 Shelf (File No. 333-224207) was declared effective on April 20, 2018 and covers the offering, issuance and sale of up to $125 million of our common stock, preferred stock, debt securities or warrants and other securities, either individually or in combination.

In November 2018, we entered into an Equity Distribution Agreement (the "Agreement") with Citigroup Global Markets Inc. and Cantor Fitzgerald & Co. (collectively, the "Sales Agents"), pursuant to which we may sell and issue shares of our common stock up to an aggregate of $50 million through the Sales Agents. The shares were offered pursuant to the April 2018 Shelf. We agreed to pay the Sales Agents a commission of up to 3% of the gross proceeds of any sales of common stock pursuant to the Agreement. We incurred approximately $0.3 million related to legal, accounting and other fees in connection with the Agreement. For the year ended December 31, 2018, under the Agreement, we sold 201,100 shares of common stock and received net proceeds of $2.2 million. In January 2019, we sold 35,362 shares of common stock and received net proceeds of $0.7 million.

On November 16, 2018, we filed a shelf registration statement (the "November 2018 Shelf") on Form S-3 with the SEC. The November 2018 Shelf (File No. 333-228430) was declared effective on November 26, 2018 and covers the offering, issuance and sale of up to $200 million of our common stock, preferred stock, debt securities or warrants and other securities, either individually or in combination, and is available for future issuances.

On June 24, 2019, we completed an underwritten public offering of 3,833,334 shares of common stock at the public offering price of $9.00 per share and received net proceeds of approximately $34.5 million, before deducting underwriting discounts and commissions of $2.1 million and estimated offering expenses of $0.2 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. No grants were received for the years ended December 31, 2020, 2019 or 2018.

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, 2020, 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 $2.7 million, including accrued LIBOR interest.

Technion Research and Development Foundation Limited Agreement

On August 29, 2013, we entered into an agreement (the "Technion Agreement") with the Technion Research and Development Foundation Limited ("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 us 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 year ended December 31, 2020 no expenses were incurred and for the years ended December 31, 2019 and 2018, we recorded research and development expenses of $0.2 million and $0.1 million, respectively, in relation to the Technion Agreement for the reimbursement of costs incurred during the preparation, filing, prosecution and maintenance of the TRDF patents rights related to Eloxx Limited (Israel). As of December 31, 2020 no amounts were recorded in accrued expenses and as of December 31, 2019, amounts recorded in accrued expenses were $0.1 million.

In addition, TRDF granted us a license to use, market, sell or sub-license the rights of the product developed under the TRDF research results (the "Licensed Product"), as defined in the Technion Agreement, for the following considerations: (a) milestone payments up to total consideration of $6.1 million, to be transferred upon meeting certain milestones as defined in the Technion Agreement; (b) certain royalties in the low- to mid-single-digit percentage of net sales (subject to change in the case of (x) sublicensing to a big pharmaceutical or biotechnology company, or (y) payment of royalties to third parties, or (z) 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 (c) a low- to mid-double-digit percentage of any non-royalty sub-license income received by us from a sub-licensed entity. During the year ended December 31, 2020, we made the first milestone payment of $0.1 million to TRDF.

Off-Balance Sheet Arrangements

As of December 31, 2020 and 2019, 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 applicable to a "smaller reporting company", 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, set forth in this Report.

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

None.

ITEM 9A. CONTROLS AND PROCEDURES

Management's Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities and Exchange Act of 1934 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.

As of December 31, 2020, our management, under the supervision and with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities and Exchange Act of 1934 (the "Exchange Act")). Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our principal executive officer and principal financial officer have concluded based upon the evaluation described above that, as of December 31, 2020, our disclosure controls and procedures were effective in ensuring that material information relating to the Company, including its consolidated subsidiaries, required to be disclosed by the Company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms, including ensuring that such material information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15d-15(f). Internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles.

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

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2020 based on the guidelines established in *Internal Control-Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO"). Based on this evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2020.

This Annual Report on Form 10-K 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 Smaller Reporting Company and a non-accelerated filer.

Changes in Internal Control over Financial Reporting

During the quarter ended December 31, 2020, there have been no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Securities Exchange Act of 1934, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this Item 10 will be included under the captions “Executive Officers,” “Election of Directors,” “Section 16(a) Beneficial Ownership Reporting Compliance,” “Code of Ethics,” “Information Regarding Committees of the Board of Directors” and “Information regarding the Board of Directors and Corporate Governance” in our definitive proxy statement to be filed pursuant to Regulation 14A within 120 days after the end of the fiscal year covered by this Report.

ITEM 11. EXECUTIVE AND DIRECTOR COMPENSATION

The information required by this Item 11 will be included under the captions “Executive Compensation” and “Director Compensation” in our definitive proxy statement to be filed pursuant to Regulation 14A within 120 days after the end of the fiscal year covered by this 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 under the captions “Security Ownership of Certain Beneficial Owners and Management” and “Equity Compensation Plan Information” in our definitive proxy statement to be filed pursuant to Regulation 14A within 120 days after the end of the fiscal year covered by this Report.

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

The information required by this Item 13 will be included, as applicable, under the captions of “Independence of the Board of Directors,” “Employment Arrangements” and “Transactions with Related Persons” in our definitive proxy statement to be filed pursuant to Regulation 14A within 120 days after the end of the fiscal year covered by this Report.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this Item 14 will be included under the captions “Principal Accountant Fees and Services” and “Pre-Approval Policies and Procedures” in our definitive proxy statement to be filed pursuant to Regulation 14A within 120 days after the end of the fiscal year covered by this 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 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 Report.

(3) Exhibits:

The exhibits listed in the Exhibit Index at the end of this report are filed or incorporated by reference as part of this 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	Agreement, dated as of May 31, 2017, by and among Sevion Therapeutics, Inc., Sevion Sub, Ltd. and Eloxx Pharmaceuticals Ltd. (incorporated by reference to Exhibit 2.1 of the Company's Current Report on Form 8-K filed on June 6, 2017, SEC File No. 001-31326)
2.2	Amendment to Agreement, dated as of August 1, 2017, by and among Sevion Therapeutics, Inc., Sevion Sub, Ltd. and Eloxx Pharmaceuticals Ltd. (incorporated by reference to Exhibit 2.3 of the Company's Annual Report on Form 10-K filed on October 13, 2017, SEC File No. 001-31326)
2.3	Second Amendment to Agreement, dated as of November 23, 2017, by and among Sevion Therapeutics, Inc., Sevion Sub, Ltd. and Eloxx Pharmaceuticals Ltd. (incorporated by reference to Exhibit 2.1 of the Company's Current Report on Form 8-K filed on November 29, 2017, SEC File No. 001-31326)
3.1	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).
3.2	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).
3.3	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).
3.4	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).
3.5	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).
3.6	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).
3.7	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).
3.8	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).
3.9	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).
3.10	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).
3.11	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).

