
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549

**FORM S-3
REGISTRATION STATEMENT**
*UNDER
THE SECURITIES ACT OF 1933*

Xilio Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

85-1623397
(I.R.S. Employer
Identification Number)

828 Winter Street, Suite 300
Waltham, Massachusetts 02451
(857) 524-2466

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

René Russo
President and Chief Executive Officer
Xilio Therapeutics, Inc.
828 Winter Street, Suite 300
Waltham, Massachusetts 02451
(857) 524-2466

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copy to:

Christopher Frankenfield
Chief Operating Officer
Xilio Therapeutics, Inc.
828 Winter Street, Suite 300
Waltham, Massachusetts 02451
(857) 524-2466

Cynthia Mazareas, Esq.
Molly W. Fox, Esq.
Wilmer Cutler Pickering Hale and Dorr LLP
60 State Street
Boston, MA 02109
(617) 526-6000

Approximate date of commencement of proposed sale to the public: As soon as practicable after this registration statement is declared effective.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

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If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of “large accelerated filer,” “accelerated filer,” “smaller reporting company,” and “emerging growth company” in Rule 12b-2 of the Exchange Act.

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input checked="" type="checkbox"/>

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until this registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The information in this prospectus is not complete and may be changed. The selling stockholders named in this prospectus may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and the selling stockholders named in this prospectus are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated April 30, 2024

PROSPECTUS



17,580,566 SHARES

COMMON STOCK

This prospectus relates to the resale from time to time of up to 17,580,566 shares of common stock, par value \$0.0001 per share, or common stock, of Xilio Therapeutics, Inc. by the selling stockholders listed on page 7 hereof, including their donees, pledgees, transferees or other respective successors-in-interest, which shares consist of (i) 1,953,125 outstanding shares of our common stock held by the selling stockholders and (ii) 15,627,441 shares of our common stock issuable upon the exercise of outstanding pre-funded warrants to purchase shares of our common stock, at an exercise price of \$0.0001 per share, held by one of the selling stockholders. We will not receive any proceeds from the sale of the shares offered by this prospectus.

We have agreed, pursuant to a registration rights agreement that we entered into with the selling stockholders, to bear all of the expenses incurred in connection with the registration of these shares. The selling stockholders will pay or assume discounts, commissions, fees of underwriters, selling brokers or dealer managers and similar expenses, if any, incurred for the sale of these shares of our common stock.

The selling stockholders identified in this prospectus, or their respective donees, pledgees, transferees or other respective successors-in-interest, may offer the shares from time to time on terms to be determined at the time of sale through ordinary brokerage transactions or through any other means described in this prospectus under the caption "Plan of Distribution" on page 10 of this prospectus. The shares may be sold at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale or at privately negotiated prices. For a list of the selling stockholders, see the section entitled "Selling Stockholders" on page 7 of this prospectus.

We may amend or supplement this prospectus from time to time by filing amendments or supplements as required. You should read the entire prospectus and any amendments or supplements carefully before you make your investment decision.

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Our common stock is traded on the Nasdaq Global Select Market under the symbol “XLO.” On April 29, 2024, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$1.04 per share. You are urged to obtain current market quotations for our common stock.

Our business and investing in our common stock involve significant risk. These risks are described in the section titled “Risk Factors” beginning on page 3 of this prospectus.

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 _____, 2024.

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You should rely only on the information contained or incorporated by reference in this prospectus. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus may only be used where it is legal to offer and sell shares of our common stock. If it is against the law in any jurisdiction to make an offer to sell these shares, or to solicit an offer from someone to buy these shares, then this prospectus does not apply to any person in that jurisdiction, and no offer or solicitation is made by this prospectus to any such person. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus, regardless of the time of delivery of this prospectus or of any sale of common stock. Our business, financial condition, results of operations and prospects may have changed since such date.

Unless the context otherwise indicates, references in this prospectus to the “our company,” “we,” “our” and “us” refer collectively to Xilio Therapeutics, Inc., a Delaware corporation, and its consolidated subsidiaries.

We own various U.S. federal trademark applications and unregistered trademarks, including our company name. All other trademarks or trade names referred to in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus are referred to without the symbols ® and ™, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

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PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus and in the other information we incorporate by reference in this prospectus. This summary does not contain all of the information you should consider before making an investment decision. You should read this entire prospectus carefully, especially the risks associated with investing in our common stock discussed under the “Risk Factors” section beginning on page 3 of this prospectus, along with our consolidated financial statements and notes to those consolidated financial statements and the other information incorporated by reference in this prospectus.

Our Business

We are a clinical-stage biotechnology company discovering and developing tumor-activated immuno-oncology, or I-O, therapies with the goal of significantly improving outcomes for people living with cancer without the systemic side effects of current I-O treatments. We are leveraging our proprietary platform to build a pipeline of novel, tumor-activated I-O molecules that are designed to optimize the therapeutic index by localizing anti-tumor activity within the tumor microenvironment, including tumor-activated cytokines and antibodies (including bispecifics) and immune cell engagers (including tumor-activated cell engagers and tumor-activated effector-enhanced cell engagers).

