

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

SCHEDULE 13D/A
Under the Securities Exchange Act of 1934
(Amendment No. 4)*

ENTASIS THERAPEUTICS HOLDINGS INC.

(Name of Issuer)

Common Stock, \$0.001 par value

(Title of Class of Securities)

293614 103

(CUSIP Number)

Pavel Raifeld
Chief Executive Officer
Innoviva, Inc.
1350 Old Bayshore Highway Suite 400
Burlingame, CA
877-202-1097

(Name, Address and Telephone Number of Person Authorized to Receive Notices and Communications)

May 3, 2021

(Date of Event which Requires Filing of this Statement)

If the filing person has previously filed a statement on Schedule 13G to report the acquisition that is the subject of this Schedule 13D, and is filing this schedule because of §§240.13d-1(e), 240.13d-1(f) or 240.13d-1(g), check the following box.

Note: Schedules filed in paper format shall include a signed original and five copies of the schedule, including all exhibits. See §240.13d-7 for other parties to whom copies are to be sent.

* The remainder of this cover page shall be filled out for a reporting person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter disclosures provided in a prior cover page.

The information required on the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934 ("Act") or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act (however, see the Notes).

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 control number.

1	NAME OF REPORTING PERSON Innoviva, Inc.	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) (b)	
3	SEC USE ONLY	
4	SOURCE OF FUNDS WC	
5	CHECK IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER 37,345,794 ⁽¹⁾
	8	SHARED VOTING POWER 7,462,050 ⁽²⁾
	9	SOLE DISPOSITIVE POWER 37,345,794 ⁽¹⁾
	10	SHARED DISPOSITIVE POWER 7,462,050 ⁽²⁾
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 44,807,844 ⁽¹⁾	
12	CHECK IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (SEE INSTRUCTIONS) <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 70.6% ⁽³⁾	
14	TYPE OF REPORTING PERSON (SEE INSTRUCTIONS) CO	

(1) Includes shares of Common Stock and warrants to purchase Common Stock acquired by INVA on April 22, 2020, June 11, 2020, and September 1, 2020.

(2) Includes shares of Common Stock and warrants to purchase Common Stock acquired by ISO on May 3, 2021.

(3) Based on 37,310,254 shares of Common Stock outstanding as April 16, 2021, as reported by the Issuer in its proxy statement on Schedule 14A filed on April 30, 2021 plus 3,731,025 shares of Common Stock and warrants to purchase 3,731,025 shares of Common Stock acquired by the Reporting Persons on May 3, 2021, plus warrants to purchase 18,672,897 shares of Common Stock previously acquired by the Reporting Persons. Does not include shares of Common Stock or warrants to purchase Common Stock to be issued by the Issuer upon the closing of the transaction described in Item 4 below.

1	NAME OF REPORTING PERSON Innoviva Strategic Opportunities LLC	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) (b)	
3	SEC USE ONLY	
4	SOURCE OF FUNDS WC	
5	CHECK IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER 0
	8	SHARED VOTING POWER 7,462,050
	9	SOLE DISPOSITIVE POWER 0
	10	SHARED DISPOSITIVE POWER 7,462,050
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 7,462,050	
12	CHECK IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (SEE INSTRUCTIONS) <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 11.8%(1)	
14	TYPE OF REPORTING PERSON (SEE INSTRUCTIONS) OO	

(1) Based on 37,310,254 shares of Common Stock outstanding as April 16, 2021, as reported by the Issuer in its proxy statement on Schedule 14A filed on April 30, 2021 plus 3,731,025 shares of Common Stock and warrants to purchase 3,731,025 shares of Common Stock acquired by ISO on May 3, 2021, plus warrants to purchase 18,672,897 shares of Common Stock previously acquired by INVA. Does not include shares of Common Stock or warrants to purchase Common Stock to be issued by the Issuer upon the second closing of the transaction described in Item 4 below

