

OMB APPROVAL	
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STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

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

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

Check this box to indicate that a transaction was made pursuant to a contract, instruction or written plan for the purchase or sale of equity securities of the issuer that is intended to satisfy the affirmative defense conditions of Rule 10b5-1(c). See Instruction 10.

1. Name and Address of Reporting Person* <u>Chimovits Erez</u> _____ (Last) (First) (Middle) <u>C/O UPSTREAM BIO, INC.</u> <u>890 WINTER STREET, SUITE 200</u> _____ (Street) <u>WALTHAM MA 02451</u> _____ (City) (State) (Zip)			2. Issuer Name and Ticker or Trading Symbol <u>Upstream Bio, Inc. [UPB]</u>			5. Relationship of Reporting Person(s) to Issuer (Check all applicable) <input checked="" type="checkbox"/> Director <input checked="" type="checkbox"/> 10% Owner Officer (give title below) Other (specify below)		
			3. Date of Earliest Transaction (Month/Day/Year) <u>10/15/2024</u>					
			4. 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 Acquired, Disposed of, or Beneficially Owned

1. Title of Security (Instr. 3)	2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any (Month/Day/Year)	3. Transaction Code (Instr. 8)		4. Securities Acquired (A) or Disposed Of (D) (Instr. 3, 4 and 5)			5. Amount of Securities Beneficially Owned Following Reported Transaction(s) (Instr. 3 and 4)	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial Ownership (Instr. 4)
			Code	V	Amount	(A) or (D)	Price			
Common Stock	10/15/2024		C		721,956	A	(1)	973,716	I	See Footnote ⁽²⁾⁽⁴⁾
Common Stock	10/15/2024		P		165,000	A	\$17	1,138,716	I	See Footnote ⁽²⁾⁽⁴⁾
Common Stock	10/15/2024		C		2,887,833	A	(1)	3,894,873	I	See Footnote ⁽³⁾⁽⁴⁾
Common Stock	10/15/2024		P		660,000	A	\$17	4,554,873	I	See Footnote ⁽³⁾⁽⁴⁾

Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)

1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative Security	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transaction Code (Instr. 8)		5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5)		6. Date Exercisable and Expiration Date (Month/Day/Year)		7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially Owned Following Reported Transaction(s) (Instr. 4)	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)	
				Code	V	(A)	(D)	Date Exercisable	Expiration Date						Title
Series A redeemable convertible preferred stock	(1)	10/15/2024		C		524,500		(1)	(1)	Common Stock	524,500	(1)	0	I	See Footnote ⁽²⁾⁽⁴⁾
Series A redeemable convertible preferred stock	(1)	10/15/2024		C		2,098,000		(1)	(1)	Common Stock	2,098,000	(1)	0	I	See Footnote ⁽³⁾⁽⁴⁾
Series B redeemable convertible preferred stock	(1)	10/15/2024		C		197,456		(1)	(1)	Common Stock	197,456	(1)	0	I	See Footnote ⁽²⁾⁽⁴⁾
Series B redeemable convertible preferred stock	(1)	10/15/2024		C		789,833		(1)	(1)	Common Stock	789,833	(1)	0	I	See Footnote ⁽³⁾⁽⁴⁾

Explanation of Responses:

- Each share of Series A redeemable convertible preferred stock and Series B redeemable convertible preferred stock automatically converted into shares of the Issuer's common stock on a one-for-1.049 basis immediately prior to the closing of the Issuer's initial public offering and have no expiration date.
- These securities are held of record by OrbiMed Israel Partners II, L.P. ("OIP II"). OrbiMed Israel GP II, L.P. ("Israel GP") is the general partner of OIP II, and OrbiMed Advisors Israel II Limited ("Advisors II") is the general partner of Israel GP. By virtue of such relationships, Israel GP and Advisors II may be deemed to have voting and investment power over the securities held by OIP II and, as a result, may be deemed to have beneficial ownership over such securities. Advisors II exercises voting and investment power through an investment committee comprised of Carl L. Gordon, David P. Bonita, and the Reporting Person, each of whom disclaims beneficial ownership of the securities held by OIP II.
- These securities are held of record by OrbiMed Private Investments VIII, LP ("OPI VIII"). OrbiMed Capital GP VIII LLC ("GP VIII") is the general partner of OPI VIII, and OrbiMed Advisors LLC ("OrbiMed Advisors") is the managing member of GP VIII. By virtue of such relationships, GP VIII and OrbiMed Advisors may be deemed to have voting power and investment power over the securities held by OPI VIII and, as a result, may be deemed to have beneficial ownership over such securities. OrbiMed Advisors exercises voting and investment power through a management committee comprised of Carl L. Gordon, Sven H. Borho, and W. Carter Neild, each of whom disclaims beneficial ownership of the securities held by OPI VIII.
- Each of the Reporting Person, Advisors II, Israel GP, OrbiMed Advisors, and GP VIII disclaims beneficial ownership of the securities reported herein for purposes of Rule 16a-1(a) under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), except to the extent of his or its pecuniary interest therein, if any. This report shall not be deemed an admission that any of the Reporting Person, Advisors II, Israel GP, OrbiMed Advisors, or GP VIII is a beneficial owner of such securities for the purpose of Section 16 of the Exchange Act, or for any other purpose.

/s/ Erez Chimovits

10/17/2024

** 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 4 (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.