

Form 5500 Department of the Treasury Internal Revenue Service Department of Labor Employee Benefits Security Administration Pension Benefit Guaranty Corporation	Annual Return/Report of Employee Benefit Plan This form is required to be filed for employee benefit plans under sections 104 and 4065 of the Employee Retirement Income Security Act of 1974 (ERISA) and sections 6057(b) and 6058(a) of the Internal Revenue Code (the Code). ▶ Complete all entries in accordance with the instructions to the Form 5500.	OMB Nos. 1210-0110 1210-0089 2021 This Form is Open to Public Inspection
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Part I	Annual Report Identification Information
For calendar plan year 2021 or fiscal plan year beginning <u>01/01/2021</u> and ending <u>12/31/2021</u>	
A This return/report is for:	☐ a multiemployer plan ☐ a multiple-employer plan (Filers checking this box must attach a list of participating employer information in accordance with the form instructions.) ☒ a single-employer plan ☐ a DFE (specify) _____
B This return/report is:	☐ the first return/report ☐ the final return/report ☐ an amended return/report ☐ a short plan year return/report (less than 12 months)
C If the plan is a collectively-bargained plan, check here.	☐
D Check box if filing under:	☒ Form 5558 ☐ automatic extension ☐ the DFVC program ☐ special extension (enter description)
E If this is a retroactively adopted plan permitted by SECURE Act section 201, check here.	☐

Part II	Basic Plan Information—enter all requested information				
1a Name of plan <u>IONIS PHARMACEUTICALS 401(K) PLAN</u>	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 80%;">1b Three-digit plan number (PN) ▶</td> <td style="width: 20%; text-align: center;"><u>001</u></td> </tr> <tr> <td colspan="2">1c Effective date of plan <u>01/01/1991</u></td> </tr> </table>	1b Three-digit plan number (PN) ▶	<u>001</u>	1c Effective date of plan <u>01/01/1991</u>	
1b Three-digit plan number (PN) ▶	<u>001</u>				
1c Effective date of plan <u>01/01/1991</u>					
2a Plan sponsor's name (employer, if for a single-employer plan) Mailing address (include room, apt., suite no. and street, or P.O. Box) City or town, state or province, country, and ZIP or foreign postal code (if foreign, see instructions) <u>IONIS PHARMACEUTICALS, INC.</u> <u>2855 GAZELLE COURT</u> <u>CARLSBAD, CA 92010</u>	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td>2b Employer Identification Number (EIN) <u>33-0336973</u></td> </tr> <tr> <td>2c Plan Sponsor's telephone number <u>760-603-3848</u></td> </tr> <tr> <td>2d Business code (see instructions) <u>541700</u></td> </tr> </table>	2b Employer Identification Number (EIN) <u>33-0336973</u>	2c Plan Sponsor's telephone number <u>760-603-3848</u>	2d Business code (see instructions) <u>541700</u>	
2b Employer Identification Number (EIN) <u>33-0336973</u>					
2c Plan Sponsor's telephone number <u>760-603-3848</u>					
2d Business code (see instructions) <u>541700</u>					

Caution: A penalty for the late or incomplete filing of this return/report will be assessed unless reasonable cause is established.

Under penalties of perjury and other penalties set forth in the instructions, I declare that I have examined this return/report, including accompanying schedules, statements and attachments, as well as the electronic version of this return/report, and to the best of my knowledge and belief, it is true, correct, and complete.

SIGN HERE	Filed with authorized/valid electronic signature.	10/12/2022	SHANNON DEVERS
	Signature of plan administrator	Date	Enter name of individual signing as plan administrator
SIGN HERE	Signature of employer/plan sponsor	Date	Enter name of individual signing as employer or plan sponsor
SIGN HERE	Signature of DFE	Date	Enter name of individual signing as DFE

For Paperwork Reduction Act Notice, see the Instructions for Form 5500.