Corporate Information

Our principal executive offices are located at 828 Winter Street, Suite 300, Waltham, Massachusetts 02451, and our telephone number is (857) 524-2466. Our website address is www.xiliotx.com. The information contained on, or accessible through, our website is not incorporated by reference into this prospectus and should not be considered to be a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

Private Placement

On March 28, 2024, we entered into a securities purchase agreement with the selling stockholders, pursuant to which we agreed to sell and issue to the selling stockholders in a private placement an aggregate of 1,953,125 shares of our common stock at a purchase price of \$0.64 per share, and to one of the selling stockholders in lieu of shares of our common stock, pre-funded warrants to purchase up to an aggregate of 15,627,441 shares of our common stock, at a purchase price of \$0.6399 per pre-funded warrant. Each pre-funded warrant is exercisable at an exercise price of \$0.0001 per share, is exercisable immediately and is exercisable until the pre-funded warrant is exercised in full. The closing of the sale and issuance of these securities occurred on April 2, 2024.

We received gross proceeds of approximately \$11.3 million from the sale of these securities, before deducting placement agent fees and offering expenses payable by us.

For a detailed description of the transactions contemplated by the securities purchase agreement with the selling stockholders and the securities issued pursuant thereto, see the section entitled “Selling Stockholders” beginning on page 7 of this prospectus. We filed the registration statement on Form S-3, of which this prospectus forms a part, to fulfill our contractual obligations under the registration rights agreement entered into concurrently with the securities purchase agreement with the selling stockholders to provide for the resale by the selling stockholders of the shares of common stock acquired pursuant to the securities purchase agreement and the shares of common stock issuable upon exercise of the pre-funded warrants acquired pursuant to the securities purchase agreement.

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THE OFFERING

Common Stock Offered by Selling Stockholders	17,580,566 shares, consisting of (i) 1,953,125 outstanding shares of our common stock held by the selling stockholders and (ii) 15,627,441 shares of our common stock issuable upon the exercise of outstanding pre-funded warrants to purchase shares of our common stock.
Use of Proceeds	We will not receive any proceeds from the sale of shares in this offering.
Risk Factors	See “Risk Factors” beginning on page 3 of this prospectus and the other information included in, or incorporated by reference into, this prospectus for a discussion of factors you should carefully consider before deciding to invest in shares of our common stock.
Nasdaq Global Select Market Symbol	“XLO”

RISK FACTORS

Investing 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 and uncertainties described under the section captioned “Risk Factors” contained in our most recent Annual Report on Form 10-K, our most recent Quarterly Report on Form 10-Q and our other filings we make with the Securities and Exchange Commission, or the SEC, from time to time, which are incorporated by reference herein in their entirety, together with other information in this prospectus and in the documents incorporated by reference in this prospectus.

The risks described in our most recent Annual Report on Form 10-K, our most recent Quarterly Report on Form 10-Q and the other filings we make with the SEC incorporated by reference herein are not the only ones facing our company. Additional risks and uncertainties may also impair our business operations. If any of the risks described in our most recent Annual Report on Form 10-K, our most recent Quarterly Report on Form 10-Q and the other filings incorporated by reference herein occurs, our business, financial condition, results of operations and future growth prospects could be harmed. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the information incorporated by reference in this prospectus contain certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act.

All statements, other than statements of historical fact, contained in or incorporated by reference in this prospectus are forward-looking statements. In some cases, you can identify forward-looking statements by words such as “aim,” “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “might,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would” or the negative words or other comparable terminology, although not all forward-looking statements contain these identifying words.

The forward-looking statements in the prospectus and the information incorporated by reference in this prospectus include, but are not limited to, statements about:

- our ability to secure sufficient additional capital in the near term or implement other strategies needed to alleviate our current doubt about our ability to continue as a going concern;
- our estimates regarding expenses, future revenue and capital requirements and our expectations regarding our ability to fund our operating expenses and capital expenditure requirements with our cash and cash equivalents;
- the initiation, timing, progress and results of our research and development programs, including preclinical studies and clinical trials;
- the potential advantages and benefits of our current and future product candidates, including our beliefs regarding the potential benefits of our current and future product candidates in combination with other agents;
- our strategic plans to develop and, if approved, subsequently commercialize any product candidates we may develop;
- the timing of and our ability to submit applications for, and obtain and, if approved, maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance of our product candidates, if approved;
- our estimates regarding the addressable patient population and potential market opportunity for our current and future product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates;
- our ability to identify additional products, product candidates or technologies with significant commercial potential that are consistent with our commercial objectives;
- the impact of government laws and regulations;
- our competitive position and expectations regarding developments and projections relating to our current or future competitors and any competing therapies that are or become available;
- developments relating to our competitors and our industry;

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- our ability to establish and maintain collaborations and strategic partnerships and realize the expected benefits of such arrangements, including our partnership with Gilead Sciences, Inc., or Gilead, and clinical collaboration with F. Hoffmann-La Roche Ltd;
- our expectations regarding milestones, equity investments and other contingent payments under our partnership with Gilead;
- our estimates regarding anticipated future cost savings associated with our strategic portfolio reprioritization and workforce reduction announced in March 2024;
- our expectations regarding the time during which we will be an emerging growth company under the Jumpstart Our Business Startups Act of 2012; and
- the impact of general economic conditions, including inflation.

