

**PROSPECTUS SUPPLEMENT**

(To Prospectus dated August 30, 2021)

**ELOXX PHARMACEUTICALS, INC.****Up to \$50,000,000****Common Stock**

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We have entered into a Sales Agreement (the “Sales Agreement”), with SVB Leerink LLC (the “SVB Leerink”), dated September 30, 2021, relating to the sale of shares of our common stock offered by this prospectus supplement. In accordance with the terms of the Sales Agreement, under this prospectus supplement we may offer and sell shares of our common stock, \$0.01 par value per share, having an aggregate offering price of up to \$50,000,000 from time to time through SVB Leerink.

Our common stock is listed on the Nasdaq Global Market under the symbol “ELOX.” On September 28, 2021, the last reported sale price of our common stock on the Nasdaq Global Market was \$1.74 per share.

Sales of our common stock, if any, under this prospectus supplement will be made by any method permitted that is deemed an “at the market offering” as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended, or the Securities Act, including sales made directly on the Nasdaq Global Market or any other trading market for our common stock. SVB Leerink is not required to sell any specific amount, but will act as our sales agent using commercially reasonable efforts consistent with their normal trading and sales practices on mutually agreed terms between SVB Leerink and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

SVB Leerink will be entitled to compensation at a commission rate of 3.0% of the gross sales price of the shares of our common stock sold through it pursuant to the Sales Agreement. See “Plan of Distribution” beginning on page [S-15](#) for additional information regarding the compensation to be paid to SVB Leerink. In connection with the sale of the common stock on our behalf, SVB Leerink may be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of SVB Leerink may be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to SVB Leerink with respect to certain liabilities, including liabilities under the Securities Act.

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**INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE “RISK FACTORS” ON PAGE [S-8](#) OF THIS PROSPECTUS SUPPLEMENT AND IN THE DOCUMENTS INCORPORATED BY REFERENCE INTO THIS PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR COMMON STOCK.**

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.**

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**SVB Leerink**

**The date of this prospectus supplement is September 30, 2021.**

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## ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement is part of a registration statement that we have filed with the U.S. Securities and Exchange Commission, or the SEC, utilizing a “shelf” registration process. By using a shelf registration statement, we may offer shares of our common stock having an aggregate offering price of up to \$200,000,000 from time to time at prices and on terms to be determined by market conditions at the time of offering.

We provide information to you about this offering of our common stock in two separate documents that are bound together: (1) this prospectus supplement, which describes the specific details regarding this offering; and (2) the accompanying prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this “prospectus supplement,” we are referring to both documents combined. If information in this prospectus supplement is inconsistent with the accompanying prospectus, you should rely on this prospectus supplement. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in any document previously filed with the SEC that are incorporated by reference in this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date — for example, a document incorporated by reference in this prospectus supplement — the statement in the document having the later date modifies or supersedes the earlier statement.

We have not, and SVB Leerink has not, authorized anyone to provide you with information other than that contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and any free writing prospectus prepared by us or on our behalf. We are not, and SVB Leerink is not, making an offer to sell or soliciting any offer to buy these securities in any jurisdiction where the offer or sale is not permitted or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein and therein and any free writing prospectus that we have authorized for use in connection with this offering is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein and therein and any free writing prospectus that we have authorized for use in connection with this offering in their entirety before making an investment decision.

Before buying any of the common stock that we are offering, we urge you to carefully read this prospectus supplement, the accompanying prospectus and all of the information incorporated by reference herein and therein, as well as the additional information described under the heading “Where You Can Find More Information; Incorporation by Reference.” These documents contain important information that you should consider when making your investment decision.

We are offering to sell, and seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

When we refer to “Eloxx,” “we,” “our” and “us” in this prospectus supplement, we mean Eloxx Pharmaceuticals, Inc. and its consolidated subsidiaries, unless otherwise specified. When we refer to “you,” we mean the holders of shares of our common stock offered by this prospectus supplement and the accompanying prospectus.

We have proprietary rights to trademarks, trade names and service marks appearing in this prospectus supplement and the accompanying prospectus that are important to our business. This prospectus supplement

and the accompanying prospectus also include trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this prospectus supplement and the accompanying prospectus appear without the ® and TM symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

## WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

### Available Information

We file reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is [www.sec.gov](http://www.sec.gov).

Our website address is [www.eloxxpharma.com](http://www.eloxxpharma.com). The information on our website, however, is not, and should not be deemed to be, a part of or incorporated by reference into this prospectus supplement and the accompanying prospectus.

This prospectus supplement and the accompanying prospectus are part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement. Statements in this prospectus supplement or the accompanying prospectus about these documents are summaries, and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement through the SEC's website, as provided above.

### Incorporation by Reference

The SEC's rules allow us to "incorporate by reference" information in this prospectus supplement, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus supplement, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement or a subsequently filed document incorporated by reference modifies or replaces that statement.

This prospectus supplement incorporates by reference the documents set forth below that have previously been filed with the SEC (other than those documents or the portions of those documents not deemed to be filed):

- [Our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 12, 2021.](#)
- The information specifically incorporated by reference into our Annual Report on [Form 10-K from our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 1, 2021.](#)
- Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2021 and June 30, 2021, filed with the SEC on [May 7, 2021](#) and [August 16, 2021.](#)
- Our Current Reports on Form 8-K and Form 8-K/A filed with the SEC on [January 13, 2021](#), [March 12, 2021](#), [March 26, 2021](#), [April 1, 2021](#) (except for Item 7.01 of such report, which shall not be deemed incorporated by reference herein), [April 29, 2021](#), [May 18, 2021](#), [May 18, 2021](#), [May 20, 2021](#), [May 27, 2021](#), [June 16, 2021](#), [July 6, 2021](#) (except for Item 7.01 of such report, which shall not be deemed incorporated by reference herein) [July 16, 2021](#), [August 20, 2021](#) and [September 30, 2021.](#)
- The description of our common stock contained in our [Registration Statement on Form 8-A, filed on April 24, 2018](#), including any amendments or reports filed for purposes of updating this description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the "Exchange Act" in this prospectus supplement, prior to the termination of this offering, including all such documents we may file with the SEC on or after the date of this prospectus supplement, will also be incorporated by reference in this prospectus supplement and deemed to be part of this prospectus supplement from the date of the filing of such reports

and documents. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed above or filed in the future, that are not deemed “filed” with the SEC, including our stock performance graph or any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

You may request a free copy of any of the documents incorporated by reference in this prospectus supplement by writing or telephoning us at the following address:

Eloxx Pharmaceuticals, Inc.  
480 Arsenal Way, Suite 130  
Watertown, Massachusetts 02472  
(781) 577-5300

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus supplement.

**PROSPECTUS SUPPLEMENT SUMMARY**

*This summary provides a general overview of selected information and does not contain all of the information you should consider before buying our common stock. Therefore, you should read this entire prospectus supplement, the accompanying prospectus and any free writing prospectus, including the information incorporated by reference, before deciding to invest in our common stock. Investors should carefully consider the information set forth under “Risk Factors” beginning on page S-8 of this prospectus supplement and incorporated by reference to our annual report on Form 10-K and our quarterly reports on Form 10-Q.*

We are a clinical-stage biopharmaceutical company engaged in the science of ribosome modulation, leveraging both our innovative TURBO-ZM chemistry technology platform in an effort to develop novel Ribosome Modulating Agents (“RMAs”) and our library of Eukaryotic Ribosome Selective Glycosides (“ERSGs”), for the treatment of 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.

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

ELX-02, is a small molecule drug candidate designed to restore production of full-length functional proteins. The investigational therapy has shown strong activity across a full range of mutations in cystic fibrosis (“CF”) preclinical models. In Phase 1 testing, ELX-02 was generally well tolerated and demonstrated high bioavailability with consistent pharmacokinetics across both single and multiple-dose studies. The Phase 2 trials are designed to validate the safety of ELX-02 and assess its biological activity.

ELX-02 is currently in Phase 2 clinical development for the treatment of CF in patients with diagnosed nonsense mutations and is being conducted at leading investigator sites in Europe, Israel and the United States. As of the end of June 2021, we believe that we have enrolled a sufficient number of patients to assess biological activity of ELX-02. We will continue to enroll additional patients to support Phase 3 clinical trial planning. We expect to present data from the first four treatment arms of the study in the fourth quarter of 2021. The Cystic Fibrosis Foundation (“CF Foundation”) is providing funding for a portion of this global clinical trial program. The FDA has granted orphan drug designation to ELX-02 for the treatment of nephropathic cystinosis, MPS I, Rett syndrome, and CF.