Exhibit No.	Description of Exhibit
3.12	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).
3.13	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).
4.1	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).
10.1*	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).
10.2*	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).
10.3	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).
10.4	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).
10.5	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).
10.6	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).
10.7	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).
10.8	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).
10.9	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).
10.10	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).

Exhibit No.	Description of Exhibit
10.11	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).
10.12	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).
10.13	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).
10.14	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).
10.15**	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).
10.16**	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).
10.17**	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).
10.18**	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).
10.19**	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).
10.20**	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)
10.21**	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).
10.22**	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).
10.23**	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).
10.24**	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).
10.25**	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).

Exhibit No.	Description of Exhibit
10.26**	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).
10.27**	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).
10.28**	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).
10.29	Lease Agreement by and between Eloxx Pharmaceuticals, Inc. and BP Bay Colony LLC, dated October 26, 2017 (incorporated by reference to Exhibit 10.31 of our Annual Report on Form 10-K filed on March 16, 2018, SEC File No. 001-31326).
10.30	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).
10.31	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).
10.32	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).
10.33	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).
10.34	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).
10.35	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).
10.36	First Amendment to Lease Agreement by and between Eloxx Pharmaceuticals, Inc. and BP Bay Colony LLC, dated June 21, 2018 (incorporated by reference to Exhibit 10.1 of our Current Report on Form 8-K filed on June 26, 2018, SEC File No. 001-31326).
10.37**	Executive Employment Agreement between Eloxx Pharmaceuticals, Inc. and Gregory C. Williams dated as of June 22, 2018 (incorporated by reference to Exhibit 10.2 of our Current Report on Form 8-K filed on June 26, 2018, SEC File No. 001-31326).
10.38	Executive Employment Agreement between Eloxx Pharmaceuticals, Inc. and David Snow dated as of June 18, 2018 (incorporated by reference to Exhibit 10.38 of our Annual Report on Form 10-K filed on March 14, 2019, SEC File No. 001-31326).
10.39	Equity Distribution Agreement, dated November 16, 2018, by and between Eloxx Pharmaceuticals, Inc., Citigroup Global Markets Inc. and Cantor Fitzgerald & Co. (incorporated by reference to Exhibit 10.1 of our Current Report on Form 8-K, filed on November 16, 2018, SEC File No. 001-31326).
10.40	Loan and Security Agreement, dated as of January 30, 2019, by and among Silicon Valley Bank, WestRiver Innovation Lending Fund VIII, L.P., Eloxx Pharmaceuticals, Inc., and Eloxx Pharmaceuticals Ltd (incorporated by reference to Exhibit 10.40 of our Annual Report on Form 10-K filed on March 14, 2019, SEC File No. 001-31326).
10.41	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).

Exhibit No.	Description of Exhibit
10.42**	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).
10.43**	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).
10.44**	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).
16.1	Letter of Kost Forer Gabbay & Kasierer, a Member of Ernst & Young Global, dated June 21, 2018 (incorporated by reference to Exhibit 16.1 of our Current Report on Form 8-K filed on June 21, 2018, SEC File No. 001-31326).
21.1	List of Subsidiaries of the Company.
23.1	Consent of Deloitte & Touche LLP, Independent Registered Public Accounting Firm.
31.1	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.
31.2	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.
32.1	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.
32.2	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.
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)

* 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

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 12, 2021

/s/ Gregory C. Williams
Gregory C. Williams, Ph.D., MBA
Chief Executive Officer
(On behalf of the Registrant and as Principal Executive Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Gregory C. Williams and Stephen G. MacDonald, and each of them, as his or her true and lawful attorneys-in-fact and agents, each with the full power of substitution, for him or her and in his or her name, place or stead, in any and all capacities, to sign any and all amendments to this report, with exhibits thereto and other documents in connection therewith, with the U.S. Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or their, his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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

Signature	Title	Date
/s/ Gregory C. Williams Gregory C. Williams, Ph.D., MBA	Chief Executive Officer (Principal Executive Officer)	March 12, 2021
/s/ Stephen G. MacDonald Stephen G. MacDonald	Vice President, Finance and Accounting, and Treasurer (Principal Financial Officer and Principal Accounting Officer)	March 12, 2021
/s/ Tomer Kariv Tomer Kariv	Chairman of the Board of Directors	March 12, 2021
/s/ Ran Nussbaum Ran Nussbaum	Director	March 12, 2021
/s/ Silvia Noiman Silvia Noiman, Ph.D.	Director	March 12, 2021
/s/ Gadi Veinrib Gadi Veinrib	Director	March 12, 2021
/s/ Zafrira Avnur Zafrira Avnur, Ph.D.	Director	March 12, 2021
/s/ Martijn Kleijwegt Martijn Kleijwegt	Director	March 12, 2021
/s/ Steven D. Rubin Steven D. Rubin	Director	March 12, 2021
/s/ Jasbir Seehra Jasbir Seehra, Ph.D.	Director	March 12, 2021

ELOXX PHARMACEUTICALS, INC. AND SUBSIDIARIES

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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 the accompanying consolidated balance sheets of Eloxx Pharmaceuticals, Inc. and subsidiaries (the "Company") as of December 31, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, stockholder's equity, and cash flows, for each of the three years in the period ended December 31, 2020, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

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

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

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

Emphasis of Matter Regarding Going Concern

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

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current-period audit of the 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 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 — Refer to Notes 2 and 5 to the financial statements

Critical Audit Matter Description

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 research 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, 2020. The cost of such services are often determined based on subjective judgments and requires management to make certain estimates as to the progress of completion.

We identified the accrued research and development expenses, specifically clinical trial costs and contract research liabilities related to contract research organizations, as a critical audit matter because of the significant estimates and assumptions management makes to measure these accrued liabilities. This required a high degree of auditor judgment 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.

How the Critical Audit Matter Was Addressed in the Audit

Our audit procedures related to the clinical trial costs and contract research liabilities included evaluating the methods and assumptions used by management to estimate the clinical trial costs and contract research liabilities, including the following, among others:

- We evaluated management's assessment of the level of services performed by clinical research organizations by performing corroborating inquiries with the Company's clinical research managers and comparing the estimates to management's clinical research progress reports, research milestone specifications, and contract research agreements.
- We evaluated the reasonableness of management's methods for the identification of services provided by contract research organizations and development of assumptions for estimating accrued clinical trial costs and contract research liabilities by:
    - Performing retrospective review on the prior period estimates to compare to actual settled costs.
    - Inspecting third-party documents such as service contracts, status reports, and other correspondence, and agreeing them to the recorded accrued research and development costs.
    - Developing independent estimates for the accrued clinical trial costs and contract research liabilities.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 12, 2021

We have served as the Company's auditor since 2018.