Any forward-looking statements in this prospectus reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. You are cautioned that these forward-looking statements are only predictions and are subject to risks, uncertainties, and assumptions that are referenced in the section of any accompanying prospectus supplement entitled “Risk Factors.”

You should also carefully review the risk factors and cautionary statements described in the other documents we file from time to time with the SEC, specifically our most recent Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K, which could cause actual results or events to differ materially from the forward-looking statements that we make. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures, collaborations, partnerships or investments we may make or enter into.

You should read this prospectus and the documents incorporated by reference in this prospectus completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this prospectus are made as of the date of this prospectus, 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 applicable law.

Unless otherwise expressly stated, we obtained this industry, business, market and other data from our own internal estimates and research as well as from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. All of the market data used in this prospectus and the information incorporated herein involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

USE OF PROCEEDS

We are filing the registration statement of which this prospectus forms a part to permit holders of the shares of our common stock described in the section entitled “Selling Stockholders” to resell such shares. We are not selling any securities under this prospectus and we will not receive any proceeds from the sale or other disposition of the shares of our common stock held by the selling stockholders and offered hereby.

The selling stockholders will pay any discounts, commissions, fees of underwriters, selling brokers or dealer managers and expenses incurred by the selling stockholders for brokerage, accounting, tax or legal services or any other expenses incurred by the selling stockholders in selling or disposing of the shares. We will bear all other costs, fees and expenses incurred in effecting the registration of the shares covered by this prospectus, including, without limitation, all registration and filing fees, printing fees, Nasdaq listing fees and fees and expenses of our counsel and our accountants.

SELLING STOCKHOLDERS

On March 28, 2024, we entered into a securities purchase agreement, or the Purchase Agreement, with the selling stockholders, pursuant to which we issued and sold an aggregate of (i) 1,953,125 shares of our common stock at a price of \$0.64 per share and (ii) to one of the investors, in lieu of shares of our common stock, pre-funded warrants to purchase 15,627,441 shares of our common stock for a price of \$0.6399 per pre-funded warrant, in a private placement to certain institutional accredited investors, which we refer to as the Private Placement. The closing of the issuance and sale of these securities occurred on April 2, 2024. Each pre-funded warrant has an exercise price of \$0.0001 per share, is exercisable immediately and is exercisable until the pre-funded warrant is exercised in full. The shares issuable upon exercise of the pre-funded warrants will become eligible for sale by the selling stockholder who holds pre-funded warrants under this prospectus only when the pre-funded warrants are exercised. We cannot predict when or whether the selling stockholder who holds pre-funded warrants will exercise its pre-funded warrants.

Under the terms of the pre-funded warrants, we may not effect the exercise of any such warrant, and a holder will not be entitled to exercise any portion of any such warrant, if, upon giving effect to such exercise, the aggregate number of shares of our common stock beneficially owned by the holder, together with such holder's affiliates and any other persons whose beneficial ownership of common stock would or could be aggregated with such holder's for purposes of Section 13(d) or Section 16 of the Exchange Act, would beneficially own more than 9.99% of the number of shares of common stock outstanding immediately after giving effect to such exercise. The selling stockholder who holds pre-funded warrants may increase or decrease such percentage, not to exceed 19.99%, by providing at least 61 days' prior notice to us. We refer to such percentage limitation as the Beneficial Ownership Limitation.

In connection with the Private Placement, we entered into a registration rights agreement with the selling stockholders, dated as of March 28, 2024, or the Registration Rights Agreement, pursuant to which we agreed to file a registration statement with the SEC covering the resale of the shares of common stock sold in the Private Placement and the shares of common stock issuable upon exercise of the pre-funded warrants sold in the Private Placement. We agreed to file such registration statement no later than 30 days following the closing of the Private Placement. We have granted the selling stockholders customary indemnification rights in connection with the registration statement. The selling stockholders have also granted us customary indemnification rights in connection with the registration statement. The registration statement of which this prospectus is a part has been filed in accordance with the Registration Rights Agreement.

The foregoing summary descriptions of the Purchase Agreement, the pre-funded warrants and the Registration Rights Agreement do not purport to be complete and are qualified in their entirety by reference to the full text of such documents, which were filed as exhibits to our Current Report on Form 8-K filed on March 28, 2024, and are incorporated by reference herein.

This prospectus covers the sale or other disposition by the selling stockholders of up to the total number of shares of our common stock that were issued to the selling stockholders pursuant to the Purchase Agreement, plus the total number of shares of our common stock issuable upon exercise of the pre-funded warrants issued to the selling stockholder who holds pre-funded warrants, without giving effect to the Beneficial Ownership Limitation described above. The table below sets forth, to our knowledge, information concerning the beneficial ownership of shares of our common stock by the selling stockholders as of April 25, 2024. The information in the table below with respect to the selling stockholders has been obtained from the selling stockholders. When we refer to the "selling stockholders" in this prospectus, we mean the selling stockholders listed in the table below as offering shares, as well as their respective donees, pledgees, transferees or other respective successors-in-interest. Throughout this prospectus, when we refer to the shares of our common stock being registered on behalf of the selling stockholders, we are referring to the shares of our common stock and the shares underlying the pre-funded warrants issued to the selling stockholder who holds pre-funded warrants pursuant to the Purchase Agreement without giving effect to the Beneficial Ownership Limitation described above. The selling stockholders may sell all, some or none of the shares of common stock subject to this prospectus. See "Plan of Distribution."

