

**STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP**

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

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>Monia Brett P</u>  (Last) (First) (Middle) C/O IONIS PHARMACEUTICALS, INC. 2855 GAZELLE COURT  (Street) CARLSBAD CA 92010  (City) (State) (Zip)	2. Issuer Name and Ticker or Trading Symbol <u>IONIS PHARMACEUTICALS INC [ IONS ]</u>  3. Date of Earliest Transaction (Month/Day/Year) 01/01/2017  4. If Amendment, Date of Original Filed (Month/Day/Year)	5. Relationship of Reporting Person(s) to Issuer (Check all applicable) Director 10% Owner X Officer (give title below) Other (specify below) <u>SVP, Antisense Drug Discovery</u>  6. Individual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person Form filed by More than One Reporting Person
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**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	01/01/2017	01/01/2017	j <sup>(1)</sup>	v	309 <sup>(1)</sup>	A	\$20.757	8,181	D	
Common Stock	01/03/2017	01/03/2017	s <sup>(2)</sup>		309 <sup>(2)</sup>	D	\$48.6	7,872	D	

**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						Amount or Number of Shares
Employee Stock Option (right to buy)	\$47.34	01/03/2017	01/03/2017	A		48,000		01/03/2018 <sup>(3)</sup>	01/02/2024	Common Stock	48,000	\$0	48,000	D	

**Explanation of Responses:**

- Reporting 309 shares acquired under the Ionis Pharmaceuticals, Inc. Amended and Restated 2000 Employee Stock Purchase Plan on January 1, 2017. These 309 shares may not be sold until July 2, 2017.
- Acquired as a result of shares owned under the Ionis Pharmaceuticals, Inc. Amended and Restated 2000 Employee Stock Purchase Plan on July 1, 2016. The sale reported on this Form 4 was effective pursuant to a Rule 10b5-1 Trading Plan adopted by the reporting person on 7/1/2014.
- Grant of 1/3/2017 to reporting person of stock options under the Ionis Pharmaceuticals, Inc. 2011 Equity Incentive Plan. 25% of the shares subject to the option vest and become exercisable on 1/3/2018. Thereafter, the remaining shares subject to the option vest and become exercisable in 36 equal monthly installments, at the rate of 12,000 shares per year. Following this transaction, the option was exercisable as to 0 on 1/3/2017.

**Remarks:**

/s/Brett P. Monia 01/04/2017  
 \*\* 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.