With the strength of our ELX-02 program for CF, the acquisition of Zikani provides us with the opportunity to amplify the potential of our innovative science by developing a new class of therapies to treat diseases with limited to no treatment options. The CF Foundation has agreed to provide funding for a portion of this research. Our preclinical programs are focused on select rare diseases including inherited diseases, cancer caused by nonsense mutations, kidney diseases, including autosomal dominant polycystic kidney disease, as well as rare ocular genetic disorders. In addition, we plan to file an IND in 2022 for what could potentially become the first oral therapy for protein restoration for patients with nonsense mutations in Recessive Dystrophic Epidermolysis Bullosa (“RDEB”) and Junctional Epidermolysis Bullosa (“JEB”). RDEB is an incurable, extremely painful and often fatal skin blistering condition caused by a lack of collagen type VII that is estimated to affect more than 3,000 people worldwide. JEB is the most severe form of Epidermolysis Bullosa, with most patients dying in infancy. By extending the application of ribosomal RNA modulation to the readthrough of nonsense mutations in tumor suppressor genes, we are also rapidly advancing preclinical research for familial adenomatous polyposis (“FAP”), an inherited pre-cancerous colorectal disease frequently caused by nonsense mutations in the adenomatous polyposis coli (“APC”) gene. We plan to target rare diseases including genetic diseases and cancers caused by nonsense mutations.

Nonsense mutations cause approximately 10-12 percent of rare inherited diseases. ELX-02 along with the TURBO-ZM library of compounds are anticipated to significantly expand to include the potential treatment of many other rare diseases and certain cancers.

We were incorporated under the laws of the State of Delaware. Our principal executive offices are located at 480 Arsenal Way, Suite 130, Watertown, Massachusetts 02472, and our telephone number is (781) 577-5300. Our website address is [www.eloxxpharma.com](http://www.eloxxpharma.com). The information contained on our website is not incorporated by reference into this prospectus supplement and the accompanying prospectus, and you should not consider any information contained on, or that can be accessed through, our website as part of this prospectus supplement and the accompanying prospectus or in deciding whether to purchase our securities. Our common stock is listed on the Nasdaq Global Market under the symbol "ELOX".



## THE OFFERING

*The following summary contains basic information about our common stock and the offering and is not intended to be complete. It does not contain all of the information that may be important to you. For a more complete understanding of our common stock, you should read this prospectus supplement, the accompanying prospectus, and the documents referred to herein and therein.*

<b>Common stock offered by us</b>	Shares of our common stock having an aggregate offering price of up to \$50,000,000.
<b>Common stock to be outstanding immediately after this offering</b>	Up to 114,937,399 shares (as more fully described in the notes following this table), assuming sales of 28,735,632 shares of our common stock in this offering at an offering price of \$1.74 per share, which was the last reported sale price of our common stock on the Nasdaq Global Market on September 28, 2021. The actual number of shares issued will vary depending on how many shares of our common stock we choose to sell and the prices at which such sales occur.
<b>Plan of Distribution</b>	“At the market offering” that may be made from time to time on the Nasdaq Capital Market or other existing trading market for our common stock through SVB Leerink. See the section entitled “Plan of Distribution” on page <a href="#">S-15</a> of this prospectus supplement.
<b>Use of Proceeds</b>	We intend to use the net proceeds of this offering, if any, for general corporate purposes, including but not limited to, working capital, capital expenditures, research and development expenditures, clinical trial expenditures and potential commercialization activities and other general corporate purposes. See the section entitled “Use of Proceeds” on page <a href="#">S-12</a> of this prospectus supplement.
<b>Risk Factors</b>	Investing in our common stock involves a high degree of risk. See “Risk Factors” beginning on page <a href="#">S-8</a> of this prospectus supplement and the other information included in, or incorporated by reference into, this prospectus supplement for a discussion of certain factors you should carefully consider before deciding to invest in shares of our common stock.
<b>Nasdaq Global Market symbol</b>	“ELOX”

The number of shares of our common stock to be outstanding upon completion of this offering is based on 86,201,767 shares of our common stock outstanding as of June 30, 2021 and excludes:

- warrants to purchase 323,892 shares of common stock at a weighted average exercise price of \$4.31 per share outstanding as of June 30, 2021;
- options to purchase 7,655,008 shares of common stock at a weighted average exercise price of \$6.19 per share outstanding as of June 30, 2021;
- 634,892 shares of our common stock reserved for issuance upon the vesting of outstanding restricted stock units as of June 30, 2021; or
- 3,384,270 shares of common stock available for issuance under our 2018 Equity Incentive Plan (the “2018 Plan”) as of June 30, 2021.

## RISK FACTORS

*Investment in any securities offered pursuant to this prospectus supplement and the accompanying prospectus involves risks. You should carefully consider the risk factors described below and in our Annual Report on Form 10-K and Quarterly Reports on Form 10-Q filed with the SEC and incorporated by reference in this prospectus supplement, any amendment or update thereto reflected in subsequent filings with the SEC, including in our Annual Reports on Form 10-K and Quarterly Reports on Form 10-Q, and all other information contained or incorporated by reference in this prospectus supplement, as updated by our subsequent filings under the Exchange Act. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities.*

### **Risks Relating to this Offering**

***If you purchase common stock in this offering, you may suffer immediate dilution of your investment. You may experience further dilution upon exercise of options and warrants.***

The price per share of our common stock being offered may be higher than the net tangible book value per share of our outstanding common stock prior to this offering. Assuming that an aggregate of 28,735,632 shares of our common stock are sold at a price of \$1.74 per share, the last reported sale price of our common stock on the Nasdaq Global Market on September 28, 2021, for aggregate gross proceeds of approximately \$50.0 million, and after deducting commissions and estimated offering expenses payable by us, new investors in this offering will incur immediate dilution of \$0.97 per share. For a more detailed discussion of the foregoing see the section entitled “Dilution” herein. To the extent outstanding stock options or warrants are exercised, there will be further dilution to new investors. In addition, to the extent we need to raise additional capital in the future and we issue additional shares of common stock or securities convertible or exchangeable for our common stock, our then existing stockholders may experience dilution and the new securities may have rights senior to those of our common stock offered in this offering.

***We have broad discretion to determine how to use the funds raised in this offering, and may use them in ways that may not enhance our operating results or the price of our common stock.***

Our management will have broad discretion over the use of proceeds from this offering, and we could spend the proceeds from this offering in ways our stockholders may not agree with or that do not yield a favorable return, if at all. We intend to use the net proceeds for general corporate purposes, including but not limited to, working capital, capital expenditures, research and development expenditures, clinical trial expenditures and potential commercialization activities and other general corporate purposes. However, our use of these proceeds may differ substantially from our current plans. If we do not invest or apply the proceeds of this offering in ways that improve our operating results, we may fail to achieve expected financial results, which could cause our stock price to decline.

***Future sales or issuances of our common stock in the public markets, or the perception of such sales, could depress the trading price of our common stock.***

The sale of a substantial number of shares of our common stock or other equity-related securities in the public markets, or the perception that such sales could occur, could depress the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. We may sell large quantities of our common stock at any time pursuant to this prospectus supplement or in one or more separate offerings. We cannot predict the effect that future sales of common stock or other equity-related securities would have on the market price of our common stock.

***The actual number of shares we will issue under the Sales Agreement, at any one time or in total, is uncertain.***

Subject to certain limitations in the Sales Agreement and compliance with applicable law, we have the discretion to deliver a placement notice to SVB Leerink at any time throughout the term of the Sales Agreement. The number of shares that are sold by SVB Leerink after delivering a placement notice will fluctuate based on the market price of our common stock during the sales period and limits we set with

SVB Leerink. Because the price per share of each share sold will fluctuate based on the market price of our common stock during the sales period, it is not possible at this stage to predict the number of shares that will be ultimately issued.

***The common stock offered hereby will be sold in “at the market offerings,” and investors who buy shares at different times will likely pay different prices.***

Investors who purchase shares in this offering at different times will likely pay different prices, and so may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and numbers of shares sold, and there is no minimum or maximum sales price. Investors may experience a decline in the value of their shares as a result of share sales made at prices lower than the prices they paid.

### CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

The information in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein and any free writing prospectus that we have authorized for use in connection with this offering contain forward-looking statements and information within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act, which are subject to the “safe harbor” created by those sections.

All statements other than statements of present and historical facts contained or incorporated by reference in this prospectus supplement, including without limitation, statements regarding expected timing of trials and results from our clinical program, strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. Without limiting the foregoing, in some cases, you can identify forward-looking statements by terms such as “aim,” “may,” “will,” “would,” “should,” “expect,” “exploring,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential,” “seeks,” or “continue” or the negative of these terms or other similar expressions, although not all forward-looking statements contain these words. No forward-looking statement is a guarantee of future results, performance, or achievements, and one should avoid placing undue reliance on such statements.

