PROSPECTUS SUPPLEMENT

(To Prospectus dated August 30, 2021 and the Prospectus Supplement dated September 30, 2021)



ELOXX PHARMACEUTICALS, INC.

Up to \$12,996,794.66 of Common Stock

This Prospectus Supplement supplements the prospectus supplement, dated September 30, 2021 (the "ATM Prospectus Supplement"), relating to the offer and sale of shares of our common stock having an aggregate offering price of up to \$50,000,000 pursuant to the terms of a sales agreement, or the Sales Agreement, with SVB Securities LLC ("SVB Securities"). Through the date hereof, we have not sold any shares of our common stock through SVB Securities under the Sales Agreement. This Prospectus Supplement should be read in conjunction with the ATM Prospectus Supplement, and is qualified by reference thereto, except to the extent that the information herein amends or supersedes the information contained in the ATM Prospectus Supplement. This Prospectus Supplement is not complete without, and may only be delivered or utilized in connection with, the ATM Prospectus Supplement, and any future amendments or supplements thereto.

On March 30, 2022, the date we filed our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, we became subject to the offering limits in General Instruction I.B.6 of Form S-3. As of the date of this Prospectus Supplement, the aggregate market value of our common stock held by non-affiliates pursuant to General Instruction I.B.6 of Form S-3 is \$38,990,384, which was calculated based on 67,224,800 shares of our outstanding common stock held by non-affiliates and a price of \$0.58 per share, the closing price of our common stock on April 4, 2022, which is the highest closing sale price of our common stock on the Nasdaq Global Market within the prior 60 days. As of the date of this Prospectus Supplement, we have not sold any securities pursuant to General Instruction I.B.6 of Form S-3 during the 12 calendar months prior to, and including, the date of this Prospectus Supplement. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell securities in public primary offerings on Form S-3 with a value exceeding one-third of our public float (as defined by General Instruction I.B.6) in any 12 calendar month period so long as our public float remains below \$75.0 million.

We are filing this Prospectus Supplement to amend the ATM Prospectus Supplement to reflect the limitations on the maximum amount of shares that we are eligible to sell under General Instruction I.B.6. As a result of these limitations, we may currently only offer and sell shares of our common stock having an aggregate offering price of up to \$12,996,794.66 pursuant to the Sales Agreement. However, in the event that our public float increases or decreases, we may sell securities in public primary offerings on Form S-3 with a value up to one-third of our public float, in each case calculated pursuant to General Instruction I.B.6 and subject to the terms of the Sales Agreement. In the event that our public float increases above \$75.0 million, we will no longer be subject to the limits in General Instruction I.B.6 of Form S-3.

Sales of common stock under this Prospectus Supplement, if any, will be made by means of ordinary brokers' transactions through the facilities of the Nasdaq Global Market, any other national securities exchange or facility thereof, a trading facility of a national securities association or an alternate trading system, to or through a market maker or directly on or through an electronic communication network or any similar market venue, at market prices, in block transactions or as otherwise agreed between us and the sales agent. Our common stock trades on the Nasdaq Global Market under the symbol "ELOX." On May 5, 2022, the last reported sale price of our common stock on the Nasdaq Global Market was \$0.33 per share.

INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE "RISK FACTORS" ON PAGE S-8 OF THE ATM PROSPECTUS
SUPPLEMENT AND IN THE DOCUMENTS INCORPORATED BY REFERENCE IN THE REGISTRATION STATEMENT 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 supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.
SVB Securities
The date of this prospectus supplement is May 6, 2022.