

**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

OMB APPROVAL	
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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>			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 10% Owner Officer (give title below) Other (specify below)		
(Last)	(First)	(Middle)	3. Date of Earliest Transaction (Month/Day/Year) <u>06/09/2026</u>			6. Individual or Joint/Group Filing (Check Applicable Line) <input checked="" type="checkbox"/> Form filed by One Reporting Person Form filed by More than One Reporting Person		
UPSTREAM BIO, INC. 890 WINTER STREET, SUITE 200			4. If Amendment, Date of Original Filed (Month/Day/Year)					
(Street) WALTHAM MA 02451								
(City) (State) (Zip)								

**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			

**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
Stock Option (Right to Buy)	\$6.69	06/09/2026		A		17,096		(1)	06/08/2036	Common Stock	17,096	\$0	17,096	D <sup>(2)</sup>	

**Explanation of Responses:**

1. The shares underlying this option shall vest in full upon the earlier of (i) June 9, 2027 and (ii) the date of the next Annual Meeting of Stockholders of the Issuer, subject to the Reporting Person's continued service on such vesting date.

2. Pursuant to an agreement with OrbiMed Advisors LLC, OrbiMed Capital GP VIII LLC, OrbiMed Israel GP II, L.P., and OrbiMed Advisors Israel II Limited, the Reporting Person is obligated to transfer any securities issued under any such stock options or other awards, or the economic benefit thereof, to OrbiMed Advisors LLC, OrbiMed Capital GP VIII LLC, OrbiMed Israel GP II, L.P., and OrbiMed Advisors Israel II Limited, which will in turn ensure that such securities or economic benefits are provided to OrbiMed Private Investments VIII, LP and OrbiMed Israel Partners II, L.P.

/s/ Allison Ambrose, Attorney-in-Fact 06/11/2026

\*\* 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.