

**STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP**

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

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

<b>1. Name and Address of Reporting Person*</b> <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)			<b>2. Issuer Name and Ticker or Trading Symbol</b> <u>IONIS PHARMACEUTICALS INC [ IONS ]</u>			<b>5. Relationship of Reporting Person(s) to Issuer</b> (Check all applicable) <input checked="" type="checkbox"/> Director 10% Owner <input checked="" type="checkbox"/> Officer (give title below) Other (specify below) <p style="text-align: center;"><b>Chairman and CEO</b></p>		
			<b>3. Date of Earliest Transaction (Month/Day/Year)</b> <u>01/03/2017</u>					
			<b>4. If Amendment, Date of Original Filed (Month/Day/Year)</b>					
			<b>6. Individual or Joint/Group Filing (Check Applicable Line)</b> <input checked="" type="checkbox"/> Form filed by One Reporting Person <input type="checkbox"/> Form filed by More than One Reporting Person					

**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	01/03/2017	01/03/2017	M <sup>(1)</sup>		5,000 <sup>(1)</sup>	A	\$7.25	30,029	D	
Common Stock	01/03/2017	01/03/2017	S <sup>(1)</sup>		5,000 <sup>(1)</sup>	D	\$47.3	25,029	D	
Common Stock	01/03/2017	01/03/2017	M <sup>(1)</sup>		5,000 <sup>(1)</sup>	A	\$7.25	30,029	D	
Common Stock	01/03/2017	01/03/2017	S <sup>(1)</sup>		5,000 <sup>(1)</sup>	D	\$48.8	25,029	D	
Common Stock	01/03/2017	01/03/2017	M <sup>(2)</sup>		500 <sup>(2)</sup>	A	\$10.29	2,670	I	By wife
Common Stock	01/03/2017	01/03/2017	S <sup>(2)</sup>		500 <sup>(2)</sup>	D	\$47.3	2,170	I	By wife
Common Stock	01/03/2017	01/03/2017	M <sup>(2)</sup>		500 <sup>(2)</sup>	A	\$10.29	2,670	I	By wife
Common Stock	01/03/2017	01/03/2017	S <sup>(2)</sup>		500 <sup>(2)</sup>	D	\$48.8	2,170	I	By wife
Common Stock	01/04/2017	01/04/2017	M <sup>(1)</sup>		7,000 <sup>(1)</sup>	A	\$7.25	32,029	D	
Common Stock	01/04/2017	01/04/2017	S <sup>(1)</sup>		7,000 <sup>(1)</sup>	D	\$50.1	25,029	D	
Common Stock	01/04/2017	01/04/2017	M <sup>(2)</sup>		700 <sup>(2)</sup>	A	\$10.29	2,870	I	By wife
Common Stock	01/04/2017	01/04/2017	S <sup>(2)</sup>		700 <sup>(2)</sup>	D	\$50.1	2,170	I	By wife
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)	\$47.34	01/03/2017	01/03/2017	A		163,013		01/03/2018 <sup>(3)</sup>	01/02/2024	Common Stock	163,013	\$0	163,013	D	
Employee Stock Option (right to buy)	\$47.34	01/03/2017	01/03/2017	A		16,157		01/03/2018 <sup>(4)</sup>	01/02/2024	Common Stock	16,157	\$0	16,157	I	By wife
Employee Stock Option (right to buy)	\$7.25	01/03/2017	01/03/2017	M			10,000	01/03/2016	01/02/2019	Common Stock	10,000	\$0	83,462	D	
Employee Stock Option (right to buy)	\$10.29	01/03/2017	01/03/2017	M			1,000	01/03/2015	01/02/2018	Common Stock	1,000	\$0	4,500	I	By wife

**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	Amount or Number of Shares				
Employee Stock Option (right to buy)	\$7.25	01/04/2017	01/04/2017	M			7,000	01/03/2016	01/02/2019	Common Stock	7,000	\$0	76,462	D	
Employee Stock Option (right to buy)	\$10.29	01/04/2017	01/04/2017	M			700	01/03/2015	01/02/2018	Common Stock	700	\$0	3,800	I	By wife

**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 9/21/2015.
- 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 9/21/2015.
- 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 40,753 shares per year. Following this transaction, the option was exercisable as to 0 on 1/3/2017.
- Grant of 1/3/2017 to reporting person's wife 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 4,039 shares per year. Following this transaction, the option was exercisable as to 0 on 1/3/2017.

**Remarks:**

/s/Stanley T. Crooke

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.

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