Eloxx Pharmaceuticals, Inc.
Form 424B5
November 16, 2018
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Filed Pursuant to Rule 424(b)(5)
Registration No. 333-224207

PROSPECTUS SUPPLEMENT
(to Prospectus dated April 20, 2018)
$50,000,000

Common Stock

This prospectus supplement and the accompanying base prospectus relate to the offer, issuance and sale from time to time of our common stock having an aggregate offering price of up to $50,000,000 through Citigroup Global Markets Inc. and Cantor Fitzgerald & Co., collectively referred to as the Sales Agents. These sales, if any, will be made pursuant to the terms of the equity distribution agreement dated November 16, 2018, between us and the Sales Agents that we will file with the Securities and Exchange Commission as an exhibit to a Current Report on Form 8-K.

Under the terms of the equity distribution agreement, we also may sell shares of our common stock to either Sales Agent as principal for its own account at a price agreed upon at the time of the sale. If we sell shares of our common stock to either Sales Agent, as principal, we will enter into a separate agreement with the respective Sales Agent and we will describe that agreement in a separate prospectus supplement or pricing supplement to the extent required by law.

Our common stock is currently listed on The Nasdaq Global Market under the symbol “ELOX.” On November 14, 2018, the last reported sale price of our common stock on The Nasdaq Global Market was $14.98 per share.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus may be made in sales deemed to be an “at the market offering” as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or the Securities Act. Neither of the Sales Agents are required to sell any specific number or dollar amount of our common stock but will use its reasonable efforts, as our agent and subject to the terms of the equity distribution agreement, to sell the shares of our common stock offered, as instructed by us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The Sales Agents will collectively be entitled to a commission of up to 3.0% of the gross sales price per share sold under the equity distribution agreement. In connection with the sale of the shares of common stock on our behalf, each of the Sales Agents may each be deemed to be an “underwriter” within the meaning of the Securities Act of 1933, as amended.

Investing in our common stock involves a high degree of risk. Please read the “ Risk Factors ” beginning on page S-4 of this prospectus supplement and found in the documents incorporated by reference into this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities, or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Citigroup Cantor
November 16, 2018

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Prospectus Supplement

Prospectus

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any free writing prospectus that we have authorized for use in connection with this offering. Neither we nor the Sales Agents have authorized anyone to provide you with information different from that contained in this prospectus supplement, the accompanying prospectus or any accompanying free writing prospectus. We are offering to sell, and seeking offers to buy, common stock only in jurisdictions where offers and sales are permitted. If anyone provides you with different or inconsistent information, you should not rely on it. We and the Sales Agents take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. The information contained in this prospectus supplement, the accompanying prospectus and any accompanying free writing prospectus is accurate only as of the date of this prospectus supplement, the accompanying prospectus and any such accompanying free writing prospectus, regardless of the time of delivery of this prospectus supplement, the accompanying prospectus, any such accompanying free writing prospectus or of any sale of our common stock. 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 in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You

should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement entitled “Where You Can Find More Information” and “Incorporation of Certain Information by Reference.”

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus form part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, utilizing a "shelf" registration process. This document contains two parts. The first part consists of this prospectus supplement, which provides you with specific information about this offering. The second part, the accompanying prospectus, provides more general information, some of which may not apply to this offering. Generally, when we refer only to the "prospectus," we are referring to both parts combined. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference herein or therein, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference herein and therein. You should read this prospectus supplement and the accompanying prospectus, including the information incorporated by reference herein and therein, and any related free writing prospectus that we have authorized for use in connection with this offering.

You should rely only on the information that we have included or incorporated by reference in this prospectus supplement, the accompanying prospectus and any related free writing prospectus that we may authorize to be provided to you. We have not authorized any dealer, salesman or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any related free writing prospectus that we may authorize to be provided to you. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any related free writing prospectus. This prospectus supplement, the accompanying prospectus and any related free writing prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus supplement, the accompanying prospectus or any related free writing prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

You should not assume that the information contained in this prospectus supplement, the accompanying prospectus or any related free writing prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference herein or therein is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus supplement, the accompanying prospectus or any related free writing prospectus is delivered, or securities are sold, on a later date.