Forward-looking statements are based on our management’s beliefs and assumptions and on information currently available to us. Such beliefs and assumptions may or may not prove to be correct. Additionally, such forward-looking statements are subject to a number of known and unknown risks, uncertainties and assumptions, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various factors, including, but not limited to:

- risks related to our dependence on our lead product candidate, ELX-02 and our ability to progress any of our product candidates in preclinical or clinical trials;
- the length and expense of preclinical and clinical trial development and the uncertain outcomes from such trials;
- risk related to doing business with collaborators, healthcare professionals, principal investigators, consultants, vendors, customers, and third-party payors;
- risks that our product candidates may cause adverse events or other properties that delay or prevent regulatory approval or market acceptance;
- risks related to the scope, rate and progress of our preclinical studies and clinical trials and other research and development activities;
- risks related to patient recruitment and enrollment in our clinical trials;
- the impact of the global COVID-19 pandemic or other public health epidemics and other factors beyond our control on our clinical trials, operations, vendors, suppliers and employees;
- risks related to regulatory approvals and other requirements applicable to our product candidates;
- risks relating to the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- risks related to our ability to obtain adequate funding to finance our operations;
- our and our stockholders ability to realize benefits from our strategic initiatives, including our acquisition of Zikani Therapeutics, Inc. in April 2021;
- general business conditions, regulatory environment, competition and market for our products; and
- our intended use of proceeds from this offering.

As more fully described under the heading “Risk Factors” and elsewhere in this prospectus supplement and under “Risk Factors” in our Annual Report on Form 10-K and our Quarterly Reports on Form 10-Q filed with the SEC, and any additional documents incorporated by reference herein and therein and any free writing prospectus, many important factors affect our ability to achieve our stated objectives and to develop and commercialize any product candidates. 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. These forward-looking statements involve risks and uncertainties that could cause our actual results to differ materially from those in the forward-looking statements, including, without limitation, the risks and uncertainties set forth in our filings with the SEC and incorporated by reference herein. You should read this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein and any free writing prospectuses that we have authorized for use in this offering with the understanding that our actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements that we make. The forward-looking statements are applicable only as of the date on which they are made, and we do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

## USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$50,000,000 from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time.

We intend to use the net proceeds of this offering, if any, for general corporate purposes, including but not limited to, working capital, capital expenditures, research and development expenditures, clinical trial expenditures and potential commercialization activities and other general corporate purposes.

The amounts and timing of our actual expenditures will depend on numerous factors, including the progress of regulatory review of our product candidates, the status of and results from clinical trials, as well as any acquisition or licensing of additional technologies, other assets or businesses that we may opportunistically identify or any other strategic investments or opportunities that we may pursue, any unforeseen cash needs, and other factors described under “Risk Factors” in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein, as well as the amount of cash used in our operations. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds. Pending the use of the net proceeds described above, we plan to invest the net proceeds from this offering in a variety of capital preservation investments, including short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

### **DIVIDEND POLICY**

We have never declared or paid any cash dividends on our capital stock and our ability to pay cash dividends is currently prohibited by the terms of our debt financing arrangements. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors after considering our financial condition, results of operations, capital requirements, business prospects and other factors the board of directors deems relevant, and subject to the restrictions contained in any future financing instruments.

## DILUTION

If you invest in this offering, your ownership interest will be diluted to the extent of the difference between the price per share you pay in this offering and the as adjusted net tangible book value per share of our common stock after this offering.

As of June 30, 2021, we had a net tangible book value of approximately \$40.6 million, or approximately \$0.47 per share of common stock based upon 86,201,767 shares outstanding. Our net tangible book value per share represents total tangible assets less total liabilities, divided by the number of shares of common stock outstanding at June 30, 2021.

After giving effect to the sale of our common stock in the aggregate amount of \$50.0 million at an assumed offering price of \$1.74 per share, the last reported sale price of our common stock on the Nasdaq Global Market on September 28, 2021, and after deducting commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2021 would have been \$88.9 million, or \$0.77 per share of common stock. This represents an immediate increase in net tangible book value of \$0.30 per share to our existing stockholders and an immediate dilution in net tangible book value of \$0.97 per share to new investors in this offering.

The following table illustrates this calculation on a per share basis. The as adjusted information is illustrative only and will adjust based on the actual price to the public, the actual number of shares sold and other terms of the offering determined at the time shares of our common stock are sold pursuant to this prospectus supplement. The as adjusted information assumes that all of our common stock in the aggregate amount of \$50.0 million is sold at the assumed offering price of \$1.74 per share, the last reported sale price of our common stock on the Nasdaq Global Market on September 28, 2021. The shares sold in this offering, if any, will be sold from time to time at various prices.

Assumed public offering price per share	\$1.74
Net tangible book value per share as of June 30, 2021	\$0.47
Increase in net tangible book value per share as of June 30, 2021 attributable to the offering	0.30
As adjusted net tangible book value per share after giving effect to the offering	0.77
Dilution per share to new investors participating in the offering	<u>\$0.97</u>

An increase of \$1.00 per share in the price at which the shares are sold from the assumed public offering price of \$1.74 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$50.0 million is sold at that price, would increase our as adjusted net tangible book value per share after this offering by \$0.08 per share and would increase the dilution per share to new investors participating in this offering to \$1.89 per share, after deducting offering commissions and estimated offering expenses payable by us. A decrease of \$1.00 per share in the price at which the shares are sold from the assumed public offering price of \$1.74 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$50.0 million is sold at that price, would decrease our as adjusted net tangible book value per share after this offering by \$0.20 per share and would decrease the dilution per share to new investors participating in this offering to \$0.16 per share, after deducting offering commissions and estimated offering expenses payable by us.

The above discussion and table are based on 86,201,767 shares of our common stock legally outstanding as of June 30, 2021, and excludes:

- warrants to purchase 323,892 shares of common stock at a weighted average exercise price of \$4.31 per share outstanding as of June 30, 2021;
- options to purchase 7,655,008 shares of common stock at a weighted average exercise price of \$6.19 per share outstanding as of June 30, 2021;
- 634,892 shares of our common stock reserved for issuance upon the vesting of outstanding restricted stock units as of June 30, 2021; or
- 3,384,270 shares of common stock available for issuance under the 2018 Plan as of June 30, 2021.



## PLAN OF DISTRIBUTION

We have entered into the Sales Agreement with SVB Leerink under which we may issue and sell shares of common stock having an aggregate offering price of up to \$50 million from time to time through SVB Leerink as our sales agent. Sales of shares of common stock, if any, under this prospectus supplement and the accompanying prospectus will be made at market prices by any method that is deemed to be an “at-the-market” offering, as defined in Rule 415 under the Securities Act, including sales made directly on the Nasdaq Global Market or any other trading market for our common stock.

SVB Leerink will offer shares of our common stock subject to the terms and conditions of the Sales Agreement on a daily basis or as otherwise agreed upon by us and SVB Leerink. We will designate the maximum amount of common stock to be sold through SVB Leerink on a daily basis or otherwise determine such maximum amount together with SVB Leerink. Subject to the terms and conditions of the Sales Agreement, SVB Leerink will use its commercially reasonable efforts consistent with its normal trading and sales practices to sell on our behalf all of the shares of common stock requested to be sold by us. We may instruct SVB Leerink not to sell shares of common stock if the sales cannot be effected at or above the price designated by us in any such instruction. SVB Leerink or we may suspend the offering of shares of our common stock being made through SVB Leerink under the Sales Agreement upon proper notice to the other party. SVB Leerink and we each have the right, by giving written notice as specified in the Sales Agreement, to terminate the Sales Agreement in each party’s sole discretion at any time. The offering of shares of our common stock pursuant to the Sales Agreement will otherwise terminate upon the termination of the Sales Agreement as provided therein.

The aggregate compensation payable to SVB Leerink as sales agent will be an amount equal to 3.0% of the gross proceeds of any shares sold through it pursuant to the Sales Agreement. We have also agreed to reimburse SVB Leerink up to \$75,000 of SVB Leerink’s actual outside legal expenses incurred by SVB Leerink in connection with this offering. We have also agreed to reimburse SVB Leerink its FINRA counsel fees in an amount up to \$15,000, plus certain ongoing fees of its legal counsel. We estimate that the total expenses of the offering payable by us, excluding commissions payable to SVB Leerink under the Sales Agreement, will be approximately \$250,000.

The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental, regulatory, or self-regulatory organization in connection with the sales, will equal our net proceeds for the sale of such shares of common stock.

SVB Leerink will provide written confirmation to us following the close of trading on the Nasdaq Global Market on each day in which shares of common stock are sold through it as sales agent under the Sales Agreement. Each confirmation will include the number of shares of common stock sold through it as sales agent on that day, the volume weighted average price of the shares of common stock sold, the percentage of the daily trading volume and the net proceeds to us.

Settlement for sales of shares of common stock will occur, unless the parties agree otherwise, on the second business day that is also a trading day following the date on which any sales were made in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

We will report at least quarterly the number of shares of common stock sold through SVB Leerink under the Sales Agreement, the net proceeds to us and the compensation paid by us to SVB Leerink in connection with the sales of shares of common stock during the relevant period.

