

INITIAL STATEMENT OF BENEFICIAL OWNERSHIP OF SECURITIES

OMB APPROVAL	
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Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Reporting Person* <u>Ruddy Marcella K.</u> (Last) (First) (Middle) UPSTREAM BIO, INC. 890 WINTER STREET, SUITE 200 (Street) WALTHAM MA 02451 (City) (State) (Zip)	2. Date of Event Requiring Statement (Month/Day/Year) 10/10/2024	3. Issuer Name and Ticker or Trading Symbol <u>Upstream Bio, Inc. [UPB]</u>	
		4. Relationship of Reporting Person(s) to Issuer (Check all applicable) <input checked="" type="checkbox"/> Director 10% Owner Officer (give title below) Other (specify below)	5. If Amendment, Date of Original Filed (Month/Day/Year) 6. Individual or Joint/Group Filing (Check Applicable Line) <input checked="" type="checkbox"/> Form filed by One Reporting Person <input type="checkbox"/> Form filed by More than One Reporting Person

Table I - Non-Derivative Securities Beneficially Owned

1. Title of Security (Instr. 4)	2. Amount of Securities Beneficially Owned (Instr. 4)	3. Ownership Form: Direct (D) or Indirect (I) (Instr. 5)	4. Nature of Indirect Beneficial Ownership (Instr. 5)
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Table II - Derivative Securities Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)

1. Title of Derivative Security (Instr. 4)	2. Date Exercisable and Expiration Date (Month/Day/Year)		3. Title and Amount of Securities Underlying Derivative Security (Instr. 4)	4. Conversion or Exercise Price of Derivative Security	5. Ownership Form: Direct (D) or Indirect (I) (Instr. 5)	6. Nature of Indirect Beneficial Ownership (Instr. 5)
	Date Exercisable	Expiration Date				
Stock Option (Right to Buy)	(1)	07/02/2032	Common Stock	13,159	3.45	D
Stock Option (Right to Buy)	(2)	03/02/2033	Common Stock	43,115	4.27	D
Stock Option (Right to Buy)	(3)	08/13/2033	Common Stock	7,867	4.87	D

Explanation of Responses:

- The shares underlying this option vest in forty-eight equal monthly installments following July 3, 2022, subject to the Reporting Person's continued service on each such vesting date.
- 25% of the shares underlying this option vested on March 3, 2024, with the remainder vesting in thirty-six equal monthly installments thereafter, subject to the Reporting Person's continued service on each such vesting date.
- 25% of the shares underlying this option vested on August 10, 2024, with the remainder vesting in thirty-six equal monthly installments thereafter, subject to the Reporting Person's continued service on each such vesting date.

Remarks:

Exhibit 24 - Power of Attorney

/s/ Michael Gray,
Attorney-in-Fact

10/10/2024

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

* If the form is filed by more than one reporting person, see Instruction 5 (b)(v).

** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB Number.

LIMITED POWER OF ATTORNEY

The undersigned hereby constitutes and appoints each of E. Rand Sutherland, Michael Paul Gray and Gabriela Morales-Rivera, signing singly, and with full power of substitution, the undersigned's true and lawful attorney-in-fact to:

(1) execute for and on behalf of the undersigned, in the undersigned's capacity as an officer, director, and/or securityholder of Upstream Bio, Inc., a Delaware corporation (the "Company"), from time to time the following U.S. Securities and Exchange Commission ("SEC") forms: (i) Form ID, including any attached documents (such as Update Passphrase Authentication), to effect the assignment of codes to the undersigned to be used in the transmission of information to the SEC using the EDGAR System; (ii) Form 3, Initial Statement of Beneficial Ownership of Securities, including any attached documents; (iii) Form 4, Statement of Changes in Beneficial Ownership of Securities, including any attached documents; (iv) Form 5, Annual Statement of Beneficial Ownership of Securities in accordance with Section 16(a) of the Securities Exchange Act of 1934, as amended, and the rules thereunder, including any attached documents; (v) Schedules 13D and 13G; and (vi) amendments of each thereof, in accordance with the Securities Exchange Act of 1934, as amended, and the rules thereunder, including any attached documents;

(2) do and perform any and all acts for and on behalf of the undersigned which may be necessary or desirable to complete and execute any such Form 3, 4 or 5, Schedule 13D or 13G, or any amendment(s) thereto and timely file such form(s) with the SEC and any securities exchange, national association or similar authority; and

(3) take any other action of any type whatsoever in connection with the foregoing which, in the opinion of such attorney-in-fact, may be of benefit to, in the best interest of, or legally required by, the undersigned, it being understood that the documents executed by such attorney-in-fact on behalf of the undersigned pursuant to this Power of Attorney shall be in such form and shall contain such terms and conditions as such attorney-in-fact may approve in such attorney-in-fact's discretion.

The undersigned hereby grants to each such attorney-in-fact, acting singly, full power and authority to do and perform any and every act and thing whatsoever requisite, necessary or proper to be done in the exercise of any of the rights and powers herein granted, as fully to all intents and purposes as the undersigned might or could do if personally present, with full power of substitution or revocation, hereby ratifying and confirming all that such attorney-in-fact, or such attorney-in-fact's substitute or substitutes, shall lawfully do or cause to be done by virtue of this power of attorney and the rights and powers herein granted. The undersigned acknowledges that the foregoing attorneys-in-fact, in serving in such capacity at the request of the undersigned, are not assuming, nor is the Company assuming, any of the undersigned's responsibilities to comply with Section 16 or Regulation 13D-G of the Securities Exchange Act of 1934, as amended. The undersigned hereby agrees to indemnify the attorneys-in-fact and the Company from and against any demand, damage, loss, cost or expense arising from any false or misleading information provided by the undersigned to the attorneys-in-fact.

This Power of Attorney shall remain in full force and effect until the undersigned is no longer required to file such forms with respect to the undersigned's holdings of and transactions in securities issued by the Company, unless earlier revoked by the undersigned in a signed writing delivered to the foregoing attorneys-in-fact. This Power of Attorney supersedes any prior power of attorney in connection with the undersigned's capacity as an officer and/or director of the Company. This Power of Attorney shall expire as to any individual attorney-in-fact if such attorney-in-fact ceases to be an employee of the Company.

IN WITNESS WHEREOF, the undersigned has caused this Power of Attorney to be executed as of October 10, 2024.

/s/ Marcella Kuhlman Ruddy, M.D., M.S.

Signature

Marcella Kuhlman Ruddy, M.D., M.S.

Print Name
