As filed with the Securities and Exchange Commission on November 10, 2026

Registration No. 333-

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

FORM S-8
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

Xilio Therapeutics, Inc.
(Exact Name of Registrant as Specified in Its Charter)

Delaware	**85-1623397**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
828 Winter Street, Suite 300 Waltham, Massachusetts	**02451**
(Address of Principal Executive Offices)	**(Zip Code)**

Third Amended and Restated 2022 Inducement Stock Incentive Plan
(Full Title of the Plan)

René Russo
President and Chief Executive Officer
Xilio Therapeutics, Inc.
828 Winter Street, Suite 300
Waltham, Massachusetts 02451
(Name and Address of Agent for Service)

(857) 524-2466
(Telephone Number, Including Area Code, of Agent for Service)

Copy to:

Ben Harshbarger
Chief Legal Officer
Xilio Therapeutics, Inc.
828 Winter Street, Suite 300
Waltham, Massachusetts 02451
(857) 524-2466

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	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☒

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. ☐

Statement of Incorporation by Reference

This Registration Statement on Form S-8, relating to the Third Amended and Restated 2022 Inducement Stock Incentive Plan, as amended (the "2022 Inducement Plan") of Xilio Therapeutics, Inc. (the "Registrant") is being filed for the purpose of registering

250,000 additional securities of the same class as other securities for which a Registration Statement on Form S-8 has previously been filed and is effective. Accordingly, this Registration Statement incorporates by reference the contents of (i) the Registration Statement on Form S-8 (File No. 333-270240) filed with the Securities and Exchange Commission ("SEC") on March 2, 2023 by the Registrant relating to the 2022 Inducement Plan, (ii) the Registration Statement on Form S-8 (File No. 333-285701) filed with the SEC on March 11, 2025 by the Registrant relating to the 2022 Inducement Plan, (iii) the Registration Statement on Form S-8 (File No. 333-294515) filed with the SEC on March 23, 2026 by the Registrant relating to the 2022 Inducement Plan, and (iv) the Registration Statement on Form S-8 (File No. 333-298250) filed with the SEC on August 12, 2026 by the Registrant relating to the 2022 Inducement Plan, except, in each case, to the extent amended or superseded by the contents hereof and for "Item 8. Exhibits" with respect to which the exhibit index set forth below is incorporated herein by reference.

Item 8. Exhibits.

The following exhibits are incorporated herein by reference:

Number	Description
4.1	Restated Certificate of Incorporation of the Registrant, as amended (incorporated by reference to Exhibit 3.1 to the Registrant's Annual Report on Form 10-K (File No. 001-40925), filed with the Securities and Exchange Commission on March 23, 2026)
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 (File No. 001-40925), filed with the Securities and Exchange Commission on April 3, 2023)
5.1*	Opinion of Wilmer Cutler Pickering Hale and Dorr LLP, counsel to the Registrant
23.1*	Consent of Ernst & Young LLP, independent registered public accounting firm
23.2*	Consent of Wilmer Cutler Pickering Hale and Dorr LLP (included in Exhibit 5.1)
24.1*	Power of attorney (included on the signature pages of this registration statement)
99.1	Third Amended and Restated 2022 Inducement Stock Incentive Plan (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-40925), filed with the Securities and Exchange Commission on August 12, 2026)
99.2	Amendment No. 1 to the Third Amended and Restated 2022 Inducement Stock Incentive Plan (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-40925), filed with the Securities and Exchange Commission on November 10, 2026)
107*	Filing Fee Table

* Filed herewith

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-8 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 this 10th day of November, 2026.

XILIO THERAPEUTICS, INC.

By: /s/ René Russo
René Russo
President and Chief Executive Officer

POWER OF ATTORNEY AND SIGNATURES

We, the undersigned officers and directors of Xilio Therapeutics, Inc., hereby severally constitute and appoint René Russo and Ben Harshbarger, and each of them singly (with full power to each of them to act alone), our true and lawful attorneys with full power of substitution and resubstitution in each of them for such person and in such person's name, place and stead, and in any and all capacities, to sign for us and in our names in the capacities indicated below, the registration statement on Form S-8 filed herewith and any and all subsequent amendments to said registration statement, and generally to do all such things in our names 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 our signatures as they may be signed by our said attorneys, or any of them, to said registration statement and any and all amendments thereto.