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The number of shares of common stock beneficially owned prior to the offering for each selling stockholder includes all shares of our common stock beneficially held by such selling stockholder as of April 25, 2024, which includes (i) all shares of common stock purchased by such selling stockholder in the Private Placement and (ii) all shares of common stock issuable upon exercise of the pre-funded warrants purchased by such selling stockholder in the Private Placement, subject to the Beneficial Ownership Limitation. The percentages of shares owned before and after the offering are based on 36,912,217 shares of common stock outstanding as of April 25, 2024, which includes the outstanding shares of common stock offered by this prospectus but does not include any shares of common stock offered by this prospectus that are issuable pursuant to pre-funded warrants and are deemed outstanding in the table below because they are beneficially owned by a person. Beneficial ownership is determined in accordance with the rules of the SEC and includes voting or investment power with respect to shares. Generally, a person “beneficially owns” shares of our common stock if the person has or shares with others the right to vote those shares or to dispose of them, or if the person has the right to acquire voting or disposition rights of shares of our common stock within 60 days. In computing the number of shares of our common stock beneficially owned by a person and the percentage ownership of that person, we deemed outstanding the shares of common stock issuable upon the exercise of pre-funded warrants held by the selling stockholder described above up to the Beneficial Ownership Limitation because such shares are exercisable within 60 days of April 25, 2024. We did not deem these shares outstanding, however, for the purpose of computing the percentage ownership of any other person.

Unless otherwise indicated below, to our knowledge, each selling stockholder named in the table has sole voting and investment power with respect to the shares of common stock beneficially owned by it, except to the extent authority is shared by spouses under applicable law. The inclusion of any shares in this table does not constitute an admission of beneficial ownership for any selling stockholder named below.

Name of Selling Stockholder	Shares of Common Stock Beneficially Owned Prior to the Offering		Number of Shares of Common Stock Being Offered (1)	Shares of Common Stock to be Beneficially Owned After the Offering (2)	
	Number	Percentage		Number	Percentage
BCLS II Equity Opportunities, LP (3)	3,687,530	9.99%	15,627,441	—	—
Entities affiliated with Rock Springs Capital Management (4)	3,003,259	8.14%	1,562,500	1,440,759	3.90%
Irving Investors, LLC (5)	390,625	1.06%	390,625	—	—

- (1) The number of shares of our common stock in the column “Number of Shares of Common Stock Being Offered” represents all of the shares of our common stock that a selling stockholder may offer and sell from time to time under this prospectus, including shares issuable upon the exercise of pre-funded warrants issued in the Private Placement, without giving effect to the Beneficial Ownership Limitation.
- (2) We do not know when or in what amounts a selling stockholder may offer shares for sale. The selling stockholders might not sell any or might sell all of the shares offered by this prospectus. Because the selling stockholders may offer all or some of the shares pursuant to this offering, and because there are currently no agreements, arrangements or understandings with respect to the sale of any of the shares, we cannot estimate the number of the shares that will be held by the selling stockholders after completion of the offering. However, for purposes of this table, we have assumed that, after completion of the offering, none of the shares covered by this prospectus will be held by the selling stockholders, including common stock issuable upon exercise of the pre-funded warrants sold in the Private Placement.

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- (3) The shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” consists of shares of common stock issuable upon exercise of pre-funded warrants held by BCLS II Equity Opportunities, LP (“BCLS II Equity”), after giving effect to the provision in such pre-funded warrants that prevents exercise of such pre-funded warrants if, as a result of such exercise, entities affiliated with BCLS II Equity would beneficially own more than 9.99% of the number of shares of our common stock outstanding immediately after giving effect to such exercise. The shares reported under “Shares of Common Stock Beneficially Owned Prior to Offering” do not include (i) 1,348,682 shares of common stock held directly by Bain Capital Life Sciences Fund II, L.P. (“BCLS Fund II”), (ii) 1,292,469 shares of common stock held directly by BCLS II Investco, LP (“BCLS II Investco”) and (iii) 164,262 shares of common stock held directly by BCIP Life Sciences Associates, L.P (“BCIPLS” and, together with BCLS II Equity, BCLS Fund II and BCLS II Investco, the “Bain Capital Life Sciences Entities”). Bain Capital Life Sciences Investors, LLC (“BCLSI”) is the ultimate general partner of each of BCLS II Equity, BCLS Fund II and BCLS II Investco and governs the investment strategy and decision-making process with respect to investments held by BCIPLS. As a result, BCLSI may be deemed to share voting and dispositive power with respect to the shares held by the Bain Capital Life Sciences Entities. The address of BCLS II Equity is c/o Bain Capital Life Sciences, LP, 200 Clarendon Street, Boston, MA 02116.
- (4) The shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” consist of 2,600,625 and 402,634 shares of common stock held by Rock Springs Capital Master Fund LP (“Rock Springs Fund”) and Four Pines Master Fund LP (“Four Pines Fund”), respectively. Rock Springs Capital Management LP (“RSCM”) is the investment adviser of Rock Springs Fund and Four Pines Fund. The general partner of RSCM is Rock Springs Capital LLC (“RSC”). RSC and RSCM may therefore be deemed to have or share beneficial ownership of the shares held directly by Rock Springs Fund and Four Pines Fund. The address for RSC and RSCM is 650 South Exeter St., Suite 1070, Baltimore, Maryland 21202.
- (5) The shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” consist of 390,625 shares of common stock held by Irving Investors, LLC. The address of Irving Investors, LLC is 205 Detroit Street, 4th Floor, Denver, Colorado 80206.