This prospectus supplement contains or incorporates by reference summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been or will be filed or have been or will be incorporated by reference as exhibits to the registration statement of which this prospectus supplement forms a part, and you may obtain copies of those documents as described in this prospectus supplement under the heading "Where You Can Find More Information."

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights information contained in other parts of this prospectus supplement. Because it is only a summary, it does not contain all of the information that you should consider before investing in shares of our common stock and it is qualified in its entirety by, and should be read in conjunction with, the more detailed information appearing elsewhere in this prospectus supplement, the accompanying prospectus, any applicable free writing prospectus and the documents incorporated by reference herein and therein. You should read all such documents carefully, especially the risk factors and our financial statements and the related notes included or incorporated by reference herein or therein, before deciding to buy shares of our common stock. Unless the context requires otherwise, references in this prospectus supplement to “Eloxx,” “we,” “us” and “our” refer to Eloxx Pharmaceuticals, Inc. and our subsidiaries.

Company Overview

We are a clinical-stage biopharmaceutical company developing novel ribonucleic acid (RNA)-modulating drug candidates (designed to be eukaryotic ribosomal selective glycosides) that are formulated to treat rare and ultra-rare premature stop codon diseases. Premature stop codons are point mutations that disrupt protein synthesis from messenger RNA. As a consequence, patients with premature stop codon diseases have reduced levels of, or no, critical functional proteins from the mutation bearing allele accounting for some of the most severe phenotypes in these genetic diseases. These premature stop codons have been identified in over 1,800 rare and ultra-rare diseases. Read-through therapeutic development is focused on extending mRNA (messenger RNA) half-life and increasing functional protein synthesis by enabling the cytoplasmic ribosome to read-through premature stop codons to produce full-length proteins. Our lead investigational drug product candidate, ELX-02, is a small molecule designed to restore production of full-length functional proteins. ELX-02 is in the early stages of clinical development focusing on cystic fibrosis and cystinosis. ELX-02 is an investigational drug that has not been approved by any global regulatory body. Our preclinical candidate pool consists of a library of novel drug candidates designed to be eukaryotic ribosomal selective glycosides identified based on read-through potential. We recently announced a new program focused on rare ocular genetic disorders. We are headquartered in Waltham, MA, with R&D operations in Rehovot, Israel.

Our research and development strategy is to target rare or ultra-rare diseases where a high unmet medical need, nonsense mutation bearing, patient population has been identified, there are established preclinical read-through or personalized medicine models that are predictive of clinical activity, and a definable path for Orphan Drug development, regulatory approval, patient access and commercialization. We believe patient advocacy to be an important element of patient focused drug development and seek opportunities to collaborate with patient advocacy groups throughout the discovery and development process. Our current clinical focus for our lead investigational drug product candidate, ELX-02, is on cystic fibrosis and cystinosis. We have initiated a new program focused on rare inherited retinal disease and are conducting IND enabling studies for several compounds from our library. We will identify an additional molecule later this year to advance into clinical development. We have entered into a multiyear partnership with the Foundation Fighting Blindness (FFB) to support our inherited retinal degenerative disease registry and educational programs. FFB will provide ELX-02 with ongoing R&D consultation and support. We believe this partnership has the potential to accelerate our development programs and support patients with ocular disease and a high unmet medical need.