In connection with the sales of shares of common stock on our behalf, SVB Leerink may be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation paid to SVB Leerink may be deemed to be underwriting commissions or discounts. We have agreed in the Sales Agreement to provide indemnification and contribution to SVB Leerink against certain liabilities, including liabilities under the Securities Act. As sales agent, SVB Leerink will not engage in any transactions that stabilize our common stock. To the extent required by Regulation M, SVB Leerink will not engage in any market making activities involving our common stock while the offering is ongoing under this prospectus supplement and the accompanying prospectus.

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent and registrar's address is 6201 15th Avenue, Brooklyn, NY 11219.

SVB Leerink and/or its affiliates have provided, and may in the future provide, various investment banking and other financial services for us for which services they have received and, may in the future receive, customary fees.

### **LEGAL MATTERS**

Latham & Watkins LLP will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of Eloxx Pharmaceuticals, Inc. Troutman Pepper Hamilton Sanders LLP has acted as counsel for SVB Leerink in connection with certain legal matters related to this offering.

### **EXPERTS**

The financial statements, incorporated in this prospectus supplement and the accompanying prospectus by reference from the Company's Annual Report on Form 10-K, have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference. Such financial statements have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

The financial statements of Zikani Therapeutics, Inc. as of December 31, 2020 and 2019 and for each of the two years in the period ended December 31, 2020 incorporated by reference in this prospectus supplement and the accompanying prospectus have been so incorporated in reliance on the report of Moody, Famiglietti, & Andronico, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting. The report on the financial statements contains an explanatory paragraph regarding Zikani Therapeutics, Inc.'s ability to continue as a going concern.

PROSPECTUS



**ELOXX PHARMACEUTICALS, INC.**

**\$200,000,000**

**Common Stock**

**Preferred Stock**

**Debt Securities**

**Warrants**

**Units**

We may offer and sell up to \$200,000,000 in the aggregate of the securities identified above from time to time in one or more offerings. This prospectus provides you with a general description of the securities.

Each time we offer and sell securities, we will provide a supplement to this prospectus that contains specific information about the offering and the amounts, prices and terms of the securities. The prospectus supplement may also add, update or change information contained in this prospectus with respect to that offering. You should carefully read this prospectus and the applicable prospectus supplement before you invest in any of our securities.

We may offer and sell the securities described in this prospectus and any prospectus supplement to or through one or more underwriters, dealers and agents, or directly to purchasers, or through a combination of these methods. If any underwriters, dealers or agents are involved in the sale of any of the securities, their names and any applicable purchase price, fee, commission or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. See the sections of this prospectus entitled "About this Prospectus" and "Plan of Distribution" for more information. No securities may be sold without delivery of this prospectus and the applicable prospectus supplement describing the method and terms of the offering of such securities.

**INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE "RISK FACTORS" ON PAGE 5 OF THIS PROSPECTUS AND ANY SIMILAR SECTION CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR SECURITIES.**

Our common stock is listed on the Nasdaq Capital Market under the symbol "ELOX." On August 19, 2021, the last reported sale price of our common stock on the Nasdaq Capital Market was \$1.34 per share.

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.**

**The date of this prospectus is August 30, 2021.**

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## ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the U.S. Securities and Exchange Commission, or the SEC, using a “shelf” registration process. By using a shelf registration statement, we may sell securities from time to time and in one or more offerings up to a total dollar amount of \$200,000,000 as described in this prospectus. Each time that we offer and sell securities, we will provide a prospectus supplement to this prospectus that contains specific information about the securities being offered and sold and the specific terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement or free writing prospectus may also add, update or change information contained in this prospectus with respect to that offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement or free writing prospectus, you should rely on the prospectus supplement or free writing prospectus, as applicable. Before purchasing any securities, you should carefully read both this prospectus and the applicable prospectus supplement (and any applicable free writing prospectuses), together with the additional information described under the heading “Where You Can Find More Information; Incorporation by Reference.”

We have not authorized anyone to provide you with any information or to make any representations other than those contained in this prospectus, any applicable prospectus supplement or any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We will not make an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus and the applicable prospectus supplement to this prospectus is accurate only as of the date on its respective cover, that the information appearing in any applicable free writing prospectus is accurate only as of the date of that free writing prospectus, and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, unless we indicate otherwise. Our business, financial condition, results of operations and prospects may have changed since those dates. This prospectus incorporates by reference, and any prospectus supplement or free writing prospectus may contain and incorporate by reference, market data and industry statistics and forecasts that are based on independent industry publications and other publicly available information. Although we believe these sources are reliable, we do not guarantee the accuracy or completeness of this information and we have not independently verified this information. In addition, the market and industry data and forecasts that may be included or incorporated by reference in this prospectus, any prospectus supplement or any applicable free writing prospectus may involve estimates, assumptions and other risks and uncertainties and are subject to change based on various factors, including those discussed under the heading “Risk Factors” contained in this prospectus, the applicable prospectus supplement and any applicable free writing prospectus, and under similar headings in other documents that are incorporated by reference into this prospectus. Accordingly, investors should not place undue reliance on this information.

When we refer to “Eloxx,” “we,” “our,” “us” and the “Company” in this prospectus, we mean Eloxx Pharmaceuticals, Inc. and its consolidated subsidiaries, unless otherwise specified. When we refer to “you,” we mean the potential holders of the applicable series of securities.

We have proprietary rights to trademarks, trade names and service marks appearing in this prospectus that are important to our business. Solely for convenience, the trademarks, trade names and service marks may appear in this prospectus without the ® and TM symbols, but any such references are not intended to indicate, in any way, that we forgo or will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensors to these trademarks, trade names and service marks. All trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners. We do not intend our use or display of other parties’ trademarks, trade names or service marks to imply, and such use or display should not be construed to imply, a relationship with, or endorsement or sponsorship of us by, these other parties.

## WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

### Available Information

We file reports, proxy statements and other information with the SEC. The SEC maintains a web site that contains reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is <http://www.sec.gov>.

Our web site address is [www.eloxxpharma.com](http://www.eloxxpharma.com). The information on our web site, however, is not, and should not be deemed to be, a part of this prospectus.

This prospectus and any prospectus supplement are part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Forms of the indenture and other documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement or documents incorporated by reference in the registration statement. Statements in this prospectus or any prospectus supplement about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement through the SEC's website, as provided above.

### Incorporation by Reference

The SEC's rules allow us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in this prospectus or a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or a subsequently filed document incorporated by reference modifies or replaces that statement.

This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that have previously been filed with the SEC (other than those documents or the portions of those documents not deemed to be filed):

- [Our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 12, 2021.](#)
- The information specifically incorporated by reference into our Annual Report on [Form 10-K from our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 1, 2021.](#)
- Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2021 and June 30, 2021, filed with the SEC on [May 7, 2021](#) and [August 16, 2021.](#)
- Our Current Reports on Form 8-K and Form 8-K/A filed with the SEC on [January 13, 2021](#), [March 12, 2021](#), [March 26, 2021](#), [April 1, 2021](#) (except for Item 7.01 of such report, which shall not be deemed incorporated by reference herein), [April 29, 2021](#), [May 18, 2021](#), [May 18, 2021](#), [May 20, 2021](#), [May 27, 2021](#), [June 16, 2021](#), [July 6, 2021](#) (except for Item 7.01 of such report, which shall not be deemed incorporated by reference herein) [July 16, 2021](#) and [August 20, 2021.](#)
- The description of our common stock contained in our [Registration Statement on Form 8-A, filed on April 24, 2018](#), including any amendments or reports filed for purposes of updating this description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the "Exchange Act" in this prospectus, prior to the termination of this offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus by writing or telephoning us at the following address:

Eloxx Pharmaceuticals, Inc.  
480 Arsenal Way  
Watertown, Massachusetts 02472  
(781) 577-5300

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus or any accompanying prospectus supplement.



## THE COMPANY

We are a clinical-stage biopharmaceutical company engaged in the science of ribosome modulation, leveraging both our innovative TURBO-ZM chemistry technology platform in an effort to develop novel Ribosome Modulating Agents (RMAs) and our library of Eukaryotic Ribosome Selective Glycosides (ERSGs), for the treatment of 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.

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

ELX-02, is a small molecule drug candidate designed to restore production of full-length functional proteins. The investigational therapy has shown strong activity across a full range of mutations in cystic fibrosis (CF) preclinical models. In Phase 1 testing, ELX-02 was generally well tolerated and demonstrated high bioavailability with consistent pharmacokinetics across both single and multiple-dose studies. The Phase 2 trials are designed to validate the safety of ELX-02 and assess its biological activity.