3a Plan administrator's name and address ☒ Same as Plan Sponsor		3b Administrator's EIN	
		3c Administrator's telephone number	
4 If the name and/or EIN of the plan sponsor or the plan name has changed since the last return/report filed for this plan, enter the plan sponsor's name, EIN, the plan name and the plan number from the last return/report: a Sponsor's name c Plan Name		4b EIN 4d PN	
5 Total number of participants at the beginning of the plan year		5	888
6 Number of participants as of the end of the plan year unless otherwise stated (welfare plans complete only lines 6a(1) , 6a(2) , 6b , 6c , and 6d).			
a(1) Total number of active participants at the beginning of the plan year.....		6a(1)	571
a(2) Total number of active participants at the end of the plan year		6a(2)	609
b Retired or separated participants receiving benefits.....		6b	3
c Other retired or separated participants entitled to future benefits		6c	400
d Subtotal. Add lines 6a(2) , 6b , and 6c		6d	1012
e Deceased participants whose beneficiaries are receiving or are entitled to receive benefits.		6e	0
f Total. Add lines 6d and 6e		6f	1012
g Number of participants with account balances as of the end of the plan year (only defined contribution plans complete this item)		6g	1008
h Number of participants who terminated employment during the plan year with accrued benefits that were less than 100% vested		6h	0
7 Enter the total number of employers obligated to contribute to the plan (only multiemployer plans complete this item).....		7	
8a If the plan provides pension benefits, enter the applicable pension feature codes from the List of Plan Characteristics Codes in the instructions: 2F 2G 2J 2K 2R 2S 2T 3D 3F 3H			
b If the plan provides welfare benefits, enter the applicable welfare feature codes from the List of Plan Characteristics Codes in the instructions:			
9a Plan funding arrangement (check all that apply) (1) ☐ Insurance (2) ☐ Code section 412(e)(3) insurance contracts (3) ☒ Trust (4) ☐ General assets of the sponsor		9b Plan benefit arrangement (check all that apply) (1) ☐ Insurance (2) ☐ Code section 412(e)(3) insurance contracts (3) ☒ Trust (4) ☐ General assets of the sponsor	
10 Check all applicable boxes in 10a and 10b to indicate which schedules are attached, and, where indicated, enter the number attached. (See instructions)			
a Pension Schedules (1) ☒ R (Retirement Plan Information) (2) ☐ MB (Multiemployer Defined Benefit Plan and Certain Money Purchase Plan Actuarial Information) - signed by the plan actuary (3) ☐ SB (Single-Employer Defined Benefit Plan Actuarial Information) - signed by the plan actuary		b General Schedules (1) ☒ H (Financial Information) (2) ☐ I (Financial Information – Small Plan) (3) ☐ <u>0</u> A (Insurance Information) (4) ☒ C (Service Provider Information) (5) ☒ D (DFE/Participating Plan Information) (6) ☐ G (Financial Transaction Schedules)	

Part III Form M-1 Compliance Information (to be completed by welfare benefit plans)

11a If the plan provides welfare benefits, was the plan subject to the Form M-1 filing requirements during the plan year? (See instructions and 29 CFR 2520.101-2.) ☐ Yes ☐ No

If "Yes" is checked, complete lines 11b and 11c.

11b Is the plan currently in compliance with the Form M-1 filing requirements? (See instructions and 29 CFR 2520.101-2.) ☐ Yes ☐ No

11c Enter the Receipt Confirmation Code for the 2021 Form M-1 annual report. If the plan was not required to file the 2021 Form M-1 annual report, enter the Receipt Confirmation Code for the most recent Form M-1 that was required to be filed under the Form M-1 filing requirements. (Failure to enter a valid Receipt Confirmation Code will subject the Form 5500 filing to rejection as incomplete.)

Receipt Confirmation Code _____

SCHEDULE C (Form 5500) Department of the Treasury Internal Revenue Service Department of Labor Employee Benefits Security Administration Pension Benefit Guaranty Corporation	Service Provider Information This schedule is required to be filed under section 104 of the Employee Retirement Income Security Act of 1974 (ERISA). ▶ File as an attachment to Form 5500.	OMB No. 1210-0110
		2021
		This Form is Open to Public Inspection.

