

**UNITED STATES SECURITIES AND EXCHANGE  
COMMISSION**

Washington, D.C. 20549

**INITIAL STATEMENT OF BENEFICIAL OWNERSHIP OF  
SECURITIES**

OMB APPROVAL

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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>Birchler Brian</u>  (Last) (First) (Middle) <u>2855 GAZELLE COURT</u>  (Street) <u>CARLSBAD CA 92010</u>  (City) (State) (Zip)	2. Date of Event Requiring Statement (Month/Day/Year) <u>03/14/2023</u>	3. Issuer Name and Ticker or Trading Symbol <u>IONIS PHARMACEUTICALS INC [ IONS ]</u>	
		4. Relationship of Reporting Person(s) to Issuer (Check all applicable) Director 10% Owner <input checked="" type="checkbox"/> Officer (give title below) Other (specify below) <u>EVP, Corp and Development Ops</u>	5. 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 Beneficially Owned**

1. Title of Security (Instr. 4)	2. Amount of Securities Beneficially Owned (Instr. 4)	3. Ownership Form: Direct (D) or Indirect (I) (Instr. 5)	4. Nature of Indirect Beneficial Ownership (Instr. 5)
<u>Common Stock</u>	<u>35,325</u>	<u>D</u>	

**Table II - Derivative Securities Beneficially Owned  
(e.g., puts, calls, warrants, options, convertible securities)**

1. Title of Derivative Security (Instr. 4)	2. Date Exercisable and Expiration Date (Month/Day/Year)		3. Title and Amount of Securities Underlying Derivative Security (Instr. 4)		4. Conversion or Exercise Price of Derivative Security	5. Ownership Form: Direct (D) or Indirect (I) (Instr. 5)	6. Nature of Indirect Beneficial Ownership (Instr. 5)
	Date Exercisable	Expiration Date	Title	Amount or Number of Shares			
<u>Non-Qualified Stock Option (right to buy)</u>	<u>(1)</u>	<u>01/02/2032</u>	<u>Common Stock</u>	<u>19,500</u>	<u>32.6</u>	<u>D</u>	
<u>Non-Qualified Stock Option (right to buy)</u>	<u>(2)</u>	<u>03/19/2032</u>	<u>Common Stock</u>	<u>15,000</u>	<u>35.25</u>	<u>D</u>	
<u>Non-Qualified Stock Option (right to buy)</u>	<u>(3)</u>	<u>01/02/2033</u>	<u>Common Stock</u>	<u>22,942</u>	<u>37.58</u>	<u>D</u>	
<u>Non-Qualified Stock Option (right to buy)</u>	<u>(4)</u>	<u>01/02/2024</u>	<u>Common Stock</u>	<u>26,982</u>	<u>47.34</u>	<u>D</u>	
<u>Non-Qualified Stock Option (right to buy)</u>	<u>(5)</u>	<u>01/01/2025</u>	<u>Common Stock</u>	<u>31,500</u>	<u>49.25</u>	<u>D</u>	
<u>Non-Qualified Stock Option (right to buy)</u>	<u>(6)</u>	<u>01/01/2026</u>	<u>Common Stock</u>	<u>23,900</u>	<u>53.77</u>	<u>D</u>	
<u>Non-Qualified Stock Option (right to buy)</u>	<u>(7)</u>	<u>01/03/2028</u>	<u>Common Stock</u>	<u>22,000</u>	<u>56.78</u>	<u>D</u>	
<u>Non-Qualified Stock Option (right to buy)</u>	<u>(8)</u>	<u>01/01/2027</u>	<u>Common Stock</u>	<u>26,063</u>	<u>60.89</u>	<u>D</u>	
<u>Non-Qualified Stock Option (right to buy)</u>	<u>(9)</u>	<u>01/01/2024</u>	<u>Common Stock</u>	<u>15,500</u>	<u>61.57</u>	<u>D</u>	
<u>Performance Restricted Stock Units<sup>(10)</sup></u>	<u>(11)</u>	<u>(11)</u>	<u>Common Stock</u>	<u>14,338</u>	<u>0.0</u>	<u>D</u>	
<u>Restricted Stock Unit<sup>(12)</sup></u>	<u>01/15/2024<sup>(13)</sup></u>	<u>01/15/2024<sup>(13)</sup></u>	<u>Common Stock</u>	<u>2,896</u>	<u>0.0</u>	<u>D</u>	
<u>Restricted Stock Unit<sup>(12)</sup></u>	<u>01/15/2024<sup>(14)</sup></u>	<u>01/15/2025<sup>(14)</sup></u>	<u>Common Stock</u>	<u>4,888</u>	<u>0.0</u>	<u>D</u>	

**Table II - Derivative Securities Beneficially Owned  
(e.g., puts, calls, warrants, options, convertible securities)**

1. Title of Derivative Security (Instr. 4)	2. Date Exercisable and Expiration Date (Month/Day/Year)		3. Title and Amount of Securities Underlying Derivative Security (Instr. 4)		4. Conversion or Exercise Price of Derivative Security	5. Ownership Form: Direct (D) or Indirect (I) (Instr. 5)	6. Nature of Indirect Beneficial Ownership (Instr. 5)
	Date Exercisable	Expiration Date	Title	Amount or Number of Shares			
Restricted Stock Unit <sup>(12)</sup>	01/15/2024 <sup>(15)</sup>	01/15/2026 <sup>(15)</sup>	Common Stock	7,312	0.0	D	
Restricted Stock Unit <sup>(12)</sup>	04/15/2023 <sup>(16)</sup>	04/15/2026 <sup>(16)</sup>	Common Stock	7,500	0.0	D	
Restricted Stock Unit <sup>(12)</sup>	01/15/2024 <sup>(17)</sup>	01/15/2027 <sup>(17)</sup>	Common Stock	17,207	0.0	D	