PLAN OF DISTRIBUTION

The selling stockholders, which as used herein includes donees, pledgees, transferees or other successors-in-interest selling shares of common stock or interests in shares of common stock received after the date of this prospectus from a selling stockholder as a gift, pledge, partnership distribution or other transfer, may, from time to time, sell, transfer or otherwise dispose of any or all of their shares of common stock or interests in shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices.

The selling stockholders may use any one or more of the following methods when disposing of shares or interests therein:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted by applicable law.

The selling stockholders may, from time to time, pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act, amending the list of selling stockholders to include the pledgee, transferee or other successors-in-interest as selling stockholders under this prospectus. The selling stockholders also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees, donees or other successors-in-interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of our common stock or interests therein, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the common stock in the course of hedging the positions they assume. The selling stockholders may also sell shares of our common stock short and deliver these securities to close out their short positions, or loan or pledge the common stock to broker-dealers that in turn may sell these securities. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the

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delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The aggregate proceeds to the selling stockholders from the sale of the common stock offered by them will be the purchase price of the common stock less discounts or commissions, if any. Each of the selling stockholders reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of common stock to be made directly or through agents. We will not receive any of the proceeds from this offering. Upon any exercise of the pre-funded warrants by payment of cash, however, we will receive the exercise price of the pre-funded warrants.

The selling stockholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, provided that they meet the criteria and conform to the requirements of that rule.

The selling stockholders and any underwriters, broker-dealers or agents that participate in the sale of the common stock or interests therein may be “underwriters” within the meaning of Section 2(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the shares may be underwriting discounts and commissions under the Securities Act. Selling stockholders who are deemed “underwriters” within the meaning of Section 2(11) of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act.

To the extent required, the shares of our common stock to be sold, the names of the selling stockholders, the respective purchase prices and public offering prices, the names of any agents, dealers or underwriters, and any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the common stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the common stock may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the selling stockholders that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of shares in the market and to the activities of the selling stockholders and their affiliates. In addition, to the extent applicable, we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling stockholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

We have agreed to indemnify the selling stockholders against liabilities, including liabilities under the Securities Act and state securities laws, relating to the registration of the shares offered by this prospectus.

We have agreed with the selling stockholders to use commercially reasonable efforts to cause the registration statement of which this prospectus constitutes a part effective and to remain continuously effective until the earlier of (1) such time as all of the shares covered by this prospectus have been disposed of pursuant to and in accordance with such registration statement, (2) the date on which all of the shares may be sold without restriction pursuant to Rule 144(c) of the Securities Act or (3) five years after the closing of the Private Placement.

LEGAL MATTERS

The validity of the shares of our common stock offered hereby is being passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP.

EXPERTS

The consolidated financial statements of Xilio Therapeutics, Inc. appearing in Xilio Therapeutics, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2023 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon (which contains an explanatory paragraph describing conditions that raise substantial doubt about the Company's ability to continue as a going concern as described in Note 1 to the consolidated financial statements) included therein, and incorporated herein by reference. Such consolidated financial statements are, and audited consolidated financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the report of Ernst & Young LLP pertaining to such consolidated financial statements (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at www.sec.gov. Copies of certain information filed by us with the SEC are also available on our website at www.xiliotx.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.

This prospectus is part of a registration statement we filed with the SEC. This prospectus omits some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information about us and the securities we are offering. Statements in this prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings and the exhibits attached thereto. You should review the complete document to evaluate these statements.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus incorporates by reference the documents listed below (File No. 001-40925) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) between the date of the initial registration statement of which this prospectus forms a part and the effectiveness of the registration statement and following the effectiveness of the registration statement until the offering of the securities under the registration statement is terminated or completed:

- [Our Annual Report on Form 10-K for the year ended December 31, 2023, filed with the SEC on April 1, 2024;](#)
- The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2023 from [our definitive proxy statement for the 2024 Annual Meeting of Stockholders, as filed with the SEC on April 25, 2024;](#)
- Our Current Reports on Form 8-K filed with the SEC on [January 3, 2024](#), [January 19, 2024](#), [March 28, 2024](#), and [March 28, 2024](#); and
- The description of our common stock contained in our Registration Statement on [Form 8-A](#), as filed with the SEC on October 18, 2021, as the description therein has been updated and superseded by the description of our capital stock contained in [Exhibit 4.3](#) to our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, as filed with the SEC on March 1, 2022, and including any amendments or reports filed for the purpose of updating such description.

