

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden hours per response:	0.5

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).

1. Name and Address of Reporting Person* <u>Perros Manoussos</u> (Last) (First) (Middle) C/O ENTASIS THERAPEUTICS HOLDINGS INC., 35 GATEHOUSE DRIVE (Street) WALTHAM MA 02451 (City) (State) (Zip)	2. Issuer Name and Ticker or Trading Symbol <u>Entasis Therapeutics Holdings Inc. [ETTX]</u>	5. Relationship of Reporting Person(s) to Issuer (Check all applicable) Director 10% Owner <input checked="" type="checkbox"/> Officer (give title below) Other (specify below) President and CEO
	3. Date of Earliest Transaction (Month/Day/Year) 07/16/2021	
4. If Amendment, Date of Original Filed (Month/Day/Year)		

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
Employee Stock Option (Right to Buy)	\$4.98	07/16/2021		D			87,462	(1)	08/11/2025	Common Stock	87,462	(2)	0	D	
Employee Stock Option (Right to Buy)	\$2.44	07/16/2021		A			58,307	(3)	07/15/2031	Common Stock	58,307	(2)	58,307	D	
Employee Stock Option (Right to Buy)	\$6.85	07/16/2021		D			166,623	(4)	04/30/2028	Common Stock	166,623	(5)	0	D	
Employee Stock Option (Right to Buy)	\$2.44	07/16/2021		A			128,531	(6)	07/15/2031	Common Stock	128,531	(5)	128,531	D	
Employee Stock Option (Right to Buy)	\$15	07/16/2021		D			79,698	(7)	09/24/2028	Common Stock	79,698	(8)	0	D	
Employee Stock Option (Right to Buy)	\$2.44	07/16/2021		A			44,276	(9)	07/15/2031	Common Stock	44,276	(8)	44,276	D	
Employee Stock Option (Right to Buy)	\$5.66	07/16/2021		D			123,500	(10)	01/17/2029	Common Stock	123,500	(11)	0	D	
Employee Stock Option (Right to Buy)	\$2.44	07/16/2021		A			95,000	(12)	07/15/2031	Common Stock	95,000	(11)	95,000	D	

Explanation of Responses:

- The option provided for vesting as follows: Twenty-five percent (25%) of the shares subject to the option will vest on May 13, 2016, and one thirty-sixth (1/36th) of the remaining shares subject to the option shall vest each month thereafter on the last day of the month, subject to Reporting Person continuing to provide service through each such date.
- On July 16, 2021, the issuer canceled, pursuant to the issuer's option exchange program, an option for 87,462 shares of issuer's common stock granted to the Reporting Person on August 11, 2015. In exchange, the Reporting Person received a replacement option for 58,307 shares of issuer's common stock, having an exercise price of \$2.44 per share.
- The shares subject to this option will vest in full on July 16, 2022, subject to the Reporting Person's continuing to provide service through such date.
- The option provided for vesting as follows: Twenty-five percent (25%) of the shares subject to the option will vest on December 6, 2018, and one thirty-sixth (1/36th) of the remaining shares subject to the option shall vest each month thereafter on the last day of the month, subject to Reporting Person continuing to provide service through each such date.
- On July 16, 2021, the issuer canceled, pursuant to the issuer's option exchange program, an option for 166,623 shares of issuer's common stock granted to the Reporting Person on May 1, 2018. In exchange, the Reporting Person received a replacement option for 128,531 shares of issuer's common stock, having an exercise price of \$2.44 per share.
- The shares subject to this option will vest in full on July 16, 2022, subject to the Reporting Person's continuing to provide service through such date.
- The option provided for vesting as follows: Twenty-five percent (25%) of the shares subject to the option shall vest on September 25, 2019, and one thirty-sixth (1/36th) of the remaining shares subject to the option shall vest each month thereafter, subject to the Reporting Person continuing to provide service through each such date.
- On July 16, 2021, the issuer canceled, pursuant to the issuer's option exchange program, an option for 79,698 shares of issuer's common stock granted to the Reporting Person on September 25, 2018. In exchange, the

Reporting Person received a replacement option for 44,276 shares of issuer's common stock, having an exercise price of \$2.44 per share.

9. Ninety-four (94%) of this award will vest on July 16, 2022, and one-third of the remaining shares subject to the option will vest monthly following July 16, 2022, subject to the Reporting Person's continuing to provide service through each such date.

10. The option provided for vesting as follows: Twenty-five percent (25%) of the shares subject to the option shall vest on January 1, 2020, and one thirty-sixth (1/36th) of the remaining shares subject to the option shall vest each month thereafter, subject to the Reporting Person continuing to provide service through each such date.

11. On July 16, 2021, the issuer canceled, pursuant to the issuer's option exchange program, an option for 123,500 shares of issuer's common stock granted to the Reporting Person on January 18, 2019. In exchange, the Reporting Person received a replacement option for 95,000 shares of issuer's common stock, having an exercise price of \$2.44 per share.

12. Eighty-five (85%) of this award will vest on July 16, 2022, and one-seventh of the remaining shares subject to the option will vest monthly following July 16, 2022, subject to the Reporting Person's continuing to provide service through each such date.

Elizabeth M. Keiley as Attorney-
in-Fact for Manoussos Perros

02/14/2022

** 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.