ELOXX PHARMACEUTICALS, INC. AND SUBSIDIARIES

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

	December 31,	
	2020	**2019**
Assets		
Current assets:		
Cash and cash equivalents	$ 24,668	$ 22,493
Marketable securities	—	33,783
Restricted cash	56	43
Prepaid expenses and other current assets	1,169	1,390
Total current assets	25,893	57,709
Property and equipment, net	133	201
Operating lease right-of-use asset	421	924
Other long-term assets	30	113
Total assets	$ 26,477	$ 58,947
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 481	$ 1,871
Accrued expenses	2,886	4,655
Current portion of long-term debt	5,239	4,336
Advances from collaboration partners	805	403
Current portion of operating lease liability	389	499
Taxes payable	38	43
Total current liabilities	9,838	11,807
Long-term debt	6,376	10,502
Operating lease liability	33	425
Total liabilities	16,247	22,734
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.01 par value per share, 5,000,000 shares authorized, no shares issued or outstanding as of December 31, 2020 and 2019	—	—
Common stock, $0.01 par value per share, 500,000,000 shares authorized, 40,350,922 and 40,186,469 shares issued, and 40,157,187 and 40,030,763 shares outstanding as of December 31, 2020 and 2019, respectively	404	402
Common stock in treasury, at cost, 193,735 and 155,706 shares as of December 31, 2020 and 2019, respectively	(1,828)	(1,703)
Additional paid-in capital	183,250	174,515
Accumulated other comprehensive income	—	18
Accumulated deficit	(171,596)	(137,019)
Total stockholders' equity	10,230	36,213
Total liabilities and stockholders' equity	$ 26,477	$ 58,947

See accompanying notes to consolidated financial statements

ELOXX PHARMACEUTICALS, INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(Amounts in thousands, except share and per share data)

	Year ended December 31,		
	2020	**2019**	**2018**
Operating expenses:			
Research and development	$ 14,590	$ 26,349	$ 20,489
General and administrative	14,847	24,206	26,482
Restructuring charges	4,018	—	—
Reverse merger related expenses	—	—	594
Total operating expenses	33,455	50,555	47,565
Loss from operations	(33,455)	(50,555)	(47,565)
Other expense (income), net	1,122	319	(502)
Loss before income taxes	(34,577)	(50,874)	(47,063)
Provision for income taxes	—	—	122
Net loss	$ (34,577)	$ (50,874)	$ (47,185)
Net loss per share, basic and diluted	$ (0.86)	$ (1.34)	$ (1.45)
Weighted average number of shares of common stock used in computing net loss per share, basic and diluted	40,124,953	38,063,173	32,436,506
Comprehensive loss:			
Net loss	$ (34,577)	$ (50,874)	$ (47,185)
Other comprehensive income (loss):			
Change in unrealized gain (loss) on available-for-sale securities	(18)	18	—
Comprehensive loss	$ (34,595)	$ (50,856)	$ (47,185)

See accompanying notes to consolidated financial statements

ELOXX PHARMACEUTICALS, INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(Amounts in thousands, except share data)

	Common Stock				Treasury Stock			
	Shares	Amount	Additional paid-in capital	Accumulated other comprehensive income	Shares	Amount	Accumulated deficit	Total stockholders' equity
Balance as of December 31, 2017	27,527,738	$ 274	$ 60,047	$ —	—	$ —	$ (38,960)	$ 21,361
Exercise of stock options	1,334,522	14	432	—		—	—	446
Issuance of common stock upon Technion settlement	569,395	6	(6)	—	—	—	—	—
Issuance of shares upon execution of warrants	60,989	1	51	—	(3,385)	(52)	—	—
Issuance of shares upon public offering	5,899,500	60	53,513	—	—	—	—	53,573
Issuance of common stock from at-the-market sales agreement	201,100	2	2,421	—	—	—	—	2,423
Repurchase of common stock	(5,076)	—	—	—	(5,000)	(31)	—	(31)
Vesting of restricted stock units	271,946	3	(3)	—	(83,038)	(1,046)	—	(1,046)
Stock-based compensation expense	—	—	13,370	—	—	—	—	13,370
Net loss	—	—	—	—	—	—	(47,185)	(47,185)
Balance as of December 31, 2018	35,860,114	360	129,825	—	(91,423)	(1,129)	(86,145)	42,911
Exercise of stock options	116,327	1	168	—	—	—	—	169
Issuance of shares upon execution of warrants	44,814	1	178	—	(14,893)	(179)	—	—
Issuance of shares upon public offering	3,833,334	38	32,134	—	—	—	—	32,172
Issuance of common stock from at-the-market sales agreement	35,362	—	455	—	—	—	—	455
Issuance of warrants	—	—	421	—	—	—	—	421
Vesting of restricted stock units	140,812	2	(2)	—	(49,390)	(395)	—	(395)
Stock-based compensation expense	—	—	11,336	—	—	—	—	11,336
Change in unrealized gain (loss) on investments	—	—	—	18	—	—	—	18
Net loss	—	—	—	—	—	—	(50,874)	(50,874)
Balance as of December 31, 2019	40,030,763	402	174,515	18	(155,706)	(1,703)	(137,019)	36,213
Exercise of stock options	17,210	1	70	—	—	—	—	71
Vesting of restricted stock units	109,214	1	(1)	—	(38,029)	(125)	—	(125)
Stock-based compensation expense	—	—	8,666	—	—	—	—	8,666
Change in unrealized gain (loss) on investments	—	—	—	(18)	—	—	—	(18)
Net loss	—	—	—	—	—	—	(34,577)	(34,577)
Balance as of December 31, 2020	40,157,187	$ 404	$ 183,250	$ —	(193,735)	$ (1,828)	$ (171,596)	$ 10,230

See accompanying notes to consolidated financial statements.