We intend to be the global leader in the application of the science of translational read-through and the associated pathway of nonsense mediated messenger ribonucleic acid (“mRNA”) decay. We believe that expanding our expertise across these basic science areas of mRNA regulation, ribosomal function, and protein translation forms a solid foundation to support our discovery and development activities. Our ERSG compounds modulate the activity of the ribosome, a complex of RNAs and proteins, and therefore, a ribonucleoprotein, responsible for protein production, a process also known as translation. These novel small molecule compounds are designed to allow the ribosome to read-through a nonsense mutation in mRNA (which is transcribed from the DNA sequence), to restore the translation process to produce full length, functional proteins and increase the amount of mRNA that would otherwise be degraded as part of a cellular process called nonsense mediated mRNA decay. As our ERSG compounds target the general mechanism for protein production in the cell, we believe they have the potential to treat hundreds of genetic diseases where nonsense mutations have impaired gene function. Our subcutaneously injected small molecules have the potential to be self-administered and to be active at most tissue locations across the body.

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We believe that our library of related novel small molecules holds the potential to be disease-modifying therapies that may change the course of hundreds of genetic diseases and improve the lives of patients. Our early preclinical data in in vitro and in vivo models of nonsense mutations suggests that drug product candidates from our read-through compound library may have potential beneficial effects for the following diseases: cystic fibrosis, cystinosis, mucopolysaccharidosis type 1, Duchenne muscular dystrophy, Rett syndrome and a variety of rare ocular genetic diseases. In preclinical studies, we have demonstrated the potential for beneficial effects in multiple organs such as the brain, kidney, muscles, eye and others.

Currently our lead program, ELX-02, is focused on development for cystic fibrosis and cystinosis patients with diagnosed nonsense mutations. Our clinical trial application ("CTA") has been approved by the Federal Agency for Medicines and Health Products (the "FAMHP") in Brussels and our IND submitted to the U.S. Food and Drug Administration (the "FDA") is now open. We expect to initiate Phase 2 studies in cystic fibrosis and cystinosis following completion of our ongoing Phase 1 multiple ascending dose ("MAD") study and report top line results in 2019.

As part of our clinical program for ELX-02, we have completed a Phase 1 single ascending dose ("SAD") study in a total of 60 healthy volunteers at sites in Israel (ClinicalTrials.gov Identifier: NCT02807961) and Belgium (ClinicalTrials.gov Identifier: NCT03292302). The results of the SAD study have been submitted for publication. Currently ongoing is the Phase 1 multiple ascending dose ("MAD") study in Belgium (ClinicalTrials.gov Identifier: NCT03309605). We have completed the first four cohorts of the MAD study and have initiated the fifth cohort.

We have initiated a new program focused on rare ocular genetic disorders and are conducting pre-IND enabling studies for several compounds from our library and will identify an additional molecule later this year to take into clinical development.

We believe there is a significant unmet medical need in the treatment of cystic fibrosis patients carrying nonsense mutations on one or both alleles of the Cystic Fibrosis Transmembrane Conductance Regulator ("CFTR") gene. Cystic fibrosis is the most prevalent genetic disease in the western world and there are no currently approved therapies that target the impairment associated with Class 1 CFTR mutations. Similarly, in cystinosis, we believe there is also a high unmet medical need as there are no currently approved therapeutics that target the nonsense mutation mediated impairment of cystinosin. Cystinosin is the cystine-selective transport channel in the lysosomal membrane that is attributed as the cause for the accumulation of cystine in this disease state. Given the high proportion of pediatric patients in each of these rare orphan diseases, we intend to apply for relevant Orphan Drug incentives in the United States and Europe, including the Rare Pediatric Disease Priority Review Voucher in the U.S.

The European Medicines Agency (the "EMA") has granted ELX-02 an orphan drug designation for the treatment of cystic fibrosis and mucopolysaccharidosis type I ("MPS I"). The FDA has granted orphan drug designation to ELX-02 for the treatment of cystinosis, MPS I, and for the treatment of Rett Syndrome.

We hold worldwide development and commercialization rights to ELX-02 and novel compounds in our read-through library, for all indications, in all territories, under a license from the Technion Research and Development Foundation Ltd. Professor Timor Baasov, the inventor of our compounds, has served as our senior consultant since our inception.

