

**FORM 5**

**UNITED STATES SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

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

Form 3 Holdings Reported.

Form 4 Transactions Reported.

**ANNUAL 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

OMB APPROVAL	
OMB Number:	3235-0362
Estimated average burden hours per response:	1.0

1. Name and Address of Reporting Person* <u>Hayden Michael R</u> _____ (Last) (First) (Middle) <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 Officer (give title below) Other (specify below)
	3. Statement for Issuer's Fiscal Year Ended (Month/Day/Year) <u>12/31/2022</u>	
	4. If Amendment, Date of Original Filed (Month/Day/Year)	6. Individual or Joint/Group Filing (Check Applicable Line) <input checked="" type="checkbox"/> Form filed by One Reporting Person 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 at end of Issuer's Fiscal Year (Instr. 3 and 4)	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Beneficial Ownership (Instr. 4)
				Amount	(A) or (D)	Price			
Common Stock							23,109	D	
Common Stock			3 <sup>(1)</sup>				2,000	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)
					(A)	(D)	Date Exercisable	Expiration Date					

**Explanation of Responses:**

1. These securities are held by Genworks 2 Consulting, Inc. ("Genworks 2"). The Reporting Person's spouse has sole voting and investment power with respect to the shares held by Genworks 2. Genworks 2 owned such shares of common stock on September 20, 2018, the date on which the reporting person became a director of Ionis Pharmaceuticals, Inc.

Patrick R. O'Neil, attorney-in-fact, Michael R. Hayden 02/14/2023

\*\* 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.