ELOXX PHARMACEUTICALS, INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF CASH FLOWS
(Amounts in thousands)

	Year ended December 31,		
	2020	**2019**	**2018**
Cash flows from operating activities:			
Net loss	$ (34,577)	$ (50,874)	$ (47,185)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	8,666	11,336	13,370
Depreciation	68	87	216
Loss (gain) on sales and disposals of property and equipment	—	(2)	12
Amortization of operating lease right-of-use asset	503	472	—
Amortization of debt discount	563	535	—
Amortization, net, of premiums and discounts on investments	15	(301)	—
Changes in operating assets and liabilities:			
Prepaid expenses and other assets	262	83	(1,121)
Accounts payable	(1,390)	1,124	(780)
Accrued expenses	(1,769)	(1,300)	3,999
Operating lease liabilities	(502)	(472)	—
Taxes payable	(5)	(79)	122
Net cash used in operating activities	(28,166)	(39,391)	(31,367)
Cash flows from investing activities:			
Purchases of marketable securities	—	(67,214)	—
Proceeds from maturities of marketable securities	33,750	33,750	—
Purchase of property and equipment	—	(40)	(235)
Proceeds from sales of property and equipment	—	2	6
Cash received (paid) for long-term deposits	42	(22)	(88)
Net cash provided by (used in) investing activities	33,792	(33,524)	(317)
Cash flows from financing activities:			
Proceeds from underwritten public offering, net of issuance costs	—	32,172	53,573
Proceeds from debt financing obligation	797	15,000	—
Payment of debt issuance costs	—	(276)	—
Repayment of term loan principal	(4,583)	—	—
Proceeds from exercises of stock options	71	169	446
Proceeds from sale of common stock under at-the-market sales agreement	—	710	2,165
Payment for settlement of taxes upon vesting of restricted stock units	(125)	(1,378)	—
Proceeds from advances from collaboration partners	402	403	—
Net cash (used in) provided by financing activities	(3,438)	46,800	56,184
Increase (decrease) in cash, cash equivalents and restricted cash	2,188	(26,115)	24,500
Cash, cash equivalents and restricted cash at the beginning of the year	22,536	48,651	24,151
Cash, cash equivalents and restricted cash at the end of the year	$ 24,724	$ 22,536	$ 48,651
Reconciliation of cash, cash equivalents and restricted cash to consolidated balance sheet:			
Cash and cash equivalents	$ 24,668	$ 22,493	$ 48,606
Restricted cash	56	43	45
Total cash, cash equivalents and restricted cash	$ 24,724	$ 22,536	$ 48,651
Supplemental disclosure of cash flow activities:			
Cash paid for interest	$ 828	$ 986	$ —
Cash paid for income taxes, net of refunds received	$ 5	$ 36	$ —
Supplemental disclosure of non-cash financing activities:			
Non-cash acquisition of treasury stock	$ —	$ —	$ 1,129
Non-cash issuance of common stock upon exercise of warrants	$ —	$ 179	$ —
Fair value of warrants issued in connection with long-term debt	$ —	$ 421	$ —
Remeasurement of operating leases	$ —	$ 176	$ —
Proceeds receivable from equity sales agreement	$ —	$ —	$ 255

See accompanying 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 developing novel ribonucleic acid (RNA)-modulating drug candidates, each designed to be a eukaryotic ribosomal selective glycoside (ERSG), formulated to treat rare and ultra-rare premature stop codon diseases. Premature stop codons are point mutations that disrupt the stability of the impacted messenger RNA (mRNA) and the protein synthesis from that mRNA. As a consequence, patients with premature stop codon diseases have reduced levels of, or no, protein from a gene whose product performs an essential function. This type of mutation accounts for some of the most severe phenotypes across genetic diseases. Nonsense mutations have been identified in over 1,800 rare and ultra-rare diseases. Read-through therapeutic development is focused on increasing functional protein synthesis by enabling the cytoplasmic ribosome to read through premature stop codons to produce full-length proteins. As opposed to a typical gene therapy approach of targeting a single, unique mutation in a target disease, this small molecule strategy enables targeting an entire class of mutations across the rare disease landscape. The small molecule approach has the potential to address a range of different premature stop codons in a single gene since the ERSG compounds are targeted to the ribosomes. ELX-02, the Company's lead investigational drug product candidate, is a small molecule designed to restore production of full-length functional proteins. ELX-02 is in clinical development for systemic administration for cystic fibrosis. ELX-02 is an investigational drug that has not been approved by any global regulatory body. The Company is also conducting investigational new drug (IND) enabling preclinical studies of ERSG compounds for autosomal dominant polycystic kidney disease (ADPKD) and in rare inherited retinal disorders (IRDs) by intravitreal administration with an initial focus on Usher Syndrome.

The Company's preclinical candidate pool consists of a library of novel ERSG drug candidates identified based on read-through potential and cytoplasmic ribosomal selectivity. The Company is headquartered in Waltham, Massachusetts, with additional offices in Morristown, New Jersey and Rehovot, Israel.

The Company's research and development strategy is to target rare or ultra-rare diseases where a high unmet medical need exists, a nonsense mutation-bearing patient population is established, preclinical read-through can be established in predictive personalized medicine models, and a defined path through Orphan Drug development, regulatory approval, patient access and commercialization is identified. The Company believes patient advocacy is an important element of patient focused drug development and seeks opportunities to collaborate with patient advocacy groups throughout the discovery and development process. The Company's current clinical program for its lead investigational drug product candidate, ELX-02, includes Phase 2 studies in cystic fibrosis in Europe, Israel and the United States. On March 25, 2020, the Company announced that enrollment in its Phase 2 clinical trials for ELX-02 in cystic fibrosis had been temporarily paused in response to the COVID-19 pandemic in order to avoid unnecessary exposure in at-risk populations, to maintain the integrity of study data and to support global healthcare providers in their commitment to ensure patient safety. On June 17, 2020, the Company announced that enrollment in its Phase 2 clinical trial in cystic fibrosis had been resumed in Israel and Europe, and on August 12, 2020, the Company announced that enrollment in its Phase 2 clinical trial in cystic fibrosis had been resumed in the U.S.

The extent and severity of the impact of the current global health crisis on the Company's business and clinical trials will be determined largely by the ability of patients and prospective patients in its clinical trials to access trial sites, the ability of personnel from clinical research organizations ("CROs") to oversee the administration of the Company's drug in accordance with trial protocols and the Company's ability to monitor and communicate effectively with CROs, staff at clinical trial sites and principal investigators. In addition, the impact of the COVID-19 pandemic on the operations of the U.S. Food and Drug Administration (the "FDA") and other health authorities may delay potential advancement of the Company's product candidates. The Company cannot reasonably estimate the extent to which these potential disruptions may materially impact its consolidated results of operations or financial position.