Corporate Information

Information concerning the Company is contained in the documents that we file with the SEC as a reporting company under the Securities Exchange Act of 1934, which are accessible at www.sec.gov. Our website address is www.eloxxpharma.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

Our mailing address is 950 Winter Street, Waltham, Massachusetts 02451. Our telephone number is (781) 577-5300.

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THE OFFERING

Common stock offered by us

Shares having an aggregate offering price of up to $50,000,000.

Manner of offering

“At-the-market” offering that may be made from time to time through our Sales Agents, Citigroup Global Markets Inc. and Cantor Fitzgerald & Co. See “Plan of Distribution” beginning on page S-10.

Use of proceeds

We intend to use the net proceeds from future sales of our common stock in this offering to fund part of the continued clinical development of ELX-02, and for working capital and other general corporate purposes. See “Use of Proceeds” beginning on page S-7 of this prospectus supplement.

Risk factors

Investing in our common stock involves a high degree of risk. See the information contained in or incorporated by reference under the heading “Risk Factors” in this prospectus supplement, in the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement and any free writing prospectus that we have authorized for use in connection with this offering.

Nasdaq Global Market symbol

ELOX

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RISK FACTORS

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should carefully consider the risks described below and those discussed under the section captioned "Risk Factors" contained in our Quarterly Reports for the quarterly periods ended September 30, 2018, June 30, 2018 and March 31, 2018 and our Annual Report on Form 10-K for the year ended December 31, 2017, as amended, which are incorporated by reference in this prospectus supplement and the accompanying prospectus, together with other information in this prospectus supplement, the accompanying prospectus, the information and documents incorporated by reference herein and therein, and in any free writing prospectus that we have authorized for use in connection with this offering. You should also carefully consider the risks incorporated by reference herein by way of any amendment or update to our risk factors reflected in subsequent SEC filings. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment.

Risks Related to This Offering and Our Common Stock

Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

Our management will have broad discretion with respect to the use of proceeds of this offering, including for any of the purposes described in the section of this prospectus supplement entitled "Use of Proceeds." You will be relying on the judgment of our management regarding the application of the proceeds of this offering. The results and effectiveness of the use of proceeds are uncertain, and we could spend the proceeds in ways that you do not agree with or that do not improve our results of operations or enhance the value of our common stock. Our failure to apply these funds effectively could have a material adverse effect on our business, delay the development of our product candidates and cause the price of our common stock to decline.

If you purchase the common stock sold in this offering, you may experience immediate and substantial dilution in the net tangible book value per share of the common stock you purchase.

Since the price per share of our common stock being offered in this offering may be higher than the net tangible book value per share of our common stock outstanding prior to this offering, you may suffer immediate and substantial dilution in the net tangible book value of any common stock you purchase in this offering. The actual amount of dilution will be based on a number of factors, including the use of proceeds, and cannot be determined at this time. See the section entitled "Dilution" below for a more detailed discussion of the dilution you may incur if you purchase shares in this offering.

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

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

Pursuant to the Share Ownership and Option Plan (2013), or the 2013 Plan, the 2008 Equity Incentive Plan, or the 2008 Plan, and together with the 2013 Plan, the Prior Plans, and the 2018 Equity Incentive Plan, or the 2018 Plan, our management is authorized to grant share options and other equity-based awards to our employees, directors and consultants. The 2018 Plan became effective on April 20, 2018. As of September 30, 2018, individuals held share options to purchase an aggregate of 3,611,400 shares of common stock. If our board of directors elects to increase the number of shares available for future grant by the maximum amount each year, our stockholders may experience additional dilution, which could have a negative effect on our share price.