For calendar plan year 2021 or fiscal plan year beginning 01/01/2021 and ending 12/31/2021		
A Name of plan IONIS PHARMACEUTICALS 401(K) PLAN	B Three-digit plan number (PN) ▶	001
C Plan sponsor's name as shown on line 2a of Form 5500 IONIS PHARMACEUTICALS, INC.	D Employer Identification Number (EIN) 33-0336973	

Part I	Service Provider Information (see instructions)
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You must complete this Part, in accordance with the instructions, to report the information required for **each person** who received, directly or indirectly, \$5,000 or more in total compensation (i.e., money or anything else of monetary value) in connection with services rendered to the plan or the person's position with the plan during the plan year. If a person received **only** eligible indirect compensation for which the plan received the required disclosures, you are required to answer line 1 but are not required to include that person when completing the remainder of this Part.

1 Information on Persons Receiving Only Eligible Indirect Compensation

- a** Check "Yes" or "No" to indicate whether you are excluding a person from the remainder of this Part because they received only eligible indirect compensation for which the plan received the required disclosures (see instructions for definitions and conditions)..... ☒ Yes ☐ No
- b** If you answered line 1a "Yes," enter the name and EIN or address of each person providing the required disclosures for the service providers who received only eligible indirect compensation. Complete as many entries as needed (see instructions).

(b) Enter name and EIN or address of person who provided you disclosures on eligible indirect compensation
FIDELITY INVESTMENTS INSTITUTIONAL
04-2647786

(b) Enter name and EIN or address of person who provided you disclosures on eligible indirect compensation

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(b) Enter name and EIN or address of person who provided you disclosures on eligible indirect compensation

2. Information on Other Service Providers Receiving Direct or Indirect Compensation. Except for those persons for whom you answered "Yes" to line 1a above, complete as many entries as needed to list each person receiving, directly or indirectly, \$5,000 or more in total compensation (i.e., money or anything else of value) in connection with services rendered to the plan or their position with the plan during the plan year. (See instructions).

(a) Enter name and EIN or address (see instructions)

WELLS FARGO CLEARING SERVICES LLC

23-2384840

(b) Service Code(s)	(c) Relationship to employer, employee organization, or person known to be a party-in-interest	(d) Enter direct compensation paid by the plan. If none, enter -0-.	(e) Did service provider receive indirect compensation? (sources other than plan or plan sponsor)	(f) Did indirect compensation include eligible indirect compensation, for which the plan received the required disclosures?	(g) Enter total indirect compensation received by service provider excluding eligible indirect compensation for which you answered "Yes" to element (f). If none, enter -0-.	(h) Did the service provider give you a formula instead of an amount or estimated amount?
27	ADVISOR	83404	Yes ☐ No ☒	Yes ☐ No ☐		Yes ☐ No ☐

(a) Enter name and EIN or address (see instructions)

FIRST LIGHT RETIREMENT LLC

86-3483132

(b) Service Code(s)	(c) Relationship to employer, employee organization, or person known to be a party-in-interest	(d) Enter direct compensation paid by the plan. If none, enter -0-.	(e) Did service provider receive indirect compensation? (sources other than plan or plan sponsor)	(f) Did indirect compensation include eligible indirect compensation, for which the plan received the required disclosures?	(g) Enter total indirect compensation received by service provider excluding eligible indirect compensation for which you answered "Yes" to element (f). If none, enter -0-.	(h) Did the service provider give you a formula instead of an amount or estimated amount?
27	ADVISOR	79042	Yes ☐ No ☒	Yes ☐ No ☐		Yes ☐ No ☐

(a) Enter name and EIN or address (see instructions)

