SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

SCHEDULE 13G

UNDER THE SECURITIES EXCHANGE ACT OF 1934

(Amendment No. 3)*

UPSTREAM BIO INC

(Name of Issuer)

COMMON STOCK

(Title of Class of Securities)

(CUSIP Number)

10/30/2026

(Date of Event Which Requires Filing of this Statement)

Check the appropriate box to designate the rule pursuant to which this Schedule is filed:

- [x] Rule 13d-1(b)
- [ ] Rule 13d-1(c)
- [ ] Rule 13d-1(d)

SCHEDULE 13G

CUSIP No.

1	Names of Reporting Persons FMR LLC	
2	Check the appropriate box if a member of a Group (see instructions)	(a) ☐ (b) ☐
3	Sec Use Only	
4	Citizenship or Place of Organization DELAWARE	

Number of Shares Beneficially Owned by Each Reporting Person With:	5	Sole Voting Power 3,790,763.00
	6	Shared Voting Power 0.00
	7	Sole Dispositive Power 3,793,955.00
	8	Shared Dispositive Power 0.00
9		Aggregate Amount Beneficially Owned by Each Reporting Person 3,793,955.00
10		Check box if the aggregate amount in row (9) excludes certain shares (See Instructions) ☐
11		Percent of class represented by amount in row (9) 6.9 %
12		Type of Reporting Person (See Instructions) HC

SCHEDULE 13G

CUSIP No.

1		Names of Reporting Persons Abigail P. Johnson
2		Check the appropriate box if a member of a Group (see instructions) ☐ (a) ☐ (b)
3		Sec Use Only
4		Citizenship or Place of Organization UNITED STATES
Number of Shares Beneficially Owned by Each Reporting Person With:	5	Sole Voting Power 0.00
	6	Shared Voting Power 0.00
	7	Sole Dispositive Power 3,793,955.00
	8	Shared Dispositive Power 0.00
9		Aggregate Amount Beneficially Owned by Each Reporting Person 3,793,955.00
10		Check box if the aggregate amount in row (9) excludes certain shares (See Instructions) ☐

11 Percent of class represented by amount in row (9)

6.9 %

12 Type of Reporting Person (See Instructions)

IN

SCHEDULE 13G

Item 1.

(a) Name of issuer:

UPSTREAM BIO INC

(b) Address of issuer's principal executive offices:

890 WINTER STREET,SUITE 200,WALTHAM,MA,USA,02451

Item 2.

(a) Name of person filing:

FMR LLC

(b) Address or principal business office or, if none, residence:

245 Summer Street, Boston, Massachusetts 02210

(c) Citizenship:

Not applicable

(d) Title of class of securities:

COMMON STOCK

(e) CUSIP No.:

Item 3. If this statement is filed pursuant to §§ 240.13d-1(b) or 240.13d-2(b) or (c), check whether the person filing is a:

(a) ☐ Broker or dealer registered under section 15 of the Act (15 U.S.C. 78o);

(b) ☐ Bank as defined in section 3(a)(6) of the Act (15 U.S.C. 78c);

(c) ☐ Insurance company as defined in section 3(a)(19) of the Act (15 U.S.C. 78c);

(d) ☐ Investment company registered under section 8 of the Investment Company Act of 1940 (15 U.S.C. 80a-8);

(e) ☐ An investment adviser in accordance with § 240.13d-1(b)(1)(ii)(E);

(f) ☐ An employee benefit plan or endowment fund in accordance with § 240.13d-1(b)(1)(ii)(F);

(g) ☑ A parent holding company or control person in accordance with § 240.13d-1(b)(1)(ii)(G);

(h) ☐ A savings associations as defined in Section 3(b) of the Federal Deposit Insurance Act (12 U.S.C. 1813);

(i) ☐ A church plan that is excluded from the definition of an investment company under section 3(c)(14) of the Investment Company Act of 1940 (15 U.S.C. 80a-3);

(j) ☐ A non-U.S. institution in accordance with § 240.13d-1(b)(1)(ii)(J). If filing as a non-U.S. institution in accordance with § 240.13d-1(b)(1)(ii)(J), please specify the type of institution:

(k) ☐ Group, in accordance with Rule 240.13d-1(b)(1)(ii)(K).

Item 4. Ownership

(a) Amount beneficially owned:

3793955.00

(b) Percent of class:

6.9 %

(c) Number of shares as to which the person has:

(i) Sole power to vote or to direct the vote:

Please see the responses to Items 5 and 6 on the cover page.