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

Our common stock began trading on The Nasdaq Global Market on April 26, 2018 under the symbol "ELOX." The trading price of our common stock has been volatile and may continue to be volatile and subject to wide fluctuations in the future. Many factors could have an impact on our stock price, including fluctuations in our or our competitors' operating results, clinical trial results or adverse events associated with our product candidates, product development by us or our competitors, changes in laws, including healthcare, regulatory, tax or intellectual property laws, intellectual property developments, acquisitions or other strategic transactions, changes in financial or operational estimates or projections and the perceptions of our investors that we are not performing or meeting expectations. The trading price of the common stock of many biopharmaceutical companies, including ours, has experienced extreme price and volume fluctuations, which have at times been unrelated to the operating performance of the companies whose stocks were affected. In addition, the securities market has from time to time experienced significant price and volume fluctuations that are not related to the operating performance of particular companies. These market fluctuations may also materially and adversely affect the market price of shares of our common stock.

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

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

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

We have never declared or paid any dividends on our common stock and do not intend to pay any dividends in the foreseeable future. We anticipate that we will retain all of our future earnings for use in the operation of our business and for general corporate purposes. Any determination to pay dividends in the future will be at the discretion of our board of directors.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the information incorporated by reference in this prospectus supplement, contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this prospectus supplement, including statements regarding our future operating results and financial position, business strategy, and plans and objectives of management for future operations, are forward-looking statements. In many cases, you can identify forward-looking statements by terms such as “may,” “should,” “expects,” “plans,” “anticipates,” “could “intends,” “target,” “projects,” “contemplates,” “believes,” “estimates,” “predicts,” “potential,” or “continue” or the negative o terms or other similar expressions. Forward looking statements include statements herein with respect to our ability to successfully develop and commercialize ELX-02; our expectations regarding approval of ELX-02 by the U.S. Food and Drug Administration; and future performance.

The forward-looking statements contained in this prospectus supplement reflect our views as of the date of this prospectus supplement about future events and are subject to risks, uncertainties, assumptions, and changes in circumstances that may cause our actual results, performance, or achievements to differ significantly from those expressed or implied in any forward-looking statement. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future events, results, performance, or achievements. A number of important factors could cause actual results to differ materially from those indicated by the forward-looking statements, including, without limitation, those factors described or referenced in “Risk Factors.” In addition, those “Risk Factors” may be updated from time to time by our filings under the Securities Exchange Act of 1934, as amended. Except as required by law, after the date of this prospectus supplement, we are under no duty to update or revise any of the forward-looking statements contained or incorporated by reference herein, whether as a result of new information, future events or otherwise.

You should read this prospectus supplement and the information that we incorporate by reference, completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

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USE OF PROCEEDS

We intend to use the net proceeds of this offering to fund part of the continued clinical development of ELX-02, and for working capital and general corporate purposes.

We have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures. As a result, our management will have broad discretion in allocating the net proceeds from this offering. Pending application of the net proceeds as described above, we intend to invest the net proceeds of this offering in short-term, investment-grade, interest-bearing securities.

These expected uses represent our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, the status of and results from clinical trials, as well as any new collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. As a result, our management will have broad discretion in the application of the net proceeds from this offering, and investors will be relying on the judgment of our management regarding the application of the net proceeds from this offering. The timing and amount of our actual expenditures will be based on many factors, including cash flows from operations and the anticipated growth of our business.

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DIVIDEND POLICY

We have never declared or paid any cash dividends on our common stock and our ability to pay cash dividends is currently prohibited by the terms of our debt financing arrangements. We do not anticipate paying cash dividends on our common stock in the foreseeable future. Payment of future dividends, if any, on our common stock will be at the discretion of our board of directors after taking into account various factors, including our financial condition, operating results, anticipated cash needs and plans for expansion.

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DILUTION

If you invest in our common stock, your interest may be diluted immediately to the extent of any difference between the public offering price per share you pay for shares of our common stock in this offering and the as adjusted net tangible book value per share of our common stock after this offering. Net tangible book value per share represents our total tangible assets less total liabilities, divided by the number of shares of our common stock outstanding.