**Explanation of Responses:**

- Grant on 01/03/2022 to reporting person of stock options under the Ionis Pharmaceuticals, Inc. Amended and Restated 2011 Equity Incentive Plan. 25% of the shares subject to the option will be vested and become exercisable on 01/03/2023. Thereafter, the remaining shares subject to the option vested and became exercisable in 36 equal monthly installments. The option is exercisable as to 5,687 shares on 03/14/2023.
- Grant on 03/20/2022 to reporting person of stock options under the Ionis Pharmaceuticals, Inc. Amended and Restated 2011 Equity Incentive Plan. 25% of the shares subject to the option will be vested and become exercisable on 03/20/2023. Thereafter, the remaining shares subject to the option vested and became exercisable in 36 equal monthly installments. The option is exercisable as to 0 shares on 03/14/2023.
- Grant on 01/03/2023 to reporting person of stock options under the Ionis Pharmaceuticals, Inc. Amended and Restated 2011 Equity Incentive Plan. 25% of the shares subject to the option will be vested and become exercisable on 01/03/2024. Thereafter, the remaining shares subject to the option vested and became exercisable in 36 equal monthly installments. The option is exercisable as to 0 shares on 03/14/2023.
- Grant on 01/03/2017 to reporting person of stock options under the Ionis Pharmaceuticals, Inc. Amended and Restated 2011 Equity Incentive Plan. 25% of the shares subject to the option vested and became exercisable on 01/03/2018. Thereafter, the remaining shares subject to the option vested and became exercisable in 36 equal monthly installments. The option is exercisable as to 26,982 shares on 03/14/2023.
- Grant on 01/02/2018 to reporting person of stock options under the Ionis Pharmaceuticals, Inc. Amended and Restated 2011 Equity Incentive Plan. 25% of the shares subject to the option vested and became exercisable on 01/02/2019. Thereafter, the remaining shares subject to the option vested and became exercisable in 36 equal monthly installments. The option is exercisable as to 31,500 shares on 03/14/2023.
- Grant on 01/02/2019 to reporting person of stock options under the Ionis Pharmaceuticals, Inc. Amended and Restated 2011 Equity Incentive Plan. 25% of the shares subject to the option vested and became exercisable on 01/02/2020. Thereafter, the remaining shares subject to the option vested and became exercisable in 36 equal monthly installments. The option is exercisable as to 23,900 shares on 03/14/2023.
- Grant on 01/04/2021 to reporting person of stock options under the Ionis Pharmaceuticals, Inc. Amended and Restated 2011 Equity Incentive Plan. 25% of the shares subject to the option will be vested and become exercisable on 01/04/2022. Thereafter, the remaining shares subject to the option vested and became exercisable in 36 equal monthly installments. The option is exercisable as to 11,916 shares on 03/14/2023.
- Grant on 01/02/2020 to reporting person of stock options under the Ionis Pharmaceuticals, Inc. Amended and Restated 2011 Equity Incentive Plan. 25% of the shares subject to the option will be vested and become exercisable on 01/02/2021. Thereafter, the remaining shares subject to the option vested and became exercisable in 36 equal monthly installments. The option is exercisable as to 20,633 shares on 03/14/2023.
- Grant on 01/02/2015 to reporting person of stock options under the Ionis Pharmaceuticals, Inc. Amended and Restated 2011 Equity Incentive Plan. 25% of the shares subject to the option vested and became exercisable on 01/02/2016. Thereafter, the remaining shares subject to the option vested and became exercisable in 36 equal monthly installments. The option is exercisable as to 15,500 shares on 03/14/2023.
- Grant to reporting person of Performance Restricted Stock Units under the Ionis Pharmaceuticals, Inc. Amended and Restated 2011 Equity Incentive Plan.
- Represents an award of performance based restricted stock units ("PRSUs"). The PRSUs may vest at the end of the three-year performance period following the date of grant based on the Issuer's relative total shareholder return as compared to a peer group of companies. The number of PRSUs reported represents the maximum that may be earned, which is 200% of the target number. No number of PRSUs is guaranteed to vest and the actual number of PRSUs that will vest at the end of the performance period may be anywhere from zero to the amount stated.
- Each restricted stock unit represents a contingent right to receive one share of Isis common stock, or its equivalent cash value.
- The restricted stock units vest in four equal annual installments, the first installment vesting on January 15, 2021. Upon vesting, the restricted stock units will be paid out in whole shares of Ionis common stock or cash as may be determined by the Company. The RSU shall be fully vested on January 15, 2024.
- The restricted stock units vest in four equal annual installments, the first installment vesting on January 15, 2022. Upon vesting, the restricted stock units will be paid out in whole shares of Ionis common stock or cash as may be determined by the Company. The RSU shall be fully vested on January 15, 2025.
- The restricted stock units vest in four equal annual installments, the first installment vesting on January 15, 2023. Upon vesting, the restricted stock units will be paid out in whole shares of Ionis common stock or cash as may be determined by the Company. The RSU shall be fully vested on January 15, 2026.
- The restricted stock units vest in four equal annual installments, the first installment vesting on April 15, 2022. Upon vesting, the restricted stock units will be paid out in whole shares of Ionis common stock or cash as may be determined by the Company. The RSU shall be fully vested on April 15, 2026.
- The restricted stock units vest in four equal annual installments, the first installment vesting on January 15, 2023. Upon vesting, the restricted stock units will be paid out in whole shares of Ionis common stock or cash as may be determined by the Company. The RSU shall be fully vested on January 15, 2027.

By: Patrick R. O'Neil,  
attorney-in-fact For: Brian 03/24/2023  
Birchler

\*\* 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 5 (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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