Explanatory Note

This Amendment No. 4 (the “Amendment No. 4”) amends and supplements the initial Statement of Beneficial Ownership on Schedule 13D, as filed with the Securities and Exchange Commission on April 23, 2020 and previously amended, (as amended, the “Schedule 13D”) with respect to shares of common stock, \$0.001 par value per share (“Common Stock”) of Entasis Therapeutics Holdings Inc., a Delaware corporation (the “Issuer”) and warrants to acquire additional shares of Common Stock of the Issuer. Innoviva, Inc. (“INVA”) and Innoviva Strategic Opportunities LLC (“ISO” and together with INVA, the “Reporting Persons”) are filing this amendment to reflect the execution of a Securities Purchase Agreement (as defined below) in respect of the acquisition of additional shares of Common Stock and Common Warrants. Except as specifically amended and supplemented by this Amendment No. 4, the Schedule 13D remains in full force and effect.

Item 2. Identity and Background

Item 2 in Schedule 13D is hereby supplemented as follows:

Innoviva Strategic Opportunities LLC (“ISO”) is a wholly-owned subsidiary of Innoviva which was formed on November 25, 2020.

The address of the principal business office of ISO is: c/o Innoviva, Inc., 1350 Old Bayshore Highway Suite 400 Burlingame, CA.

Neither Reporting Person has been, (a) with respect to INVA, in the last five years, and (b) with respect to ISO, since the date of its formation: (i) convicted in a criminal proceeding, or (ii) a party to any other civil proceeding of a judicial or administrative body of competent jurisdiction, as a result of which the Reporting Person is or has been subject to a judgment, decree or final order enjoining future violations of, or prohibiting or mandating activities subject to, federal or state securities laws or finding any violation with respect to such laws.

Item 3. Source and Amount of Funds or Other Consideration

Item 3 of Schedule 13D is hereby supplemented as follows:

ISO acquired the shares and Common Warrants for an aggregate purchase price of approximately \$7.5 million. The Securities were acquired with funds provided from working capital of the Reporting Persons.

Item 4. Purpose of Transaction

Item 4 in Schedule 13D is hereby supplemented as follows:

On May 3, 2021, the Issuer entered into a securities purchase agreement (the “Securities Purchase Agreement”) with ISO, pursuant to which the Issuer agreed to initially issue and sell to ISO (i) 3,731,025 shares of Common Stock (the “Shares”), and (ii) warrants to purchase 3,731,025 shares of Common Stock (the “Common Warrants”), with each Share and Common Warrant being issued and sold as a unit, for a per unit price of \$2.00. In addition to the Shares and Common Warrants referenced in the preceding sentence, ISO may acquire an additional 6,268,975 shares of Common Stock and additional Warrants to purchase 6,268,975 shares of Common Stock of the Issuer, subject to satisfaction of certain conditions set forth in the Securities Purchase Agreement, including that the Securities Purchase Agreement and the transactions contemplated thereby having been approved by the stockholders of the Issuer as may be required by the applicable rules and regulations of Nasdaq Stock Market LLC.

The exercise price and the number of shares of Common Stock issuable upon exercise of each Common Warrant is subject to appropriate adjustments in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting the Common Stock. Each Common Warrant issued to ISO is exercisable from the date of issuance and has a term of five years and an initial exercise price of \$2.00.

The foregoing summaries of the Securities Purchase Agreement and Common Warrants do not purport to be complete and are subject to, and qualified in their entirety by, the full text of the Securities Purchase Agreement and the form of Common Warrant, respectively, which are filed as Exhibit 10.1 to the Form 8-K of the Issuer filed with the SEC on May 3, 2021 and are incorporated herein by reference; any description herein of the Securities Purchase Agreement is qualified in its entirety by reference to the Securities Purchase Agreement so filed by the Issuer.