As of September 30, 2018, our net tangible book value was approximately $51.5 million, or $1.46 per share of common stock. After giving effect to the sale of our common stock in the aggregate amount of $50.0 million at an assumed offering price of $14.98 per share, the last reported sale price of our common stock on The Nasdaq Global Market on November 14, 2018, and after deducting estimated commissions and estimated expenses payable by us, our net tangible book value as of September 30, 2018 would have been approximately $99.6 million, or $2.59 per share of common stock. This represents an immediate increase in as adjusted net tangible book value to existing stockholders of $1.13 per share and an immediate dilution to new investors purchasing common stock in this offering of $12.39 per share.

The following table illustrates this per share dilution to the new investors purchasing shares of common stock in this offering:

Assumed public offering price per share		$ 14.98
Net tangible book value per share at September 30, 2018	$ 1.46	
Increase in net tangible book value per share attributable to new investors purchasing shares in this offering		1.13
As adjusted net tangible book value per share after giving effect to this offering		2.59
Dilution per share to new investors in this offering		$ 12.39

The table above assumes for illustrative purposes that an aggregate of 3,337,783 shares of our common stock are sold at a price of $14.98 per share, the last reported sale price of our common stock on The Nasdaq Global Market on November 14, 2018, for aggregate gross proceeds of $50.0 million. The shares sold in this offering, if any, will be sold from time to time at various prices. An increase of $1.00 per share in the price at which the shares are sold from the assumed offering price of $14.98 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 result in our adjusted net tangible book value per share after this offering being $2.60 and would increase the dilution in net tangible book value per share to new investors in this offering to $13.38 per share, after deducting estimated 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 offering price of $14.98 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 result in our adjusted net tangible book value per share after this offering being $2.57 per share, and would decrease the dilution in net tangible book value per share to new investors in this offering to $11.41 per share, after deducting estimated commissions and estimated offering expenses payable by us. This information is supplied for illustrative purposes only.

The foregoing table and calculations are based on 35,124,844 shares of our common stock outstanding as of September 30, 2018, and excludes:

- warrants to purchase 347,241 shares of common stock;
- options to purchase 3,611,400 shares of common stock; and
- restricted stock units for 767,743 shares of common stock.

To the extent that outstanding options are exercised or outstanding restricted stock units are settled, you may experience further dilution. We may choose to raise additional capital due to market conditions or strategic considerations even if at that time we believe we have sufficient funds for our current or future operating plans. To the

extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

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PLAN OF DISTRIBUTION

We have entered into an equity distribution agreement with Citigroup Global Markets Inc. and Cantor Fitzgerald & Co., each, a Sales Agent, under which we may offer and sell common stock having an aggregate offering price of up to $50,000,000 from time to time through either Sales Agent. We will file the equity distribution agreement as an exhibit to a Current Report on Form 8-K, which is incorporated by reference in this prospectus supplement. Sales of our common stock, if any, will be made at market prices by any method that is deemed to be an "at-the-market" equity offering as defined in Rule 415 under the Securities Act of 1933, as amended, the Securities Act, including sales made directly on or through The Nasdaq Global Market or any other trading market for our common stock. Neither Sales Agent will engage in any transactions that stabilize the price of our common stock.

Under the terms of the equity distribution agreement, we also may sell common stock to either Sales Agent as principal for its own account at a price agreed upon at the time of sale. If we sell common stock to either Sales Agent as principal, we will enter into a separate agreement with such Sales Agent, and we will describe that agreement in a separate prospectus supplement or pricing supplement to the extent required by law.

We will designate the maximum amount of common stock to be sold through the Sales Agents on a daily basis or otherwise as we and the Sales Agents agree, and the minimum price per share at which such common stock may be sold. Subject to the terms and conditions of the equity distribution agreement, each Sales Agent will use its reasonable efforts to sell, on our behalf, all of the designated common stock. We may instruct the Sales Agents not to sell any common stock if the sales cannot be effected at or above the price designated by us in any such instruction. We or the Sales Agents may suspend the offering of common stock at any time and from time to time by notifying the other party.