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
/s/ René Russo René Russo	President and Chief Executive Officer, Director *(Principal Executive Officer)*	November 10, 2026
/s/ Christopher Frankenfield Christopher Frankenfield	Chief Financial Officer and Chief Operating Officer *(Principal Financial and Accounting Officer)*	November 10, 2026
/s/ Sara M. Bonstein Sara M. Bonstein	Chair of the Board	November 10, 2026
/s/ Akintunde Bello Akintunde Bello	Director	November 10, 2026
/s/ Cheryl R. Blanchard Cheryl R. Blanchard	Director	November 10, 2026
/s/ Aoife Brennan Aoife Brennan	Director	November 10, 2026
/s/ Daniel Curran Daniel Curran	Director	November 10, 2026
/s/ Robert Ross Robert Ross	Director	November 10, 2026
/s/ James Shannon James Shannon	Director	November 10, 2026
/s/ Yuan Xu Yuan Xu	Director	November 10, 2026

Exhibit 5.1

WILMERHALE

November 10, 2026

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

Re: Xilio Therapeutics, Inc. Third Amended and Restated 2022 Inducement Stock Incentive Plan, as amended

Ladies and Gentlemen:

We have assisted in the preparation of a Registration Statement on Form S-8 (the "Registration Statement") to be filed with the Securities and Exchange Commission (the "Commission") under the Securities Act of 1933, as amended (the "Securities Act"), relating to an aggregate of 250,000 shares of common stock, $0.0001 par value per share (the "Shares"), of Xilio Therapeutics, Inc., a Delaware corporation (the "Company"), issuable under the Company's Third Amended and Restated 2022 Inducement Stock Incentive Plan, as amended (the "Plan").

We have examined the Certificate of Incorporation and By-Laws of the Company, each as amended and restated to date, and originals, or copies certified to our satisfaction, of all pertinent records of the meetings of the board of directors and stockholders of the Company, the Registration Statement, the Plan and such other documents relating to the Company as we have deemed material for the purposes of this opinion.

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 certified, photostatic or other copies, the authenticity of the originals of any such documents and the legal competence of all signatories to such documents.

We assume that the appropriate action will be taken, prior to the offer and sale of the Shares in accordance with the Plan, to register and qualify the Shares for sale under all applicable state securities or "blue sky" laws.

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.

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.

Based on the foregoing, we are of the opinion that the Shares have been duly authorized for issuance and, when the Shares are issued and paid for in accordance with the terms and conditions of the Plan, the Shares will be validly issued, fully paid and nonassessable.

We hereby consent to the filing of this opinion with the Commission in connection with the Registration Statement in accordance with the requirements of Item 601(b)(5) of Regulation S-K under the Securities Act. 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

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement (Form S-8) pertaining to the Third Amended and Restated 2022 Inducement Stock Incentive Plan of Xilio Therapeutics, Inc. of our report dated March 23, 2026, 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, 2025, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Boston, Massachusetts
November 10, 2026

Calculation of Filing Fee Tables

S-8

Xilio Therapeutics, Inc.

Table 1: Newly Registered Securities

	Security Type	Security Class Title	Fee Calculation Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee
1	Equity	Common stock, par value $0.0001 per share	Other	250,000	$ 8.64	$ 2,160,000.00	0.000087	$ 187.92
				Total Offering Amounts:		$ 2,160,000.00		$ 187.92
				Total Fee Offsets:				$ 0.00
				Net Fee Due:				$ 187.92

Offering Note

1

(1) In accordance with Rule 416(a) under the Securities Act of 1933, as amended (the "Securities Act"), this Registration Statement shall be deemed to cover any additional shares of common stock that may from time to time be offered or issued to prevent dilution resulting from stock splits, stock dividends or similar transactions.

(2) Consists of 250,000 shares of common stock issuable under the Xilio Therapeutics, Inc. Third Amended and Restated 2022 Inducement Stock Incentive Plan, as amended.

(3) Estimated solely for the purpose of calculating the registration fee pursuant to Rules 457(c) and 457(h) of the Securities Act and based upon the average of the high and low prices of the registrant's common stock as reported on the Nasdaq Capital Market on November 4, 2026.

Table 2: Fee Offset Claims and Sources ☑Not Applicable

	Registrant or Filer Name	Form or Filing Type	File Number	Initial Filing Date	Filing Date	Fee Offset Claimed	Security Type Associated with Fee Offset Claimed	Security Title Associated with Fee Offset Claimed	Unsold Securities Associated with Fee Offset Claimed	Unsold Aggregate Offering Amount Associated with Fee Offset Claimed	Fee Paid with Fee Offset Source
					Rule 457(p)						
Fee Offset Claims											
Fee Offset Sources											