Filed Pursuant to Rule 433 Issuer Free Writing Prospectus dated June 1, 2023 Relating to Preliminary Prospectus Supplement dated May 31, 2023 Registration Statement No. 333-258564



NEWS RELEASE

FOR IMMEDIATE RELEASE

LEXICON ANNOUNCES PRICING OF \$125 MILLION PUBLIC OFFERING AND CONCURRENT PRIVATE PLACEMENT

The Woodlands, Texas, June 1, 2023 – Lexicon Pharmaceuticals, Inc. (Nasdaq: LXRX) ("Lexicon") today announced the pricing of its previously announced underwritten public offering of 23,924,705 shares of its common stock, par value \$0.001. The shares of common stock being offered pursuant to the public offering are being offered at a public offering price of \$2.60 per share. All of the shares are being offered by Lexicon. The gross proceeds from the public offering are expected to be approximately \$62.2 million, before deducting underwriting discounts and commissions and other offering expenses. In addition, Lexicon has granted the underwriters a 30-day option to purchase up to an additional 3,588,705 shares of common stock at the public offering price, less underwriting discounts and commissions. The public offering is expected to close on or about June 5, 2023, subject to the satisfaction of customary closing conditions.

In addition to the shares being sold in the underwritten public offering, Lexicon has agreed to sell 24,152,218 shares of its common stock to raise gross proceeds of approximately \$62.8 million in a concurrent private placement (together with the underwritten public offering described above, the "offering") at \$2.60 per share to an affiliate (the "Private Placement Purchaser") of Invus, L.P., Lexicon's largest stockholder, pursuant to its preemptive right under Lexicon's Fifth Amended and Restated Certificate of Incorporation. The Private Placement Purchaser will have the option to purchase, on a pro rata basis, up to an additional 3,622,832 shares of common stock at the public offering price to the extent the underwriters exercise their option to purchase additional shares of common stock. The shares of common stock being offered pursuant to the concurrent private placement will not be registered under the Securities Act of 1933, as amended (the "Securities Act"). The concurrent private placement is also scheduled to close on or about June 5, 2023, subject to the closing of the public offering and the satisfaction of certain other customary closing conditions. The closing of the underwritten public offering is not conditioned on the closing of the concurrent private placement.

Lexicon currently intends to use a portion of the net proceeds that it will receive from the offering, together with its existing cash and cash equivalents and short-term investments, to (i) fund the commercial launch of INPEFA $^{\text{TM}}$ (sotagliflozin) and (ii) fund the continued research and development of its drug candidates and for working capital and other general corporate purposes.

Citigroup, Jefferies and Piper Sandler are acting as joint book-running managers for the public offering.

A shelf registration statement on Form S-3 relating to the public offering was filed with the U.S. Securities and Exchange Commission ("SEC") on August 6, 2021 and declared effective by the SEC on September 14, 2021 (File No. 333-258564). The shares of common stock proposed to be issued in the concurrent private placement have not been registered under the Securities Act, or the securities laws of any state or other jurisdiction in the United States, and may not be offered, pledged, sold, delivered or otherwise transferred, directly or indirectly, in the United States except pursuant to registration under the Securities Act or an applicable exemption from the registration requirements of the Securities Act and, in each case, in compliance with other applicable securities laws. A preliminary prospectus supplement and accompanying prospectus relating to the public offering have been filed with the SEC and are available on the SEC's website at www.sec.gov. A final prospectus supplement and accompanying prospectus may also be obtained from Citigroup, c/o Broadridge Financial Services, 1155 Long Island Avenue, Edgewood, NY 11717 (Tel: 800-831-9146); Jefferies LLC, Attention: Equity Syndicate Prospectus Department, 520 Madison Avenue, New York, NY 10022, by e-mail at prospectus_department@jefferies.com or by telephone at (877) 821-7388; or Piper Sandler & Co., Attention: Prospectus Department, 800 Nicollet Mall, J12S03, Minneapolis, Minnesota 55402, by telephone at (800) 747-3924, or by email at prospectus@psc.com.

This press release does not constitute an offer to sell, or the solicitation of an offer to buy, these securities, nor will there be any sale of these securities in any state or jurisdiction in which such offer, solicitation or sale is not permitted.

About Lexicon Pharmaceuticals

Lexicon is a biopharmaceutical company with a mission of pioneering medicines that safely and effectively treat disease. Lexicon advanced two of these medicines to market and has additional drug candidates in discovery and clinical and preclinical development in heart failure, neuropathic pain, diabetes and metabolism and other indications.

Safe Harbor Statement

This press release contains "forward-looking statements" within the meaning of Section 27A of the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended. All forward-looking statements, including, without limitation, statements about the completion and timing of the public offering and concurrent private placement and the use of proceeds from the offering are based on management's current assumptions and expectations and involve risks, uncertainties and other important factors, specifically including Lexicon's ability to meet its capital requirements, successfully commercialize INPEFA in heart failure on the timeline and/or at the prices currently contemplated or at all, conduct preclinical and clinical development and obtain necessary regulatory approvals of INPEFA (in other indications), LX9211 and its other drug candidates on its anticipated timelines, achieve its operational objectives, obtain patent protection for its discoveries and establish strategic alliances, as well as additional factors relating to manufacturing, intellectual property rights, and the therapeutic or commercial value of its drug candidates. Any of these risks, uncertainties and other factors may cause Lexicon's actual results to be materially different from any future results expressed or implied by such forward-looking statements. Information identifying such important factors is contained under "Risk Factors" in Lexicon's annual report on Form 10-K for the year ended December 31, 2022, quarterly report on Form 10-Q for the quarter ended March 31, 2023 and other subsequent disclosure documents filed with the SEC. Lexicon undertakes no obligation to update or revise any such forward-looking statements, whether as a result of new information, future events or otherwise.

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Registration Statement

Lexicon has filed a registration statement (including a prospectus) with the SEC for the equity offering to which this communication relates. Before you invest, you should read the preliminary prospectus supplement and the accompanying prospectus in that registration statement and other documents Lexicon has filed with the SEC for more complete information about Lexicon and the equity offering. You may get these documents for free by visiting EDGAR on the SEC's website at www.sec.gov. Copies of the preliminary prospectus supplement and accompanying prospectus may also be obtained from Citigroup, c/o Broadridge Financial Services, 1155 Long Island Avenue, Edgewood, NY 11717 (Tel: 800-831-9146); Jefferies LLC, Attention: Equity Syndicate Prospectus Department, 520 Madison Avenue, New York, NY 10022, by e-mail at prospectus_department@jefferies.com or by telephone at (877) 821-7388; or Piper Sandler & Co., Attention: Prospectus Department, 800 Nicollet Mall, J12S03, Minneapolis, Minnesota 55402, by telephone at (800) 747-3924, or by email at prospectus@psc.com