If shares of our common stock are sold by the Sales Agents in an at-the-market offering, the Sales Agents will provide written confirmation to us promptly following the close of trading on The Nasdaq Global Market each trading day on which shares of our common stock are sold under the equity distribution agreement. Each confirmation will include the number of shares of our common stock sold on the preceding day, the gross sales price, the net proceeds to us and the compensation payable by us to the Sales Agents in connection with the sales.

We will pay the Sales Agents a commission of up to 3.0% of the gross sales price per share of common stock sold through the Sales Agents under the equity distribution agreement. We have also agreed to reimburse the Sales Agents for certain specified expenses, including the fees and disbursements of its legal counsel in an amount not to exceed $50,000. We estimate that the total expenses payable by us in connection with the establishment of the program to offer shares of our common stock described in this prospectus supplement, excluding commissions and reimbursements payable to the Sales Agents under the equity distribution agreement, will be approximately $350,000.

Settlement for sales of our common stock under the equity distribution agreement will occur on the second trading day following the date on which any sales are made, or on some other date that is agreed upon by us and the Sales Agents in connection with a particular transaction, 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.

The offering of common stock pursuant to the equity distribution agreement will terminate upon the earlier of (1) the sale of all common stock subject to the equity distribution agreement or (2) the termination of the equity distribution agreement by us, by the Sales Agents or by its terms, as applicable.

In connection with the sale of the common stock on our behalf, the Sales Agents may be deemed to be "underwriters" within the meaning of the Securities Act and the compensation paid to the Sales Agents may be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to the Sales Agents against certain liabilities, including civil liabilities under the Securities Act.

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Other Relationships

Each Sales Agent is a full service financial institution engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, principal investment, hedging, financing and brokerage activities. The Sales Agents and their affiliates have in the past performed commercial banking, investment banking and advisory services for us from time to time for which they have received no more than customary fees and reimbursement of expenses and may, from time to time, engage in transactions with and perform services for us in the ordinary course of their business for which they may receive customary fees and reimbursement of expenses. In the ordinary course of its various business activities, the Sales Agents and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (which may include bank loans and/or credit default swaps) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The Sales Agents and their respective affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments. To the extent required by Regulation M, the Sales Agents will not engage in any market making activities involving our common stock while the offering is ongoing under this prospectus.

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LEGAL MATTERS

The validity of the common stock being offered in this offering will be passed upon for us by Proskauer Rose LLP, New York, New York. Goodwin Procter LLP, New York, New York, is counsel to the Sales Agents in connection with this offering.

EXPERTS

The consolidated financial statements of Eloxx Pharmaceuticals Inc. at December 31, 2017 and 2016, and for the three years in the period ended December 31, 2017, incorporated in this prospectus supplement by reference from the Company's Annual Report on Form 10-K have been audited by Kost Forer Gabbay & Kasierer, a member of Ernst & Young Global, independent registered public accounting firm, as stated in their report which is incorporated by reference herein. 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.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement and the accompanying prospectus form part of a registration statement on Form S-3 that we filed with the SEC. This prospectus supplement and the accompanying prospectus do not contain all of the information set forth in the registration statement and the exhibits to the registration statement or the documents incorporated by reference herein and therein. For further information with respect to us and the securities that we are offering under this prospectus supplement, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement and the documents incorporated by reference herein and therein. You should rely only on the information contained in this prospectus supplement or the accompanying prospectus or incorporated by reference herein or therein. We have not authorized anyone else to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus supplement is accurate as of any date other than the date on the front page of this prospectus supplement, regardless of the time of delivery of this prospectus supplement or any sale of the securities offered hereby.

We maintain a website at www.eloxxpharma.com. Information contained in or accessible through our website does not constitute a part of this prospectus.

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INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus.

