

**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

OMB APPROVAL	
OMB Number:	3235-0287
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1. Name and Address of Reporting Person* <u>CROOKE STANLEY T</u>  (Last) (First) (Middle) <u>C/O IONIS PHARMACEUTICALS, INC.</u> <u>2855 GAZELLE COURT</u>  (Street) <u>CARLSBAD CA 92010</u>  (City) (State) (Zip)	2. Issuer Name and Ticker or Trading Symbol <u>IONIS PHARMACEUTICALS INC [ IONS ]</u>	5. Relationship of Reporting Person(s) to Issuer (Check all applicable) <input checked="" type="checkbox"/> Director 10% Owner <input checked="" type="checkbox"/> Officer (give title below) Other (specify below) <u>Chairman and CEO</u>
	3. Date of Earliest Transaction (Month/Day/Year) <u>08/20/2019</u>	
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			
Common Stock	08/20/2019	08/20/2019	M <sup>(1)</sup>		10,000 <sup>(1)</sup>	A	\$39.87	79,634	D	
Common Stock	08/20/2019	08/20/2019	S <sup>(1)</sup>		10,000 <sup>(1)</sup>	D	\$71	69,634	D	
Common Stock	08/20/2019	08/20/2019	M <sup>(2)</sup>		2,000 <sup>(2)</sup>	A	\$39.87	7,532	I	By wife
Common Stock	08/20/2019	08/20/2019	S <sup>(2)</sup>		2,000 <sup>(2)</sup>	D	\$71	5,532	I	By wife
Common Stock	08/21/2019	08/21/2019	M <sup>(1)</sup>		10,000 <sup>(1)</sup>	A	\$39.87	79,634	D	
Common Stock	08/21/2019	08/21/2019	S <sup>(1)</sup>		10,000 <sup>(1)</sup>	D	\$72.15 <sup>(3)</sup>	69,634	D	
Common Stock								725,391	I	By trust

**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)	\$39.87	08/20/2019	08/20/2019	M			10,000	01/02/2018	01/01/2021	Common Stock	10,000	\$0	37,180	D	
Employee Stock Option (right to buy)	\$39.87	08/20/2019	08/20/2019	M			2,000	01/02/2018	01/01/2021	Common Stock	2,000	\$0	500	I	By wife
Employee Stock Option (right to buy)	\$39.87	08/21/2019	08/21/2019	M			10,000	01/02/2018	01/01/2021	Common Stock	10,000	\$0	27,180	D	

**Explanation of Responses:**

- Acquired as a result of exercising a stock option pursuant to Rule 10b5-1 Trading Plan. The purchase and sale reported on this Form 4 was effective pursuant to Rule 10b5-1 Trading Plan adopted by the reporting person on 3/13/2019.
- Acquired as a result of exercising a stock option pursuant to Rule 10b5-1 Trading Plan. The purchase and sale reported on this Form 4 was effective pursuant to Rule 10b5-1 Trading Plan adopted by the reporting person's wife on 3/13/2019.
- The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from \$72.10 to \$72.20, inclusive. The reporting person undertakes to provide to Ionis Pharmaceuticals, Inc., any security holder of Ionis Pharmaceuticals, Inc. or the staff of the Securities and Exchange Commission, upon request, full information regarding the number of shares sold at each separate price within the ranges set forth in footnote (3) on this Form 4.

**Remarks:**

/s/Patrick R. O'Neil, attorney-in-fact 08/22/2019

\*\* Signature of Reporting Person Date

\* 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.

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