ELX-02 is currently in Phase 2 clinical development for the treatment of CF in patients with diagnosed nonsense mutations and is being conducted at leading investigator sites in Europe, Israel and the United States. As of the end of June 2021, we believe that we have enrolled a sufficient number of patients to assess biological activity of ELX-02. We will continue to enroll additional patients to support Phase 3 clinical trial planning. We expect to present data from the first four treatment arms of the study in the fourth quarter of 2021. The Cystic Fibrosis Foundation (“CF Foundation”) is providing funding for a portion of this global clinical trial program. The FDA has granted orphan drug designation to ELX-02 for the treatment of nephropathic cystinosis, MPS I, Rett syndrome, and CF.

With the strength of our ELX-02 program for CF, the acquisition of Zikani provides us with the opportunity to amplify the potential of our innovative science by developing a new class of therapies to treat diseases with limited to no treatment options. The CF Foundation has agreed to provide funding for a portion of this research. Our preclinical programs are focused on select rare diseases including inherited diseases, cancer caused by nonsense mutations, kidney diseases, including autosomal dominant polycystic kidney disease, as well as rare ocular genetic disorders. In addition, we plan to file an IND in 2022 for what could potentially become the first oral therapy for protein restoration for patients with nonsense mutations in Recessive Dystrophic Epidermolysis Bullosa (RDEB) and Junctional Epidermolysis Bullosa (JEB). RDEB is an incurable, extremely painful and often fatal skin blistering condition caused by a lack of collagen type VII that is estimated to affect more than 3,000 people worldwide. JEB is the most severe form of EB, with most patients dying in infancy. By extending the application of ribosomal RNA modulation to the readthrough of nonsense mutations in tumor suppressor genes, we are also rapidly advancing preclinical research for familial adenomatous polyposis (FAP), an inherited pre-cancerous colorectal disease frequently caused by nonsense mutations in the adenomatous polyposis coli (APC) gene. We plan to target rare diseases including genetic diseases and cancers caused by nonsense mutations.

Nonsense mutations cause approximately 10-12 percent of rare inherited diseases. ELX-02 along with the TURBO-ZM library of compounds are anticipated to significantly expand to include the potential treatment of many other rare diseases and certain cancers.

We were incorporated under the laws of the State of Delaware. Our principal executive offices are located at 480 Arsenal Way, Watertown, Massachusetts 02472, and our telephone number is (781) 577-5300. Our website address is [www.eloxpharma.com](http://www.eloxpharma.com). The information contained on our website is not incorporated by reference into this prospectus, and you should not consider any information contained on, or that can be accessed through, our website as part of this prospectus or in deciding whether to purchase our securities. Our common stock is listed on the Nasdaq Global Market under the symbol “ELOX”.

## **RISK FACTORS**

Investment in any securities offered pursuant to this prospectus and the applicable prospectus supplement involves risks. You should carefully consider the risk factors incorporated by reference to our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K, and all other information contained or incorporated by reference into this prospectus, as updated by our subsequent filings under the Exchange Act, and the risk factors and other information contained in the applicable prospectus supplement and any applicable free writing prospectus before acquiring any of such securities. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities.

**USE OF PROCEEDS**

We intend to use the net proceeds from the sale of the securities as set forth in the applicable prospectus supplement.

## DESCRIPTION OF CAPITAL STOCK

As of the date of this prospectus, our certificate of incorporation authorizes us to issue up to 500,000,000 shares of common stock, \$0.01 par value per share, and 5,000,000 shares of preferred stock, \$0.01 par value per share. The following summary describes the material terms and provisions affecting the rights of holders of our capital stock, which is qualified in its entirety by reference to our certificate of incorporation and our bylaws, in each case as amended.

As of June 30, 2021, there were 86,201,767 shares of common stock outstanding, no shares of preferred stock outstanding, and warrants to purchase 323,892 shares of common stock, options to purchase 7,655,008 shares of common stock, and restricted stock units for 634,892 shares of common stock were outstanding.

### Common Stock

Our common stock is listed on the Nasdaq Capital Market under the symbol “ELOX.”

*Voting rights.* Each holder of our common stock is entitled to one vote for each share of common stock on all matters submitted to a vote of the stockholders, including the election of directors.

*Dividend rights.* Subject to preferences that may be applicable to any then outstanding preferred stock, holders of our common stock are entitled to receive ratably such dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

*Liquidation.* In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of preferred stock.

*Rights and Preferences.* Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to and may be adversely affected by, the rights of the holders of shares of any series of our preferred stock that we may designate in the future. All outstanding shares of common stock are fully paid and nonassessable, and the shares of common stock to be issued under this prospectus, when they are paid for, will be fully paid and nonassessable.

### Transfer Agent

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC.

### Dividend

Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of outstanding preferred stock. We have never declared or paid any cash dividends on our common stock. We do not intend to pay cash dividends for the foreseeable future. We currently expect to retain all future earnings, if any, for use in the development, operation and expansion of our business. Any determination to pay cash dividends in the future will depend upon, among other things, our results of operations, plans for expansion, tax considerations, available net profits and reserves, limitations under law, financial condition, capital requirements and other factors that our board of directors considers to be relevant.

### Preferred Stock

Our board of directors has the authority, without further action by our stockholders, to issue preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the

likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change of control of our company or other corporate action.

Our board of directors will fix the designations, voting powers, preferences and rights of the preferred stock of each series we issue under this prospectus, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that contains the terms of the series of preferred stock we are offering. We will describe in the applicable prospectus supplement the terms of the series of preferred stock being offered, including, to the extent applicable:

- the title and stated value;
- the number of shares we are offering;
- the liquidation preference per share;
- the purchase price;
- the dividend rate, period and payment date and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if applicable;
- the provisions for a sinking fund, if applicable;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock or other equity securities, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;
- voting rights, if any;
- preemptive rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of material or special U.S. federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- any limitations on the issuance of any class or series of preferred stock ranking senior to or on parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

The laws of the state of Delaware, the state of our incorporation, provide that the holders of preferred stock will have the right to vote separately as a class on any proposal involving fundamental changes in the rights of holders of such preferred stock. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

If we issue and sell shares of preferred stock pursuant to this prospectus, the shares will be fully paid and nonassessable and will not have, or be subject to, any preemptive or similar rights. The issuance of

preferred stock could adversely affect the voting power, conversion or other rights of holders of common stock and reduce the likelihood that common stockholders will receive dividend payments and payments upon liquidation. Preferred stock could be issued quickly with terms designed to delay, deter or prevent a change in control of our company or make removal of management more difficult. Additionally, the issuance of preferred stock may have the effect of decreasing the market price of our common stock.

### **Section 203 of the Delaware General Corporation Law**

We are subject to Section 203 of the Delaware General Corporation Law, which prohibits a publicly-held Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years after the date that such stockholder became an interested stockholder, with the following exceptions:

- before such date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested holder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction began, excluding for purposes of determining the voting stock outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (i) by persons who are directors and also officers and (ii) employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- on or after such date, the business combination is approved by the board of directors and authorized at an annual or special meeting of the stockholders, and not by written consent, by the affirmative vote of at least 50% of the outstanding voting stock that is not owned by the interested stockholder.

In general, Section 203 defines business combination to include the following:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;
- subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- any transaction involving the corporation that has the effect of increasing the proportionate share of the stock or any class or series of the corporation beneficially owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loss, advances, guarantees, pledges or other financial benefits by or through the corporation.

In general, Section 203 defines an “interested stockholder” as an entity or person who, together with the person’s affiliates and associates, beneficially owns, or within three years prior to the time of determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation.

## DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplement or free writing prospectus, summarizes certain general terms and provisions of the debt securities that we may offer under this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a supplement to this prospectus. We will also indicate in the supplement to what extent the general terms and provisions described in this prospectus apply to a particular series of debt securities.

We may issue debt securities either separately, or together with, or upon the conversion or exercise of or in exchange for, other securities described in this prospectus. Debt securities may be our senior, senior subordinated or subordinated obligations and, unless otherwise specified in a supplement to this prospectus, the debt securities will be our direct, unsecured obligations and may be issued in one or more series.

The debt securities will be issued under an indenture between us and a trustee. We have summarized select portions of the indenture below. The summary is not complete. The form of the indenture has been filed as an exhibit to the registration statement of which this prospectus forms a part and you should read the indenture for provisions that may be important to you. In the summary below, we have included references to the section numbers of the indenture so that you can easily locate these provisions. Capitalized terms used in the summary and not defined herein have the meanings specified in the indenture.

As used in this section only, “Eloxx,” “we,” “our” or “us” refer to Eloxx Pharmaceuticals, Inc., excluding our subsidiaries, unless expressly stated or the context otherwise requires.

### General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in a resolution of our board of directors, in an officer’s certificate or by a supplemental indenture. The particular terms of each series of debt securities will be described in a prospectus supplement relating to such series (including any pricing supplement or term sheet).