During 2019, the Company announced that the Cystic Fibrosis Foundation (the "CF Foundation") is providing funding for a portion of the U.S. Phase 2 cystic fibrosis clinical trial and in December of 2020, expanded its support to include our global clinical trial program. The Company has since formed a joint program advisory group with the CF Foundation focused on the development of ELX-02 for cystic fibrosis. The Cystic Fibrosis Therapeutics Development Network ("TDN") has sanctioned the Phase 2 study protocol, which is being conducted at TDN member sites. On August 4, 2020, the Company announced that the FDA granted orphan drug designation for ELX-

02 for the treatment of cystic fibrosis. The FDA's Office of Orphan Drug Products grants orphan status to support the development of medicines for underserved patient populations, or rare disorders, that affect fewer than 200,000 people in the U.S. Orphan drug designation qualifies Eloxx for certain benefits, including seven years of market exclusivity upon regulatory approval (if received), exemption from FDA application fees, tax credits on qualified U.S. clinical trials and eligibility for grant funding opportunities that can be used for clinical trial costs. ELX-02 had previously been granted orphan medicinal product designation for the treatment of cystic fibrosis by the European Medicines Agency.

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, 2020, had an accumulated deficit of $(171.6) million. The Company expects to continue to incur net losses and use cash in its operations for the foreseeable future. To date, the Company has not generated revenue from the sale of any product or service and does not expect to generate significant revenue unless and until 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. As discussed in Note 17, on February 24, 2020, the Company's Board of Directors approved a leadership and organizational realignment, aimed at supporting the Company's efforts to improve operating performance, and concentrate development efforts on core programs. The Company believes that its cash and cash equivalents of $24.7 million will enable it to meet the anticipated cash needs required to reach top line Phase 2 data in cystic fibrosis; however, this amount is not 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").

Reclassification

The Company has reclassified certain items from the prior year's consolidated financial statements to conform to the current year's presentation. Specifically, the Company allocated certain facilities and support costs between Research and development expenses and General and administrative expenses that were previously reported within General and administrative expenses only. For the year ended December 31, 2019, $0.5 million is reclassified from General and administrative expenses to Research and development expenses, which resulted in General and administrative expenses decreasing from $24.7 million to $24.2 million, and Research and development expenses increasing from $25.8 million to $26.3 million. This reclassification within the consolidated statements of operations and cash flows for the year ended December 31, 2019 had no impact on previously reported Total operating expenses, Loss from operations, Net loss, or Net cash used in operating activities.

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 the consolidated financial statements in conformity with U.S. GAAP requires management to make estimates, judgments and assumptions. The Company's management believes that the estimates, judgments and assumptions used are reasonable based upon information available at the time they are made. These estimates, judgments and assumptions can affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the dates of the consolidated financial statements, and the reported amounts of expenses during the reporting period. The Company evaluates estimates on an ongoing basis in light of changes in circumstances, facts and experiences. 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.

Comprehensive Loss

Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. Comprehensive loss consists of net loss and other comprehensive loss. Other comprehensive loss consists of changes in unrealized gains and losses from available-for-sale securities.

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, 2020 and 2019 the balances of cash and cash equivalents were $24.7 million and $22.5 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, 2020, and 2019, restricted cash consisted of bank guarantees related to Eloxx Limited's corporate facilities lease and credit card program.

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 and marketable securities. The Company mitigates its risk with respect to cash and cash equivalents and marketable securities by maintaining its deposits and investments at high-quality financial institutions. The Company invests any excess cash in money market funds and U.S. treasuries, and the management of these investments is not discretionary on the part of the financial institution.

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. 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 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.

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, 2020, 2019 and 2018 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 know 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. At December 31, 2020 and 2019, the Company's financial assets valued based on Level 1 inputs consisted of cash, cash equivalents and, at December 31, 2019, marketable securities (U.S. treasuries). The Company did not have any transfers of financial assets between Level 2 and 3 during 2020 or 2019.

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 2020 and 2019 and using the binomial lattice-based option valuation model for options awarded in 2018. 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.

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, 2020 and 2019, 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 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

The Company adopted the provisions of ASC topic 842, “Leases”, on January 1, 2019. The Company has operating leases for its principal offices in the U.S. and Israel. Operating lease assets represent the Company’s right to use an underlying asset for the lease term and operating lease liabilities represent the Company’s obligation to make lease payments arising from its operating leases. Lease expense for these leases is recognized on a straight-line basis over the lease term, with variable lease payments recognized in the period those payments are incurred. In determining the length of the lease term to its long-term lease, the Company determined not to consider an embedded renewal option for one operating lease primarily due to the facts that (i) the renewal rate is at a future market rate to be determined, and (ii) the Company does not have significant leasehold improvements that would restrict its ability to consider relocation. The Company applied its incremental borrowing rate based upon information available in determining the present value of the lease payments. The Company’s incremental borrowing rate is determined using a secured borrowing rate for the same currency and term as the associated lease. The Company made an accounting policy election to not recognize assets or liabilities for leases with a term of less than twelve months.

Recent Accounting Pronouncements

In June 2016, the FASB issued ASU No. 2016-13, *Measurement of Credit Losses on Financial Instruments*. This standard requires that for most financial assets, losses must be based on an expected loss approach which includes estimates of losses over the life of exposure that considers historical, current and forecasted information. Expanded disclosures related to the methods used to estimate the losses as well as a specific disaggregation of balances for financial assets are also required. The Company adopted the new standard on January 1, 2020 and adoption did not have a material impact on the consolidated financial statements.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework-Changes to the Disclosure Requirements for Fair Value Measurement*, which modifies the disclosure requirements for certain fair value measurements. The Company adopted the new standard on January 1, 2020 and adoption did not have a material impact on the consolidated financial statements.

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,	
	2020	**2019**
Research and development	$ 631	$ 448
Insurance	170	217
VAT receivables	—	26
Other	368	699
Totals	$ 1,169	$ 1,390

4. Property and Equipment, net

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

	December 31,	
	2020	2019
Computers and software	$ 124	$ 166
Office furniture and equipment	164	164
Leasehold improvements	158	158
Total property and equipment, at cost	446	488
Less: Accumulated depreciation	(313)	(287)
Property and equipment, net	$ 133	$ 201

Depreciation expense was $68 thousand, $87 thousand and $216 thousand for the years ended December 31, 2020, 2019 and 2018, respectively.

5. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31,	
	2020	2019
Research and development	$ 802	$ 1,560
Payroll, bonus and other employee-related expenses	1,315	2,200
Restructuring	258	—
Professional services	415	664
Other	39	137
Interest on debt	57	94
Total	$ 2,886	$ 4,655

6. Leases

Operating lease costs under the leases for the year ended December 31, 2020 and 2019 were approximately $0.6 million and $0.5 million, respectively. The weighted average remaining lease term at December 31, 2020 was 0.86 years and the weighted average incremental borrowing rate was 8.0%.

The following table summarizes the Company's maturities of operating lease liabilities as of December 31, 2020 (in thousands):

2021	$ 404
2022	32
Total lease payments	436
Less: present value discount	(14)
Total operating lease liabilities	422
Less: current portion	(389)
Long-term portion	$ 33

7. Debt

Term Loan

On January 30, 2019, the Company entered into a Loan and Security Agreement (the "SVB 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 "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 following the funding of the loan. On December 31, 2020, the rate was 5.75%. The Company commenced making payments on the outstanding principal balance of the loan on February 1, 2020, which is payable in 36 equal monthly installments. Amounts outstanding under the loan are due and payable on January 1, 2023.