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You may request a copy of these filings, at no cost, by writing or calling us at the following address or telephone number:

Xilio Therapeutics, Inc.
828 Winter Street, Suite 300
Waltham, Massachusetts 02451
Attn: Investor Relations
Phone: (857) 524-2466
E-mail: investors@xiliotx.com



17,580,566 SHARES

COMMON STOCK

PROSPECTUS

, 2024

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

The following table sets forth the various expenses to be incurred in connection with the sale and distribution of the securities being registered hereby, all of which will be borne by Xilio Therapeutics, Inc. (except any underwriting discounts and commissions and expenses incurred by the selling stockholders for brokerage, accounting, tax or legal services or any other expenses incurred by the selling stockholders in disposing of the shares). All amounts shown are estimates except the SEC registration fee.

SEC registration fee	\$	2,637
Legal fees and expenses	\$	40,000
Accounting fees and expenses	\$	20,000
Miscellaneous fees and expenses	\$	8,339
Total expenses	\$	<u>70,976</u>

Item 15. Indemnification of Directors and Officers.

The following summary is qualified in its entirety by reference to the complete Delaware General Corporation Law, or DGCL, and our restated certificate of incorporation and second amended and restated bylaws.

Section 145 of the DGCL provides, generally, that a corporation shall have the power to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding (except actions by or in the right of the corporation) by reason of the fact that such person is or was a director, officer, employee or agent of the corporation against all expenses, judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with such action, suit or proceeding if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the corporation and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful. A corporation may similarly indemnify such person for expenses actually and reasonably incurred by such person in connection with the defense or settlement of any action or suit by or in the right of the corporation, provided that such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, and, in the case of claims, issues and matters as to which such person shall have been adjudged liable to the corporation, provided that a court shall have determined, upon application, that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which such court shall deem proper.

Section 102(b)(7) of the DGCL provides, generally, that our restated certificate of incorporation may contain a provision eliminating or limiting the personal liability of a director to the corporation or its shareholders for monetary damages for breach of fiduciary duty as a director, provided that such provision may not eliminate or limit the liability of a director (i) for any breach of the director's duty of loyalty to the corporation or its shareholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under section 174 of the DGCL, or (iv) for any transaction from which the director derived an improper personal benefit. No such provision may eliminate or limit the liability of a director for any act or omission occurring prior to the date when such provision became effective.

Our restated certificate of incorporation provides that we will indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of us), by reason of the fact that he or she is or was,

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or has agreed to become, our director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan) (all such persons being referred to as an Indemnitee), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974) and amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding and any appeal therefrom if such Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, and, with respect to any criminal action or proceeding, he or she had no reasonable cause to believe his or her conduct was unlawful.

Our restated certificate of incorporation also provides that we will indemnify any Indemnitee who was or is a party or threatened to be made a party to any threatened, pending or completed action or suit by or in the right of us to procure a judgment in our favor by reason of the fact that the Indemnitee is or was, or has agreed to become, our director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding, and any appeal therefrom, if the Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, except that no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to us, unless and only to the extent that the Court of Chancery of Delaware or the court in which such action or suit was brought determines that, despite such adjudication but in view of all of the circumstances, he or she is fairly and reasonably entitled to indemnification of such expenses (including attorney's fees). Notwithstanding the foregoing, to the extent that any Indemnitee has been successful, on the merits or otherwise, he or she will be indemnified by us against all expenses (including attorneys' fees) actually and reasonably incurred by him or her or on his or her behalf in connection therewith. If we do not assume the defense, expenses must be advanced to an Indemnitee under certain circumstances.

In addition, we have entered into indemnification agreements with all of our directors and executive officers. In general, these agreements provide that we will indemnify the directors or executive officers to the fullest extent permitted by law for claims arising in his or her capacity as a director or executive officer of our company or in connection with his or her service at our request for another corporation or entity. The indemnification agreements also provide for procedures that will apply in the event that a director or executive officer makes a claim for indemnification and establish certain presumptions that are favorable to the executive officer or director.

We maintain a general liability insurance policy that covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers.

Item 16. Exhibits

Exhibit Number	Description
4.1	Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed with the SEC on October 26, 2021)
4.2	Second Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed with the SEC on April 3, 2023)
4.3	Securities Purchase Agreement, dated March 28, 2024, by and among the Registrant and the persons party thereto (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed with the SEC on March 28, 2024)

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4.4	Form of Pre-Funded Warrant to Purchase Common Stock (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K filed with the SEC on March 28, 2024)
4.5	Registration Rights Agreement, dated March 28, 2024, by and among the Registrant and the persons party thereto (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed with the SEC on March 28, 2024)
4.6	Specimen Stock Certificate evidencing the shares of common stock (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1 filed with SEC on October 1, 2021)
5.1*	Opinion of Wilmer Cutler Pickering Hale and Dorr LLP
23.1*	Consent of Ernst & Young LLP, independent registered public accounting for the Registrant
23.2*	Consent of Wilmer Cutler Pickering Hale and Dorr LLP (included in Exhibit 5.1 filed herewith)
24.1*	Power of Attorney (included on the signature page of this registration statement)
107*	Filing Fee Table

* Filed herewith

Item 17. Undertakings.