We can issue an unlimited amount of debt securities under the indenture that may be in one or more series with the same or various maturities, at par, at a premium, or at a discount. We will set forth in a prospectus supplement (including any pricing supplement or term sheet) relating to any series of debt securities being offered, the aggregate principal amount and the following terms of the debt securities, if applicable:

- the title and ranking of the debt securities (including the terms of any subordination provisions);
- the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities;
- any limit on the aggregate principal amount of the debt securities;
- the date or dates on which the principal of the securities of the series is payable;
- the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;
- the place or places where principal of, and interest, if any, on the debt securities will be payable (and the method of such payment), where the securities of such series may be surrendered for registration of transfer or exchange, and where notices and demands to us in respect of the debt securities may be delivered;
- the period or periods within which, the price or prices at which and the terms and conditions upon which we may redeem the debt securities;

- any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities and the period or periods within which, the price or prices at which and in the terms and conditions upon which securities of the series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;
- the dates on which and the price or prices at which we will repurchase debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;
- the denominations in which the debt securities will be issued, if other than denominations of \$1,000 and any integral multiple thereof;
- whether the debt securities will be issued in the form of certificated debt securities or global debt securities;
- the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;
- the currency of denomination of the debt securities, which may be United States Dollars or any foreign currency, and if such currency of denomination is a composite currency, the agency or organization, if any, responsible for overseeing such composite currency;
- the designation of the currency, currencies or currency units in which payment of principal of, premium and interest on the debt securities will be made;
- if payments of principal of, premium or interest on the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;
- the manner in which the amounts of payment of principal of, premium, if any, or interest on the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index;
- any provisions relating to any security provided for the debt securities;
- any addition to, deletion of or change in the Events of Default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;
- any addition to, deletion of or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;
- any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities;
- the provisions, if any, relating to conversion or exchange of any debt securities of such series, including if applicable, the conversion or exchange price and period, provisions as to whether conversion or exchange will be mandatory, the events requiring an adjustment of the conversion or exchange price and provisions affecting conversion or exchange;
- any other terms of the debt securities, which may supplement, modify or delete any provision of the indenture as it applies to that series, including any terms that may be required under applicable law or regulations or advisable in connection with the marketing of the securities; and
- whether any of our direct or indirect subsidiaries will guarantee the debt securities of that series, including the terms of subordination, if any, of such guarantees.

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of and any premium and interest on any series of debt



securities is payable in a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

### **Transfer and Exchange**

Each debt security will be represented by either one or more global securities registered in the name of The Depository Trust Company, or the Depository, or a nominee of the Depository (we will refer to any debt security represented by a global debt security as a “book-entry debt security”), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a “certificated debt security”) as set forth in the applicable prospectus supplement. Except as set forth under the heading “Global Debt Securities and Book-Entry System” below, book-entry debt securities will not be issuable in certificated form.

*Certificated Debt Securities.* You may transfer or exchange certificated debt securities at any office we maintain for this purpose in accordance with the terms of the indenture. No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange.

You may effect the transfer of certificated debt securities and the right to receive the principal of, premium and interest on certificated debt securities only by surrendering the certificate representing those certificated debt securities and either reissuance by us or the trustee of the certificate to the new holder or the issuance by us or the trustee of a new certificate to the new holder.

*Global Debt Securities and Book-Entry System.* Each global debt security representing book-entry debt securities will be deposited with, or on behalf of, the Depository, and registered in the name of the Depository or a nominee of the Depository. Please see “Global Securities.”

### **Covenants**

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue of debt securities.

### **No Protection in the Event of a Change of Control**

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions which may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control) which could adversely affect holders of debt securities.

### **Consolidation, Merger and Sale of Assets**

We may not consolidate with or merge with or into, or convey, transfer or lease all or substantially all of our properties and assets to any person (a “successor person”) unless:

- we are the surviving corporation or the successor person (if other than Eloxx) is a corporation organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes our obligations on the debt securities and under the indenture; and
- immediately after giving effect to the transaction, no Default or Event of Default, shall have occurred and be continuing.

Notwithstanding the above, any of our subsidiaries may consolidate with, merge into or transfer all or part of its properties to us.

## Events of Default

“Event of Default” means with respect to any series of debt securities, any of the following:

- default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of such default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);
- default in the payment of principal of any security of that series at its maturity;
- default in the performance or breach of any other covenant or warranty by us in the indenture (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 90 days after we receive written notice from the trustee or Eloxx and the trustee receive written notice from the holders of not less than 25% in principal amount of the outstanding debt securities of that series as provided in the indenture;
- certain voluntary or involuntary events of bankruptcy, insolvency or reorganization of Eloxx;
- any other Event of Default provided with respect to debt securities of that series that is described in the applicable prospectus supplement.

No Event of Default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an Event of Default with respect to any other series of debt securities. The occurrence of certain Events of Default or an acceleration under the indenture may constitute an event of default under certain indebtedness of ours or our subsidiaries outstanding from time to time.

We will provide the trustee written notice of any Default or Event of Default within 30 days of becoming aware of the occurrence of such Default or Event of Default, which notice will describe in reasonable detail the status of such Default or Event of Default and what action we are taking or propose to take in respect thereof.

If an Event of Default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than 25% in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal of (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) and accrued and unpaid interest, if any, on all debt securities of that series. In the case of an Event of Default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the holders of a majority in principal amount of the outstanding debt securities of that series may rescind and annul the acceleration if all Events of Default, other than the non-payment of accelerated principal and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the indenture. We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an Event of Default.

The indenture provides that the trustee may refuse to perform any duty or exercise any of its rights or powers under the indenture unless the trustee receives indemnity satisfactory to it against any cost, liability or expense which might be incurred by it in performing such duty or exercising such right or power. Subject to certain rights of the trustee, the holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to the debt securities of that series.

No holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

- that holder has previously given to the trustee written notice of a continuing Event of Default with respect to debt securities of that series; and
- the holders of not less than 25% in principal amount of the outstanding debt securities of that series have made written request, and offered indemnity or security satisfactory to the trustee, to the trustee to institute the proceeding as trustee, and the trustee has not received from the holders of not less than a majority in principal amount of the outstanding debt securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days. Notwithstanding any other provision in the indenture, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, premium and any interest on that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment.

The indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a statement as to compliance with the indenture. If a Default or Event of Default occurs and is continuing with respect to the securities of any series and if it is known to a responsible officer of the trustee, the trustee shall mail to each Securityholder of the securities of that series notice of a Default or Event of Default within 90 days after it occurs or, if later, after a responsible officer of the trustee has knowledge of such Default or Event of Default. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any Default or Event of Default (except in payment on any debt securities of that series) with respect to debt securities of that series if the trustee determines in good faith that withholding notice is in the interest of the holders of those debt securities.

#### **Modification and Waiver**

We and the trustee may modify, amend or supplement the indenture or the debt securities of any series without the consent of any holder of any debt security:

- to cure any ambiguity, defect or inconsistency;
- to comply with covenants in the indenture described above under the heading “Consolidation, Merger and Sale of Assets”;
- to provide for uncertificated securities in addition to or in place of certificated securities;
- to add guarantees with respect to debt securities of any series or secure debt securities of any series;
- to surrender any of our rights or powers under the indenture;
- to add covenants or events of default for the benefit of the holders of debt securities of any series;
- to comply with the applicable procedures of the applicable depository;
- to make any change that does not adversely affect the rights of any holder of debt securities;
- to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;
- to effect the appointment of a successor trustee with respect to the debt securities of any series and to add to or change any of the provisions of the indenture to provide for or facilitate administration by more than one trustee; or
- to comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act.

We may also modify and amend the indenture with the consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the modifications or amendments. We may not make any modification or amendment without the consent of the holders of each affected debt security then outstanding if that amendment will:

- reduce the amount of debt securities whose holders must consent to an amendment, supplement or waiver;
- reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;
- reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;
- reduce the principal amount of discount securities payable upon acceleration of maturity;
- waive a default in the payment of the principal of, premium or interest on any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of that series and a waiver of the payment default that resulted from such acceleration);
- make the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security;
- make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of, premium and interest on those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or
- waive a redemption payment with respect to any debt security.

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration.

#### **Defeasance of Debt Securities and Certain Covenants in Certain Circumstances**

*Legal Defeasance.* The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, we may be discharged from any and all obligations in respect of the debt securities of any series (subject to certain exceptions). We will be so discharged upon the irrevocable deposit with the trustee, in trust, of money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money or U.S. government obligations in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities.

This discharge may occur only if, among other things, we have delivered to the trustee an opinion of counsel stating that we have received from, or there has been published by, the United States Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable United States federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit, defeasance and discharge had not occurred.