We incorporate by reference into this prospectus and the registration statement of which this prospectus forms a part the information or documents listed below that we have filed with the SEC:

- our Annual Report on Form 10-K for the year ended December 31, 2017, filed on March 16, 2018 and as amended on April 19, 2018;

- our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2018, June 30, 2018 and September 30, 2018, filed on May 10, 2018, August 10, 2018 and November 8, 2018, respectively;

- our Current Reports on Form 8-K filed on March 2, 2018, March 16, 2018, March 30, 2018, April 26, 2018, May 22, 2018, June 14, 2018, June 21, 2018, June 26, 2018 and August 3, 2018;

- our Current Reports on Form 8-K/A filed on March 8, 2018 and March 16, 2018;

- our Notifications on Form 12b-25/A, each filed on March 8, 2018; and

- 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.

We also incorporate by reference any filings we may make with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act (i) after the date of the filing of the registration statement of which this prospectus is a part and prior to effectiveness of such registration statement, and (ii) after the date of this prospectus but prior to the termination of the offering of the securities covered by this prospectus. We will not, however, incorporate by reference in this prospectus any documents or portions thereof that are not deemed "filed" with the SEC, including any information furnished pursuant to Item 2.02 or Item 7.01 of our current reports on Form 8-K unless, and except to the extent, specified in such current reports.

We will furnish without charge to each person, including any beneficial owner, to whom a prospectus is delivered, on written or oral request, a copy of any or all of the documents incorporated by reference in this prospectus, including exhibits to these documents. You should direct any requests for documents to Gregory Weaver, Chief Financial Officer, Eloxx Pharmaceuticals, Inc., 950 Winter Street, Waltham, Massachusetts 02451; telephone: (781) 577-5300.

Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus will be deemed modified, superseded or replaced for purposes of this prospectus to the extent that a statement contained in this prospectus or in any other subsequently filed document that also is or is deemed to be incorporated by reference in this prospectus modifies, supersedes or replaces such statement. Any statement that is modified or superseded will not constitute a part of this prospectus, except as modified or superseded.

This prospectus is part of a registration statement we filed with the SEC. That registration statement and the exhibits filed along with the registration statement contain more information about us and the shares in this offering. Because information about documents referred to in this prospectus is not always complete, you should read the full documents which are filed as exhibits to the registration statement. You may read and copy the full registration statement and its

exhibits at the SEC's public reference rooms or its website.

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PROSPECTUS

$125,000,000
Common Stock
Preferred Stock
Debt Securities
Warrants

From time to time, we may offer and sell up to an aggregate amount of $125,000,000 of any combination of our common stock, preferred stock, debt securities or warrants described in this prospectus, either individually or in combination, in one or more offerings. We may also offer common stock or preferred stock upon the conversion of debt securities, common stock upon the conversion of preferred stock, or common stock, preferred stock or debt securities upon the exercise of warrants.

This prospectus provides a general description of the securities we may offer. Each time we offer securities we will provide the specific terms of the securities offered in a supplement to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before you invest in any of the securities being offered.

Our common stock is traded on the OTCQB Market under the symbol “ELOX.” On April 3, 2018, the closing sale price of our common stock on the OTCQB Market was $9.59 per share. The applicable prospectus supplement will contain information, where applicable, as to other listings, if any, on the OTCQB Market or any other securities exchange of the securities covered by the applicable prospectus supplement.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading “Risk Factors” on page 5 of this prospectus and any similar section contained in the applicable prospectus supplement and in any free writing prospectuses we have authorized for use in connection with a specific offering, and under similar headings in the other documents that are incorporated by reference into this prospectus.

This prospectus may not be used to consummate a sale of securities unless accompanied by a prospectus supplement.

The securities may be sold directly by us to investors, through agents designated from time to time or to or through underwriters or dealers, on a continuous or delayed basis. For additional information on the methods of sale, you should refer to the section titled “Plan of Distribution” in this prospectus. If any agents or underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents or underwriters and any applicable fees, commissions, discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

Neither the U.S. Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Prospectus dated April 20, 2018.

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