The undersigned registrant hereby undertakes:

(a)(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933, as amended, or the Securities Act;

(ii) To reflect in the prospectus any facts or events arising after the effective date of this registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in this registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Securities and Exchange Commission, or the Commission, pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in this registration statement or any material change to such information in this registration statement;

provided, however, that paragraphs (1)(i), (1)(ii) and (1)(iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, that are incorporated by reference in this registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of this registration statement.

(2) That, for the purposes of determining any liability under the Securities Act, each post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at the time shall be deemed to be the initial *bona fide* offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act to any purchaser:

(i) each prospectus filed by the Registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(ii) each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof; provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the registrant's annual report pursuant to Section 13(a) or 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in this registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(c) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the indemnification provisions described herein, or otherwise, the registrant has been advised that in the opinion of the Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Waltham, Commonwealth of Massachusetts, on April 30, 2024.

XILIO THERAPEUTICS, INC.

By: /s/ René Russo

Name: René Russo

Title: President and Chief Executive Officer

SIGNATURES AND POWER OF ATTORNEY

We, the undersigned officers and directors of Xilio Therapeutics, Inc. hereby severally constitute and appoint René Russo and Christopher Frankenfield, and each of them singly, our true and lawful attorneys-in-fact with full power to any of them, and to each of them singly, to sign for us and in our names in the capacities indicated below the Registration Statement on Form S-3 filed herewith and any and all amendments (including post-effective amendments) to said Registration Statement, and any registration statement filed pursuant to Rule 462 under the Securities Act of 1933, as amended, in connection with said Registration Statement, and to file or cause to be filed the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, and generally to do all such things in our name and on our behalf in our capacities as officers and directors to enable Xilio Therapeutics, Inc. to comply with the provisions of the Securities Act of 1933, as amended, and all requirements of the Securities and Exchange Commission, hereby ratifying and confirming all that said attorneys, and each of them, or their substitute or substitutes, shall do or cause to be done by virtue hereof.

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Pursuant to the requirements of the Securities Act of 1933, as amended, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
<u>/s/ René Russo</u> René Russo	President and Chief Executive Officer, Director (<i>Principal Executive Officer</i>)	April 30, 2024
<u>/s/ Kevin Brennan</u> Kevin Brennan	Senior Vice President, Finance and Accounting (<i>Principal Financial and Accounting Officer</i>)	April 30, 2024
<u>/s/ Paul J. Clancy</u> Paul J. Clancy	Chairman of the Board of Directors	April 30, 2024
<u>/s/ Sara M. Bonstein</u> Sara M. Bonstein	Director	April 30, 2024
<u>/s/ Daniel Curran</u> Daniel Curran	Director	April 30, 2024
<u>/s/ Tomas J. Heyman</u> Tomas J. Heyman	Director	April 30, 2024
<u>/s/ Robert Ross</u> Robert Ross	Director	April 30, 2024
<u>/s/ Christina Rossi</u> Christina Rossi	Director	April 30, 2024
<u>/s/ Yuan Xu</u> Yuan Xu	Director	April 30, 2024

April 30, 2024

Xilio Therapeutics, Inc.
828 Winter Street, Suite 300
Waltham, Massachusetts 02451

Re: Registration Statement on Form S-3

Ladies and Gentlemen:

This opinion is furnished to you in connection with a Registration Statement on Form S-3 (the "Registration Statement") filed with the Securities and Exchange Commission (the "Commission") under the Securities Act of 1933, as amended (the "Securities Act"), for the registration of the resale of an aggregate of 17,580,566 shares (the "Shares") of common stock, \$0.0001 par value per share (the "Common Stock"), of Xilio Therapeutics, Inc., a Delaware corporation (the "Company"). All of the Shares are being registered for resale on behalf of certain stockholders of the Company (each, a "Selling Stockholder" and together, the "Selling Stockholders"). The Shares consist of (i) 1,953,125 outstanding shares of Common Stock (the "Outstanding Shares") that are held by certain of the Selling Stockholders and (ii) 15,627,441 shares of Common Stock (the "Pre-Funded Warrant Shares") issuable upon the exercise of outstanding pre-funded warrants to purchase shares of Common Stock (the "Pre-Funded Warrants") that are held by one of the Selling Stockholders.

We are acting as counsel for the Company in connection with the registration for resale of the Shares. We have examined signed copies of the Registration Statement as filed with the Commission. We have also examined and relied upon minutes of meetings of the Board of Directors of the Company as provided to us by the Company, stock record books of the Company as provided to us by the Company, the Pre-Funded Warrants, the Restated Certificate of Incorporation and Second Amended and Restated Bylaws of the Company, each as restated and/or amended to date, and such other documents as we have deemed necessary for purposes of rendering the opinions hereinafter set forth.