*Defeasance of Certain Covenants.* The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, upon compliance with certain conditions:

- we may omit to comply with the covenant described under the heading “Consolidation, Merger and Sale of Assets” and certain other covenants set forth in the indenture, as well as any additional covenants which may be set forth in the applicable prospectus supplement; and
- any omission to comply with those covenants will not constitute a Default or an Event of Default with respect to the debt securities of that series (“covenant defeasance”).

The conditions include:

- depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities; and
- delivering to the trustee an opinion of counsel to the effect that the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred.

#### **No Personal Liability of Directors, Officers, Employees or Securityholders**

None of our past, present or future directors, officers, employees or securityholders, as such, will have any liability for any of our obligations under the debt securities or the indenture or for any claim based on, or in respect or by reason of, such obligations or their creation. By accepting a debt security, each holder waives and releases all such liability. This waiver and release is part of the consideration for the issue of the debt securities. However, this waiver and release may not be effective to waive liabilities under U.S. federal securities laws, and it is the view of the SEC that such a waiver is against public policy.

#### **Governing Law**

The indenture and the debt securities, including any claim or controversy arising out of or relating to the indenture or the securities, will be governed by the laws of the State of New York.

The indenture will provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably waive, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to the indenture, the debt securities or the transactions contemplated thereby.

The indenture will provide that any legal suit, action or proceeding arising out of or based upon the indenture or the transactions contemplated thereby may be instituted in the federal courts of the United States of America located in the City of New York or the courts of the State of New York in each case located in the City of New York, and we, the trustee and the holder of the debt securities (by their acceptance of the debt securities) irrevocably submit to the non-exclusive jurisdiction of such courts in any such suit, action or proceeding. The indenture will further provide that service of any process, summons, notice or document by mail (to the extent allowed under any applicable statute or rule of court) to such party’s address set forth in the indenture will be effective service of process for any suit, action or other proceeding brought in any such court. The indenture will further provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the courts specified above and irrevocably and unconditionally waive and agree not to plead or claim any such suit, action or other proceeding has been brought in an inconvenient forum.

## DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of shares of our common stock or preferred stock or of debt securities. We may issue warrants independently or together with other securities, and the warrants may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and the investors or a warrant agent. The following summary of material provisions of the warrants and warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to a particular series of warrants. The terms of any warrants offered under a prospectus supplement may differ from the terms described below. We urge you to read the applicable prospectus supplement and any related free writing prospectus, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants.

The particular terms of any issue of warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

- the number of shares of common stock or preferred stock purchasable upon the exercise of warrants to purchase such shares and the price at which such number of shares may be purchased upon such exercise;
- the designation, stated value and terms (including, without limitation, liquidation, dividend, conversion and voting rights) of the series of preferred stock purchasable upon exercise of warrants to purchase preferred stock;
- the principal amount of debt securities that may be purchased upon exercise of a debt warrant and the exercise price for the warrants, which may be payable in cash, securities or other property;
- the date, if any, on and after which the warrants and the related debt securities, preferred stock or common stock will be separately transferable;
- the terms of any rights to redeem or call the warrants;
- the date on which the right to exercise the warrants will commence and the date on which the right will expire;
- United States Federal income tax consequences applicable to the warrants; and
- any additional terms of the warrants, including terms, procedures, and limitations relating to the exchange, exercise and settlement of the warrants.

Holders of equity warrants will not be entitled:

- to vote, consent or receive dividends;
- receive notice as shareholders with respect to any meeting of shareholders for the election of our directors or any other matter; or
- exercise any rights as shareholders of Eloxx.

Each warrant will entitle its holder to purchase the principal amount of debt securities or the number of shares of preferred stock or common stock at the exercise price set forth in, or calculable as set forth in, the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

A holder of warrant certificates may exchange them for new warrant certificates of different denominations, present them for registration of transfer and exercise them at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement. Until any warrants to purchase debt securities are exercised, the holder of the warrants will not have any rights of holders of the debt securities that can be purchased upon exercise, including any rights to receive payments of principal, premium or interest on the underlying debt securities or to enforce covenants in the applicable indenture. Until any warrants to purchase common stock or preferred stock are exercised, the holders of the warrants

will not have any rights of holders of the underlying common stock or preferred stock, including any rights to receive dividends or payments upon any liquidation, dissolution or winding up on the common stock or preferred stock, if any.

## DESCRIPTION OF UNITS

We may issue units consisting of any combination of the other types of securities offered under this prospectus in one or more series. We may evidence each series of units by unit certificates that we will issue under a separate agreement. We may enter into unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units.

The following description, together with the additional information included in any applicable prospectus supplement, summarizes the general features of the units that we may offer under this prospectus. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreements that contain the terms of the units. Specific unit agreements will contain additional important terms and provisions and we will file as an exhibit to the registration statement of which this prospectus is a part or will incorporate by reference from another report that we file with the SEC, the form of each unit agreement relating to units offered under this prospectus.

If we offer any units, certain terms of that series of units will be described in the applicable prospectus supplement, including, without limitation, the following, as applicable:

- the title of the series of units;
- identification and description of the separate constituent securities comprising the units;
- the price or prices at which the units will be issued;
- the date, if any, on and after which the constituent securities comprising the units will be separately transferable;
- a discussion of certain United States federal income tax considerations applicable to the units; and
- any other terms of the units and their constituent securities.



## GLOBAL SECURITIES

### Book-Entry, Delivery and Form

Unless we indicate differently in any applicable prospectus supplement or free writing prospectus, the securities initially will be issued in book-entry form and represented by one or more global notes or global securities, or, collectively, global securities. The global securities will be deposited with, or on behalf of, The Depository Trust Company, New York, New York, as depository, or DTC, and registered in the name of Cede & Co., the nominee of DTC. Unless and until it is exchanged for individual certificates evidencing securities under the limited circumstances described below, a global security may not be transferred except as a whole by the depository to its nominee or by the nominee to the depository, or by the depository or its nominee to a successor depository or to a nominee of the successor depository.

DTC has advised us that it is:

- a limited-purpose trust company organized under the New York Banking Law;
- a “banking organization” within the meaning of the New York Banking Law;
- a member of the Federal Reserve System;
- a “clearing corporation” within the meaning of the New York Uniform Commercial Code; and
- a “clearing agency” registered pursuant to the provisions of Section 17A of the Exchange Act.

DTC holds securities that its participants deposit with DTC. DTC also facilitates the settlement among its participants of securities transactions, such as transfers and pledges, in deposited securities through electronic computerized book-entry changes in participants’ accounts, thereby eliminating the need for physical movement of securities certificates. “Direct participants” in DTC include securities brokers and dealers, including underwriters, banks, trust companies, clearing corporations and other organizations. DTC is a wholly-owned subsidiary of The Depository Trust & Clearing Corporation, or DTCC. DTCC is the holding company for DTC, National Securities Clearing Corporation and Fixed Income Clearing Corporation, all of which are registered clearing agencies. DTCC is owned by the users of its regulated subsidiaries. Access to the DTC system is also available to others, which we sometimes refer to as indirect participants, that clear through or maintain a custodial relationship with a direct participant, either directly or indirectly. The rules applicable to DTC and its participants are on file with the SEC.

Purchases of securities under the DTC system must be made by or through direct participants, which will receive a credit for the securities on DTC’s records. The ownership interest of the actual purchaser of a security, which we sometimes refer to as a beneficial owner, is in turn recorded on the direct and indirect participants’ records. Beneficial owners of securities will not receive written confirmation from DTC of their purchases. However, beneficial owners are expected to receive written confirmations providing details of their transactions, as well as periodic statements of their holdings, from the direct or indirect participants through which they purchased securities. Transfers of ownership interests in global securities are to be accomplished by entries made on the books of participants acting on behalf of beneficial owners. Beneficial owners will not receive certificates representing their ownership interests in the global securities, except under the limited circumstances described below.

To facilitate subsequent transfers, all global securities deposited by direct participants with DTC will be registered in the name of DTC’s partnership nominee, Cede & Co., or such other name as may be requested by an authorized representative of DTC. The deposit of securities with DTC and their registration in the name of Cede & Co. or such other nominee will not change the beneficial ownership of the securities. DTC has no knowledge of the actual beneficial owners of the securities. DTC’s records reflect only the identity of the direct participants to whose accounts the securities are credited, which may or may not be the beneficial owners. The participants are responsible for keeping account of their holdings on behalf of their customers.

So long as the securities are in book-entry form, you will receive payments and may transfer securities only through the facilities of the depository and its direct and indirect participants. We will maintain an office or agency in the location specified in the prospectus supplement for the applicable securities, where notices and demands in respect of the securities and the indenture may be delivered to us and where certificated securities may be surrendered for payment, registration of transfer or exchange.

Conveyance of notices and other communications by DTC to direct participants, by direct participants to indirect participants and by direct participants and indirect participants to beneficial owners will be governed by arrangements among them, subject to any legal requirements in effect from time to time.