(ii) Shared power to vote or to direct the vote:

0.00

(iii) Sole power to dispose or to direct the disposition of:

3793955.00

(iv) Shared power to dispose or to direct the disposition of:

0.00

Item 5. Ownership of 5 Percent or Less of a Class.

Item 6. Ownership of more than 5 Percent on Behalf of Another Person.

If any other person is known to have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of, such securities, a statement to that effect should be included in response to this item and, if such interest relates to more than 5 percent of the class, such person should be identified. A listing of the shareholders of an investment company registered under the Investment Company Act of 1940 or the beneficiaries of employee benefit plan, pension fund or endowment fund is not required.

One or more other persons are known to have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of, the COMMON STOCK of UPSTREAM BIO INC. No one other person's interest in the COMMON STOCK of UPSTREAM BIO INC is more than five percent of the total outstanding COMMON STOCK.

Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on by the Parent Holding Company or Control Person.

If a parent holding company has filed this schedule, pursuant to Rule 13d-1(b)(ii)(G), so indicate under Item 3(g) and attach an exhibit stating the identity and the Item 3 classification of the relevant subsidiary. If a parent holding company has filed this schedule pursuant to Rule 13d-1(c) or Rule 13d-1(d), attach an exhibit stating the identification of the relevant subsidiary.

See attached Exhibit 99.

Item 8. Identification and Classification of Members of the Group.

Not Applicable

Item 9. Notice of Dissolution of Group.

Not Applicable

Item 10. Certifications:

By signing below I certify that, to the best of my knowledge and belief, the securities referred to above were acquired and are held in the ordinary course of business and were not acquired and are not held for the purpose of or with the effect of changing or influencing the control of the issuer of the securities and were not acquired and are not held in connection with or as a participant in any transaction having that purpose or effect, other than activities solely in connection with a nomination under § 240.14a-11.

SIGNATURE

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

FMR LLC

Signature: Stephanie J. Brown

Name/Title: Duly authorized under Power of Attorney effective as of January 3, 2023, by and on behalf of FMR LLC and its direct and indirect subsidiaries*

Date: 11/05/2026

Abigail P. Johnson

Signature: Stephanie J. Brown

Name/Title: Duly authorized under Power of Attorney effective as of January 26, 2023, by and on behalf of Abigail P. Johnson**

Date: 11/05/2026

Comments accompanying signature: * This power of attorney is incorporated herein by reference to Exhibit 24 to the Schedule 13G filed by FMR LLC on January 10, 2023, accession number: 0000315066-23-000003. ** This power of attorney is incorporated herein by reference to Exhibit 24 to the Schedule 13G filed by FMR LLC on January 31, 2023, accession number: 0000315066-23-000038.

Exhibit Information

Please see Exhibit 99 for 13d-1(k) (1) agreement.

Exhibit 99

Pursuant to the instructions in Item 7 of Schedule 13G, the following table lists the identity and Item 3 classification, if applicable, of each relevant entity that beneficially owns shares of the security class being reported on this Schedule 13G.

Entity	ITEM 3 Classification
FIAM LLC	IA
Fidelity Institutional Asset Management Trust Company	BK
Fidelity Management & Research Company LLC	IA

Abigail P. Johnson is a Director, the Chairman and the Chief Executive Officer of FMR LLC.

Members of the Johnson family, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC.

This filing reflects the securities beneficially owned, or that may be deemed to be beneficially owned, by FMR LLC, certain of its subsidiaries and affiliates, and other companies (collectively, the "FMR Reporters"). This filing does not reflect securities, if any, beneficially owned by certain other companies whose beneficial ownership of securities is disaggregated from that of the FMR Reporters in accordance with Securities and Exchange Commission Release No. 34-39538 (January 12, 1998).

RULE 13d-1(k)(1) AGREEMENT

The undersigned persons, on November 5, 2026, agree and consent to the joint filing on their behalf of this Schedule 13G in connection with their beneficial ownership of the COMMON STOCK of UPSTREAM BIO INC at October 30, 2026.

FMR LLC

By /s/ Stephanie J. Brown
Stephanie J. Brown
Duly authorized under Power of Attorney effective as of January 3, 2023, by and on behalf of FMR LLC and its direct and indirect subsidiaries*

Abigail P. Johnson

By /s/ Stephanie J. Brown
Stephanie J. Brown
Duly authorized under Power of Attorney effective as of January 26, 2023, by and on behalf of Abigail P. Johnson**

* This power of attorney is incorporated herein by reference to Exhibit 24 to the Schedule 13G filed by FMR LLC on January 10, 2023, accession number: 0000315066-23-000003.

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