In conjunction with the initial loan advance, the Company issued warrants (the "Warrants") to SVB and WestRiver to purchase an aggregate of 40,834 shares of the Company's common stock at a warrant exercise price of $11.02 (subject to certain adjustments), which price was calculated using the 10-day average bid price of the Company's common stock prior to the date of the SVB Loan Agreement.

The Company may prepay the outstanding principal balance of the loans advanced by SVB 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 SVB Loan Agreement.

Under the terms of the SVB Loan Agreement, the Company granted first priority liens and security interests in substantially all of the Company's assets (excluding all of its intellectual property, which is subject to a negative pledge) and a pledge by the Company of the shares of one of its wholly-owned subsidiaries as collateral for the obligations thereunder. The SVB Loan Agreement also contains representations and warranties by the Company and SVB and indemnification provisions in favor of SVB and customary covenants (including limitations on other indebtedness, liens, acquisitions, investments and dividends, but no financial covenants), and events of default (including payment defaults, breaches of covenants following any applicable cure period, events relating to bankruptcy or insolvency, and a material adverse change, including a material impairment in the perfection or priority of SVB's security interest in the collateral, a material adverse change in the Company's business, or a material impairment of the prospect of repayment of any Obligations (as defined in the SVB Loan Agreement)).

As of December 31, 2020, the carrying value of the outstanding loan consists of $10.4 million in principal less the unamortized debt discount of approximately $0.5 million. The debt issuance costs, the valuation of the Warrants, and the final maturity payment of $0.9 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 period ended December 31, 2020 and 2019 was $1.3 million and $1.6 million, respectively. Interest expense is calculated using the effective interest method and is inclusive of non-cash amortization of the debt discount. At December 31, 2020, the effective interest rate was 10.85%.

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 expects to use the loan proceeds for payroll and other covered costs in accordance with the relevant terms and conditions of the CARES Act. The Company issued a promissory note for the PPP Loan with a maturity date of April 21, 2022 and an interest rate of 1.0% per annum. Monthly payments of principal and interest will be due beginning on September 21, 2021, although interest accrues from the issuance date. The Company may prepay the PPP Loan without penalty or premium, and the promissory note provides for customary events of default. A PPP loan may be partially or entirely forgiven based on employee retention for the 24-week period starting on the loan date through October 2020, and the use of loan proceeds for payroll or other specified costs during the same period. Forgiveness is also based on the employer maintaining or restoring headcount and maintaining salary levels. Forgiveness is reduced if headcount declines or if salaries decrease. Any loan forgiveness will be made subject to SVB approval in accordance with SBA requirements.

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

	December 31, 2020
2021	$ 5,398
2022	5,398
2023	417
Total future principal payments	11,213
Less: unamortized discount	(498)
Carrying value of long-term debt	10,715
Less: current portion	(5,239)
Add: final Term Loan fee due at maturity in 2023	900
Long-term portion	$ 6,376

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 year ended December 31, 2020 no expenses were incurred and for the years ended December 31, 2019 and 2018, the Company recorded research and development expenses of $0.2 million and $0.1 million, respectively, in relation to the Technion Agreement for the reimbursement of costs incurred during the preparation, filing, prosecution and maintenance of the TRDF patents rights related to Eloxx Limited. As of December 31, 2020 no amounts were recorded in accrued expenses and December 31, 2019, amounts recorded in accrued expenses were $0.1 million.

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. During the year ended December 31, 2020, the Company made the first milestone payment of $0.1 million to TRDF.

9. Commitments and Contingencies

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, 2020, 2019 and 2018.

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, 2020, 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 $2.7 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.

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, 2020 and 2019, 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.

During 2019, the Company received a funding award from the Cystic Fibrosis Foundation and entered into an agreement relating to the award, which agreement was amended in December 2020 providing for an additional award amount. 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 would be required to repay amounts received from the Cystic Fibrosis Foundation (or specified multiples of such amounts) in certain circumstances, pursuant to the terms of the agreement, as amended. In the event of a disposition transaction (as defined in the agreement), the Company would be obligated to use up to 5% of the amounts received 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, 2020 and 2019, the Company had received payments of $0.8 million and $0.4 million, respectively, which are recorded as liabilities captioned 'Advances from collaboration partners'. Additional payments totaling $2.6 million were received in the first quarter of 2021, for a total of $3.4 million received to date.

10. Stockholders’ Equity

As of December 31, 2020, the Company had 500,000,000 shares authorized of common stock, $0.01 par value, of which 40,157,187 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 April 30, 2018, the Company closed an underwritten public offering of 5,899,500 shares of its common stock, including the exercise in full by the underwriter of its overallotment option to purchase an additional 769,500 shares, at the public offering price of $9.75 per share for gross proceeds of approximately $57.5 million, before deducting the underwriting discounts and commissions and offering expenses of approximately $3.9 million. The shares of common stock were offered by the Company pursuant to a shelf registration statement on Form S-3 (File No. 333-224207) that was filed with the U.S. Securities and Exchange Commission (the “SEC”) on April 10, 2018 and declared effective on April 20, 2018, which covers the offering, issuance and sale of up to $125 million of its common stock, preferred stock, debt securities or warrants and other securities, either individually or in combination (the “April 2018 Shelf”).

On June 24, 2019, the Company completed an underwritten public offering of 3,833,334 shares of common stock of the Company at the public offering price of $9.00 per share and received net proceeds of approximately $32.2 million after deducting underwriting discounts and commissions of $2.1 million and estimated offering expenses of $0.2 million.

Form S-3 and Equity Sales Agreement

In November 2018, the Company entered into an Equity Distribution Agreement (the "Agreement") with Citigroup Global Markets Inc. and Cantor Fitzgerald & Co. (collectively, the "Sales Agents"), pursuant to which the Company may sell and issue shares of its common stock up to an aggregate of $50 million through the Sales Agents. The shares were offered pursuant to the April 2018 Shelf. The Company agreed to pay the Sales Agents a commission of up to 3% of the gross proceeds of any sales of common stock pursuant to the Agreement. The Company incurred approximately $0.3 million related to legal, accounting and other fees in connection with the Agreement. For the year ended December 31, 2018, under the Agreement, the Company sold 201,100 shares of common stock and received net proceeds of $2.2 million. In January 2019, the Company sold 35,362 shares of common stock and received net proceeds of $0.7 million.