The Reporting Persons may, from time to time and at any time, either alone or together with others: (i) acquire additional Common Stock and warrants and/or other equity, debt, notes, instruments or other securities (collectively, “Securities”) of the Issuer in the open market or otherwise; (ii) dispose of any or all of its Securities in the open market or otherwise; or (iii) engage in any hedging or similar transactions with respect to the Securities. The Reporting Persons agreed to purchase the Common Stock and Common Warrants reported in this Amendment No. 4 for investment purposes.

Item 5. Interest in Securities of the Issuer

Item 5 in Schedule 13D is hereby amended and restated as follows:

The information contained in the cover page and in Item 4 to this Schedule 13D is hereby incorporated by reference into this Item 5. The Reporting Persons did not acquire or sell any shares of Common Stock or other securities of the Issuer during the last 60 days.

Item 6. Contracts, Arrangements, Understandings or Relationships with Respect to Securities of the Issuer

Item 6 in Schedule 13D is hereby supplemented as follows:

The information contained above in Item 4 is hereby incorporated by reference into this Item 6.

In connection with the Securities Purchase Agreement, the Issuer entered into a Registration Rights Agreement (the "Registration Rights Agreement") with ISO. Pursuant to the Registration Rights Agreement, the Issuer agreed to prepare and file a registration statement with the SEC for purposes of registering the resale of the Shares, the shares of Common Stock issuable upon exercise of the Common Warrants, the Common Warrants and any shares of Common Stock issued as a dividend or other distribution with respect to the Shares or shares of Common Stock issuable upon exercise of the Common Warrants.

The form of Registration Rights Agreement is attached as Exhibit 10.2 to the Form 8-K of the Issuer filed with the SEC on May 3, 2021 and is incorporated by reference in this Schedule 13D; any description herein of the Registration Rights Agreement is qualified in its entirety by reference to the Registration Rights Agreement so filed by the Issuer.

Item 7. Material to Be Filed as Exhibits

Exhibit 9 – Securities Purchase Agreement, dated as of May 3, 2021, by and between Entasis Therapeutics Holdings Inc. and Innoviva Strategic Opportunities LLC (incorporated by reference to Exhibit 10.1 to the Form 8-K of the Issuer filed with the SEC on May 3, 2021)

Exhibit 10 – Registration Rights Agreement, dated as of May 3, 2021, by and between Entasis Therapeutics Holdings Inc. and Innoviva Strategic Opportunities LLC (incorporated by reference to Exhibit 10.2 to the Form 8-K of the Issuer filed with the SEC on May 3, 2021)

Exhibit 99.1 – Joint Filing Agreement, dated as of May 3, 2021, by and between the Reporting Persons

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.

Dated: May 3, 2021

INNOVIVA, INC.

By: /s/ Pavel Raifeld
Name: Pavel Raifeld
Title: Chief Executive Officer

INNOVIVA STRATEGIC OPPORTUNITIES LLC
By: **Innoviva, Inc., its managing member**

By: /s/ Pavel Raifeld
Name: Pavel Raifeld
Title: Chief Executive Officer

JOINT FILING AGREEMENT

The undersigned acknowledge and agree that the foregoing amendment to Schedule 13D is filed on behalf of each of the undersigned and that all subsequent amendments to the Schedule 13D shall be filed on behalf of each of the undersigned without the necessity of filing additional joint filing agreements. The undersigned acknowledge that each shall be responsible for the timely filing of such amendments, and for the completeness and accuracy of the information concerning it contained therein, but shall not be responsible for the completeness and accuracy of the information concerning the others, except to the extent that it knows or has reason to believe that such information is inaccurate. This Agreement may be executed in any number of counterparts and all of such counterparts taken together shall constitute one and the same instrument.

[Remainder of page intentionally blank]

Dated: May 3, 2021

INNOVIVA, INC.

By: /s/ Pavel Raifeld

Name: Pavel Raifeld

Title: Chief Executive Officer

Dated: May 3, 2021

INNOVIVA STRATEGIC OPPORTUNITIES LLC

By: Innoviva, Inc., its managing member

By: /s/ Pavel Raifeld

Name: Pavel Raifeld

Title: Chief Executive Officer