Redemption notices will be sent to DTC. If less than all of the securities of a particular series are being redeemed, DTC's practice is to determine by lot the amount of the interest of each direct participant in the securities of such series to be redeemed.

Neither DTC nor Cede & Co. (or such other DTC nominee) will consent or vote with respect to the securities. Under its usual procedures, DTC will mail an omnibus proxy to us as soon as possible after the record date. The omnibus proxy assigns the consenting or voting rights of Cede & Co. to those direct participants to whose accounts the securities of such series are credited on the record date, identified in a listing attached to the omnibus proxy.

So long as securities are in book-entry form, we will make payments on those securities to the depository or its nominee, as the registered owner of such securities, by wire transfer of immediately available funds. If securities are issued in definitive certificated form under the limited circumstances described below and unless if otherwise provided in the description of the applicable securities herein or in the applicable prospectus supplement, we will have the option of making payments by check mailed to the addresses of the persons entitled to payment or by wire transfer to bank accounts in the United States designated in writing to the applicable trustee or other designated party at least 15 days before the applicable payment date by the persons entitled to payment, unless a shorter period is satisfactory to the applicable trustee or other designated party.

Redemption proceeds, distributions and dividend payments on the securities will be made to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC. DTC's practice is to credit direct participants' accounts upon DTC's receipt of funds and corresponding detail information from us on the payment date in accordance with their respective holdings shown on DTC records. Payments by participants to beneficial owners will be governed by standing instructions and customary practices, as is the case with securities held for the account of customers in bearer form or registered in "street name." Those payments will be the responsibility of participants and not of DTC or us, subject to any statutory or regulatory requirements in effect from time to time. Payment of redemption proceeds, distributions and dividend payments to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC, is our responsibility, disbursement of payments to direct participants is the responsibility of DTC, and disbursement of payments to the beneficial owners is the responsibility of direct and indirect participants.

Except under the limited circumstances described below, purchasers of securities will not be entitled to have securities registered in their names and will not receive physical delivery of securities. Accordingly, each beneficial owner must rely on the procedures of DTC and its participants to exercise any rights under the securities and the indenture.

The laws of some jurisdictions may require that some purchasers of securities take physical delivery of securities in definitive form. Those laws may impair the ability to transfer or pledge beneficial interests in securities.

DTC may discontinue providing its services as securities depository with respect to the securities at any time by giving reasonable notice to us. Under such circumstances, in the event that a successor depository is not obtained, securities certificates are required to be printed and delivered.

As noted above, beneficial owners of a particular series of securities generally will not receive certificates representing their ownership interests in those securities. However, if:

- DTC notifies us that it is unwilling or unable to continue as a depository for the global security or securities representing such series of securities or if DTC ceases to be a clearing agency registered under the Exchange Act at a time when it is required to be registered and a successor depository is not appointed within 90 days of the notification to us or of our becoming aware of DTC's ceasing to be so registered, as the case may be;

- we determine, in our sole discretion, not to have such securities represented by one or more global securities; or
- an Event of Default has occurred and is continuing with respect to such series of securities,

we will prepare and deliver certificates for such securities in exchange for beneficial interests in the global securities. Any beneficial interest in a global security that is exchangeable under the circumstances described in the preceding sentence will be exchangeable for securities in definitive certificated form registered in the names that the depository directs. It is expected that these directions will be based upon directions received by the depository from its participants with respect to ownership of beneficial interests in the global securities.

#### ***Euroclear and Clearstream***

If so provided in the applicable prospectus supplement, you may hold interests in a global security through Clearstream Banking S.A., which we refer to as “Clearstream,” or Euroclear Bank S.A./N.V., as operator of the Euroclear System, which we refer to as “Euroclear,” either directly if you are a participant in Clearstream or Euroclear or indirectly through organizations which are participants in Clearstream or Euroclear. Clearstream and Euroclear will hold interests on behalf of their respective participants through customers’ securities accounts in the names of Clearstream and Euroclear, respectively, on the books of their respective U.S. depositories, which in turn will hold such interests in customers’ securities accounts in such depositories’ names on DTC’s books.

Clearstream and Euroclear are securities clearance systems in Europe. Clearstream and Euroclear hold securities for their respective participating organizations and facilitate the clearance and settlement of securities transactions between those participants through electronic book-entry changes in their accounts, thereby eliminating the need for physical movement of certificates.

Payments, deliveries, transfers, exchanges, notices and other matters relating to beneficial interests in global securities owned through Euroclear or Clearstream must comply with the rules and procedures of those systems. Transactions between participants in Euroclear or Clearstream, on one hand, and other participants in DTC, on the other hand, are also subject to DTC’s rules and procedures.

Investors will be able to make and receive through Euroclear and Clearstream payments, deliveries, transfers and other transactions involving any beneficial interests in global securities held through those systems only on days when those systems are open for business. Those systems may not be open for business on days when banks, brokers and other institutions are open for business in the United States.

Cross-market transfers between participants in DTC, on the one hand, and participants in Euroclear or Clearstream, on the other hand, will be effected through DTC in accordance with the DTC’s rules on behalf of Euroclear or Clearstream, as the case may be, by their respective U.S. depositories; however, such cross-market transactions will require delivery of instructions to Euroclear or Clearstream, as the case may be, by the counterparty in such system in accordance with the rules and procedures and within the established deadlines (European time) of such system. Euroclear or Clearstream, as the case may be, will, if the transaction meets its settlement requirements, deliver instructions to its U.S. depository to take action to effect final settlement on its behalf by delivering or receiving interests in the global securities through DTC, and making or receiving payment in accordance with normal procedures for same-day fund settlement. Participants in Euroclear or Clearstream may not deliver instructions directly to their respective U.S. depositories.

Due to time zone differences, the securities accounts of a participant in Euroclear or Clearstream purchasing an interest in a global security from a direct participant in DTC will be credited, and any such crediting will be reported to the relevant participant in Euroclear or Clearstream, during the securities settlement processing day (which must be a business day for Euroclear or Clearstream) immediately following the settlement date of DTC. Cash received in Euroclear or Clearstream as a result of sales of interests in a global security by or through a participant in Euroclear or Clearstream to a direct participant in DTC will be received with value on the settlement date of DTC but will be available in the relevant Euroclear or Clearstream cash account only as of the business day for Euroclear or Clearstream following DTC’s settlement date.

***Other***

The information in this section of this prospectus concerning DTC, Clearstream, Euroclear and their respective book-entry systems has been obtained from sources that we believe to be reliable, but we do not take responsibility for this information. This information has been provided solely as a matter of convenience. The rules and procedures of DTC, Clearstream and Euroclear are solely within the control of those organizations and could change at any time. Neither we nor the trustee nor any agent of ours or of the trustee has any control over those entities and none of us takes any responsibility for their activities. You are urged to contact DTC, Clearstream and Euroclear or their respective participants directly to discuss those matters. In addition, although we expect that DTC, Clearstream and Euroclear will perform the foregoing procedures, none of them is under any obligation to perform or continue to perform such procedures and such procedures may be discontinued at any time. Neither we nor any agent of ours will have any responsibility for the performance or nonperformance by DTC, Clearstream and Euroclear or their respective participants of these or any other rules or procedures governing their respective operations.

## PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods or through underwriters or dealers, through agents and/or directly to one or more purchasers. The securities may be distributed from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Each time that we sell securities covered by this prospectus, we will provide a prospectus supplement or supplements that will describe the method of distribution and set forth the terms and conditions of the offering of such securities, including the offering price of the securities and the proceeds to us, if applicable.

Offers to purchase the securities being offered by this prospectus may be solicited directly. Agents may also be designated to solicit offers to purchase the securities from time to time. Any agent involved in the offer or sale of our securities will be identified in a prospectus supplement.

If a dealer is utilized in the sale of the securities being offered by this prospectus, the securities will be sold to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If an underwriter is utilized in the sale of the securities being offered by this prospectus, an underwriting agreement will be executed with the underwriter at the time of sale and the name of any underwriter will be provided in the prospectus supplement that the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we or the purchasers of securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for which they may act as agent. Unless otherwise indicated in a prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase securities as a principal, and may then resell the securities at varying prices to be determined by the dealer.

Any compensation paid to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers will be provided in the applicable prospectus supplement. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act of 1933, as amended, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof and to reimburse those persons for certain expenses.

Any common stock will be listed on the Nasdaq Global Market, but any other securities may or may not be listed on a national securities exchange. To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than were sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option, if any. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

**LEGAL MATTERS**

Latham & Watkins LLP will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of the Company. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

**EXPERTS**

The financial statements, incorporated in this Prospectus by reference from the Company's Annual Report on Form 10-K, have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference. Such financial statements have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

**Up to \$50,000,000**



**Common Stock**

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**PROSPECTUS SUPPLEMENT**

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**SVB Leerink**

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**September 30, 2021**

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