On November 16, 2018, the Company filed a shelf registration statement (the "November 2018 Shelf") on Form S-3 with the SEC. The November 2018 Shelf (File No. 333-228430) was declared effective on November 26, 2018 and covers the offering, issuance and sale of up to $200 million of the Company's common stock, preferred stock, debt securities or warrants and other securities, either individually or in combination.

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 (further described above in Note 7, "Debt"). During the year ended December 31, 2020, transactions related to warrants were as follows:

	Shares	Weighted average exercise price	Weighted average remaining contractual life (years)
Warrants outstanding at December 31, 2019	323,894	$ 4.32	3.74
Granted	-		
Exercised	-		
Forfeited	(2)	520.00	
Warrants outstanding at December 31, 2020	323,892	$ 4.31	2.74
Warrants exercisable at December 31, 2020	323,892	$ 4.31	2.74

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 5,000,000 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.

In 2017, the Company issued inducement awards outside of its stock plans to its former Chief Executive Officer in the form of options to purchase 663,212 shares of the Company's common stock with an exercise price per share equal to $8.00, and awards of restricted stock units for 663,212 shares of the Company's common stock. The employment of the grantee terminated in February 2020, as part of the organizational realignment, and the unvested portions of the awards were cancelled.

Summary of Stock Option Activity

Transactions during the year ended December 31, 2020 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
Options outstanding as of December 31, 2019	4,737,670	$ 11.17	8.54	$ 3,629,073
Granted	1,400,010	3.52		
Exercised	(17,210)	4.08		
Forfeited	(2,317,409)	(9.86)		
Options outstanding as of December 31, 2020	3,803,061	$ 10.16	8.20	$ 1,936,183
Options exercisable at December 31, 2020	1,766,009	$ 13.80	7.29	$ 1,266,440

As of December 31, 2020, the unrecognized compensation cost related to the outstanding options was $7.6 million and is expected to be recognized over a weighted-average period of 2.40 years.

The weighted average grant date fair values of stock options granted during the years ended December 31, 2020, 2019, and 2018 were $2.29, $6.28 and $18.06 per share, 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,		
	2020	2019	2018
Dividend yield	0%	0%	0%
Volatility	72%-80%	76%-92%	90%-92%
Risk-free interest rate	0.36%-1.63%	1.51%-2.62%	2.55%-3.20%
Expected term (years)	5.5-6.0	5.5-6.0	—
Contractual term (years)	10	10	10
Forfeiture rate post-vesting	—	—	10%
Suboptimal exercise	—	—	2.3

Summary of Restricted Stock Unit Activity

Transactions during the year ended December 31, 2020 related to RSUs granted to employees were as follows:

	Shares	Weighted average grant date fair value per share
Unvested at December 31, 2019	463,945	$ 9.45
Granted	300,000	3.59
Vested	(147,243)	10.32
Forfeited	(266,977)	8.65
Unvested at December 31, 2020	349,725	$ 4.67

As of December 31, 2020, the unrecognized compensation cost related to the outstanding RSUs was $1.4 million and is expected to be recognized over a weighted-average period of 3.01 years.

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,		
	2020	2019	2018
Research and development	$ 979	$ 2,458	$ 1,745
General and administrative	5,563	8,878	11,625
Restructuring charges	2,124	—	—
Total stock-based compensation expense	$ 8,666	$ 11,336	$ 13,370

12. Income Taxes

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

	Year ended December 31,		
	2020	2019	2018
U.S.	$ (18,582)	$ (22,242)	$ (24,439)
Israel	(15,995)	(28,632)	(22,624)
Loss before taxes on income	$ (34,577)	$ (50,874)	$ (47,063)

There were no taxes on income during the year ended December 31, 2020 or 2019. Taxes on income during the year ended December 31, 2018 resulted primarily from subsidiary income as a result of the implementation of an intercompany cost-plus arrangement. The current income tax provision consisted of the following (in thousands):

	Year ended December 31,		
	2020	2019	2018
Federal	$ —	$ —	$ 94
State and local	—	—	28
Foreign	—	—	—
Income tax provision	$ —	$ —	$ 122

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

	December 31,	
	2020	2019
Deferred tax assets:		
Net operating loss carryforwards	$ 43,759	$ 38,357
Stock-based compensation	2,200	2,801
Reserves and allowances	431	615
U.S. tax credits and other credits	3,624	2,980
Research and development credits	2,511	1,831
Operating lease right-of-use assets	(98)	(169)
Operating lease liabilities	98	169
Other	59	98
Total deferred tax assets	52,584	46,682
Valuation allowance	(52,584)	(46,682)
Net deferred tax assets	$ —	$ —

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, 2020 and 2019, 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, 2020 and 2019.

As of December 31, 2020 and 2019, the Company provided valuation allowances of approximately $52.6 million and $46.7 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 $5.9 million and $10.8 million during the years ended December 31, 2020 and 2019, respectively. For the year ended December 31, 2020, 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 year ended December 31, 2019, the increase in the valuation allowance was primarily related to losses generated during the period, partially offset by a reduction in the stock-based compensation deferred tax asset associated with cancelled awards.

For the years ended December 31, 2020, 2019 and 2018 the expected tax expense based on the federal statutory rate is reconciled with the actual tax expense as follows:

	Year ended December 31,		
	2020	2019	2018
U.S. federal statutory rate	21.0%	21.0%	21.0%
State tax rate, net of federal benefit	1.0	0.9	2.4
Permanent differences	(2.0)	(1.5)	(3.0)
Adjustment to deferred taxes	—	—	(1.8)
Tax credits	2.9	—	—
Effect of rate differences from statutory	0.9	1.1	0.8
Tax reform - federal tax rate change	—	—	0.1
Tax reform - change in valuation allowance	—	—	(0.1)
Change in valuation allowance	(23.8)	(21.5)	(19.5)
Other	—	—	(0.2)
Income tax provision	0.0%	0.0%	-0.3%

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, 2020 and 2019, the Company had U.S. federal net operating loss ("NOL") carryforwards of $108.9 million and $99.4 million, respectively. U.S. federal NOL carryforwards will begin to expire, if not utilized, beginning in 2021 through 2037. Included in the U.S. federal NOL carryforward as of December 31, 2020 are $34.9 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, 2020 and 2019, the Company had U.S. state NOL carryforwards of $13.7 million and $31.9 million, respectively, which may be available to offset future income tax liabilities.

As of December 31, 2020 and 2019, the Company had federal research tax credit carryforwards of $3.6 million and $3.0 million, respectively, available to reduce future tax liabilities and which expire at dates beginning in 2026 through 2040.

As of December 31, 2020 and 2019, the Company had Israeli NOL carryforwards of $86.9 million and $73.7 million, respectively, which carry forward indefinitely.