In our examination of the foregoing documents, we have assumed the genuineness of all signatures, the authenticity of all documents submitted to us as originals, the conformity to original documents of all documents submitted to us as copies, the authenticity of the originals of such latter documents and the legal competence of all signatories to such documents.

Our opinion below, insofar as it relates to the Outstanding Shares being fully paid, is based solely on a certificate of the Senior Vice President, Finance and Accounting of the Company confirming the Company's receipt of the consideration called for by the applicable resolutions authorizing the issuance of such Outstanding Shares.

We assume that appropriate action will be taken, prior to the offer and sale of the Shares by the Selling Stockholders, to register and qualify the Shares for sale under all applicable state securities or "blue sky" laws, to the extent required.

We express no opinion herein as to the laws of any state or jurisdiction other than the General Corporation Law of the State of Delaware.

Based upon and subject to the foregoing, we are of the opinion that (i) the Outstanding Shares have been duly authorized for issuance and are validly issued, fully paid and nonassessable, and (ii) the Pre-Funded Warrant Shares have been duly authorized for issuance and, when issued, delivered and paid for in accordance with the terms of the

Wilmer Cutler Pickering Hale and Dorr LLP, 60 State Street, Boston, Massachusetts 02109

Beijing Berlin Boston Brussels Denver Frankfurt London Los Angeles New York Palo Alto San Francisco Washington

April 30, 2024
Page 2

Pre-Funded Warrants, including the payment of the exercise price therefor, will be validly issued, fully paid and nonassessable.

It is understood that this opinion is to be used only in connection with the offer and sale of the Shares while the Registration Statement is in effect.

Please note that we are opining only as to the matters expressly set forth herein, and no opinion should be inferred as to any other matters. This opinion is based upon currently existing statutes, rules, regulations and judicial decisions, and we disclaim any obligation to advise you of any change in any of these sources of law or subsequent legal or factual developments which might affect any matters or opinions set forth herein.

We hereby consent to the filing of this opinion with the Commission as an exhibit to the Registration Statement in accordance with the requirements of Item 601(b)(5) of Regulation S-K under the Securities Act and to the use of our name therein and in the related Prospectus under the caption "Legal Matters." In giving such consent, we do not hereby admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission.

Very truly yours,

/s/ Wilmer Cutler Pickering Hale and Dorr LLP

WILMER CUTLER PICKERING
HALE AND DORR LLP

Wilmer Cutler Pickering Hale and Dorr LLP, 60 State Street, Boston, Massachusetts 02109

Beijing Berlin Boston Brussels Denver Frankfurt London Los Angeles New York Palo Alto San Francisco Washington

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption "Experts" in the Registration Statement (Form S-3) and related Prospectus of Xilio Therapeutics, Inc. for the registration of 17,580,566 shares of its common stock and to the incorporation by reference therein of our report dated April 1, 2024, with respect to the consolidated financial statements of Xilio Therapeutics, Inc. included in its Annual Report (Form 10-K) for the year ended December 31, 2023, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP
Boston, Massachusetts
April 30, 2024

Calculation of Filing Fee Tables

Form S-3
(Form Type)

Xilio Therapeutics, Inc.

(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered and Carry Forward Securities

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee	Carry Forward Form Type	Carry Forward File Number	Carry Forward Initial Effective Date	Filing Fee Previously Paid In Connection with Unsold Securities to be Carried Forward
Newly Registered Securities												
Fees to Be Paid	Equity	Common Stock, \$0.0001 par value per share	Other	17,580,566 (1)	\$1.016 (2)	\$17,861,855.06 (2)	0.00014760	\$2,636.41				
Fees Previously Paid	—	—	—	—	—	—	—	—				
Carry Forward Securities												
Carry Forward Securities	—	—	—	—	—	—	—	—	—	—	—	—
	Total Offering Amounts					\$17,861,855.06 (2)	—	\$2,636.41				
	Total Fees Previously Paid							—				
	Total Fee Offsets							—				
	Net Fee Due							\$2,636.41				

- (1) The shares of common stock will be offered for resale by the selling stockholders pursuant to the prospectus contained in the registration statement to which this exhibit is attached. The registration statement registers the resale of an aggregate of 17,580,566 shares of the Registrant's common stock, which consists of (i) 1,953,125 outstanding shares of common stock and (ii) 15,627,441 shares of common stock issuable upon the exercise of outstanding pre-funded warrants. Pursuant to Rule 416 under the Securities Act of 1933, as amended (the "Securities Act"), the shares of common stock being registered hereunder include such indeterminate number of shares of common stock as may be issuable upon stock splits, stock dividends, or other distribution, recapitalization or similar events.
- (2) This estimate is made pursuant to Rule 457(c) of the Securities Act solely for purposes of calculating the registration fee. The price per share and aggregate offering price are based upon the average of the high and low prices of the Registrant's common stock on April 25, 2024, as reported on the Nasdaq Global Select Market.