The enactment of the Tax Act in December 2017, as further discussed below, resulted in the remeasurement of the Company's net deferred tax assets due to the reduction in the corporate statutory rate from 35% to 21%. The effect on deferred tax assets and liabilities of a change in law or tax rates is recognized in income in the period that includes the enactment date. The Tax Act also includes a provision designed to currently tax global intangible low-taxed income ("GILTI"). The Company will record the U.S. income tax effect of future GILTI inclusions in the period in which they arise, if ever. After the enactment of the Tax Act, the SEC issued Staff Accounting Bulletin No. 118 ("SAB 118") which provided guidance on accounting for the enactment effect of the Tax Act. SAB 118 addressed the application of U.S. GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of the Tax Act. SAB 118 provided for a measurement period of up to one year from the Tax Act enactment date for companies to complete their accounting under ASC 740. The Company had calculated a provisional estimate of deferred tax expense of $10.2 million related to the remeasurement of its U.S. deferred tax assets in the future, which was fully and equally offset by a corresponding reduction in the valuation allowance. During the quarter ended December 31, 2018, the Company completed the accounting for the income tax effects of the Tax Act, which resulted in an immaterial change in the net deferred tax asset, before valuation allowance, as of the enactment date.

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 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. 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 beginning in June 30, 2015 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. 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, 2020, 2019, and 2018, are as follows (in thousands, except share and per share data):

	Year ended December 31,		
	2020	2019	2018
Numerator:			
Net loss	$ (34,577)	$ (50,874)	$ (47,185)
Denominator:			
Weighted average number of shares of common stock used in computing net loss per share, basic and diluted	40,124,953	38,063,173	32,436,506
Net loss per share, basic and diluted	$ (0.86)	$ (1.34)	$ (1.45)

For the years ended December 31, 2020, 2019, and 2018, 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 4,476,678, 5,525,509 and 4,163,107, respectively.

14. Other Expense (Income), net

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

	Year ended December 31,		
	2020	2019	2018
Interest and other income	$ (337)	$ (1,072)	$ (601)
Foreign currency exchange losses (gains), net	35	76	92
Investment income, net	15	(301)	—
Interest and other expense	1,409	1,616	7
Total other expense (income), net	$ 1,122	$ 319	$ (502)

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 two geographic regions: the U.S. and Israel. Substantially all of the Company's assets are located in the U.S.

16. Marketable Securities

Below is a summary of cash, cash equivalents and marketable securities at December 31, 2020 (in thousands):

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash and cash equivalents	$ 24,668	$ —	$ —	$ 24,668
Marketable securities - U.S. treasuries	—	—	—	—
Total cash, cash equivalents and marketable securities	$ 24,668	$ —	$ —	$ 24,668

Below is a summary of cash, cash equivalents and marketable securities at December 31, 2019 (in thousands):

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash and cash equivalents	$ 22,493	$ —	$ —	$ 22,493
Marketable securities - U.S. treasuries	33,765	19	(1)	33,783
Total cash, cash equivalents and marketable securities	$ 56,258	$ 19	$ (1)	$ 56,276

As of December 31, 2020 and 2019, no credit losses were identified related to the cash equivalents or marketable securities.

17. Restructuring

On February 24, 2020, the Company's Board of Directors approved a leadership and organizational realignment aimed at supporting its efforts to improve operating performance and concentrate development efforts on its core programs. The organizational realignment reduced managerial layers and consolidated roles across the organization, resulting in the elimination of 13 full-time positions during the first quarter of 2020. This resulted in a one-time charge of $4.0 million, including $2.1 million in stock-based compensation expense, with the severance portion being paid out over a one-year period. The accrued charges and associated payments that occurred for the year ended December 31, 2020, are as follows (amounts in thousands):

	Beginning Balance	Additions	Deductions	Ending Balance
Severance and related costs	$ —	$ 1,729	$ (1,471)	$ 258
Contract termination costs	—	165	(165)	—
Total restructuring charges	$ —	$ 1,894	$ (1,636)	$ 258

Exhibit 21.1

Subsidiaries of Eloxx Pharmaceuticals, Inc.
as of December 31, 2020

Eloxx Pharmaceuticals Ltd., a private limited company organized under the laws of Israel

EXHIBIT 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement Nos. 333-228430 and 333-224207 on Form S-3 and Registration Statement Nos. 333-236952, 333-224860, 333-222499, and 333-201891 on Form S-8 of our report dated March 12, 2021 relating to the consolidated financial statements of Eloxx Pharmaceuticals, Inc., appearing in this Annual Report on Form 10-K for the year ended December 31, 2020.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 12, 2021

Exhibit 31.1

CERTIFICATION

I, Gregory C. Williams, certify that:

1. I have reviewed this annual report on Form 10-K of Eloxx Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

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

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

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

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

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 12, 2021

/s/ Gregory C. Williams
Gregory C. Williams, PhD, MBA
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

I, Stephen G. MacDonald, certify that:

1. I have reviewed this annual report on Form 10-K of Eloxx Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

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

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

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

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

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 12, 2021

/s/ Stephen G. MacDonald
Stephen G. MacDonald
Vice President, Finance and Accounting, and Treasurer
(Principal Financial Officer and Principal Accounting Officer)

Exhibit 32.1

CERTIFICATION[1]

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), I, Gregory C. Williams, Chief Executive Officer of Eloxx Pharmaceuticals, Inc. (the "Company"), hereby certify that, to the best of my knowledge:

1. The Company's Annual Report on Form 10-K for the period ended December 31, 2020, to which this Certification is attached as Exhibit 32.1 (the "Annual Report") fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act, and

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

IN WITNESS WHEREOF, the undersigned have set their hands hereto as of the 12th day of March, 2021.

/s/ Gregory C. Williams
Gregory C. Williams, PhD, MBA
Chief Executive Officer
(Principal Executive Officer)

(1) This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Eloxx Pharmaceuticals, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.

Exhibit 32.2

CERTIFICATION[1]

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), I, Stephen G. MacDonald, Vice President, Finance and Accounting, and Treasurer of Eloxx Pharmaceuticals, Inc. (the "Company"), hereby certify that, to the best of my knowledge:

1. The Company's Annual Report on Form 10-K for the period ended December 31, 2020, to which this Certification is attached as Exhibit 32.2 (the "Annual Report") fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act, and

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

IN WITNESS WHEREOF, the undersigned have set their hands hereto as of the 12th day of March, 2021.

/s/ Stephen G. MacDonald
Stephen G. MacDonald
Vice President, Finance and Accounting, and Treasurer
(Principal Financial Officer and Principal Accounting Officer)

(1) This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Eloxx Pharmaceuticals, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.