FIDELITY INVESTMENTS INSTITUTIONAL

04-2647786

(b) Service Code(s)	(c) Relationship to employer, employee organization, or person known to be a party-in-interest	(d) Enter direct compensation paid by the plan. If none, enter -0-.	(e) Did service provider receive indirect compensation? (sources other than plan or plan sponsor)	(f) Did indirect compensation include eligible indirect compensation, for which the plan received the required disclosures?	(g) Enter total indirect compensation received by service provider excluding eligible indirect compensation for which you answered "Yes" to element (f). If none, enter -0-.	(h) Did the service provider give you a formula instead of an amount or estimated amount?
37 60 64 65 71	RECORDKEEPER	-89574	Yes ☒ No ☐	Yes ☒ No ☐	0	Yes ☒ No ☐

2. Information on Other Service Providers Receiving Direct or Indirect Compensation. Except for those persons for whom you answered "Yes" to line 1a above, complete as many entries as needed to list each person receiving, directly or indirectly, \$5,000 or more in total compensation (i.e., money or anything else of value) in connection with services rendered to the plan or their position with the plan during the plan year. (See instructions).

(a) Enter name and EIN or address (see instructions)

(b) Service Code(s)	(c) Relationship to employer, employee organization, or person known to be a party-in-interest	(d) Enter direct compensation paid by the plan. If none, enter -0-.	(e) Did service provider receive indirect compensation? (sources other than plan or plan sponsor)	(f) Did indirect compensation include eligible indirect compensation, for which the plan received the required disclosures?	(g) Enter total indirect compensation received by service provider excluding eligible indirect compensation for which you answered "Yes" to element (f). If none, enter -0-.	(h) Did the service provider give you a formula instead of an amount or estimated amount?
			Yes ☐ No ☐	Yes ☐ No ☐		Yes ☐ No ☐

(a) Enter name and EIN or address (see instructions)

(b) Service Code(s)	(c) Relationship to employer, employee organization, or person known to be a party-in-interest	(d) Enter direct compensation paid by the plan. If none, enter -0-.	(e) Did service provider receive indirect compensation? (sources other than plan or plan sponsor)	(f) Did indirect compensation include eligible indirect compensation, for which the plan received the required disclosures?	(g) Enter total indirect compensation received by service provider excluding eligible indirect compensation for which you answered "Yes" to element (f). If none, enter -0-.	(h) Did the service provider give you a formula instead of an amount or estimated amount?
			Yes ☐ No ☐	Yes ☐ No ☐		Yes ☐ No ☐

(a) Enter name and EIN or address (see instructions)

(b) Service Code(s)	(c) Relationship to employer, employee organization, or person known to be a party-in-interest	(d) Enter direct compensation paid by the plan. If none, enter -0-.	(e) Did service provider receive indirect compensation? (sources other than plan or plan sponsor)	(f) Did indirect compensation include eligible indirect compensation, for which the plan received the required disclosures?	(g) Enter total indirect compensation received by service provider excluding eligible indirect compensation for which you answered "Yes" to element (f). If none, enter -0-.	(h) Did the service provider give you a formula instead of an amount or estimated amount?
			Yes ☐ No ☐	Yes ☐ No ☐		Yes ☐ No ☐

Part I Service Provider Information (continued)

3. If you reported on line 2 receipt of indirect compensation, other than eligible indirect compensation, by a service provider, and the service provider is a fiduciary or provides contract administrator, consulting, custodial, investment advisory, investment management, broker, or recordkeeping services, answer the following questions for (a) each source from whom the service provider received \$1,000 or more in indirect compensation and (b) each source for whom the service provider gave you a formula used to determine the indirect compensation instead of an amount or estimated amount of the indirect compensation. Complete as many entries as needed to report the required information for each source.

(a) Enter service provider name as it appears on line 2	(b) Service Codes (see instructions)	(c) Enter amount of indirect compensation
FIDELITY INVESTMENTS INSTITUTIONAL	60	0
(d) Enter name and EIN (address) of source of indirect compensation	(e) Describe the indirect compensation, including any formula used to determine the service provider's eligibility for or the amount of the indirect compensation.	
AB LG CAP GRTH I - ALLIANCEBERNSTE 18, RUE EUGNE RUPPERT LUXEMBOURG, LU L-245 LU	0.15%	
(a) Enter service provider name as it appears on line 2	(b) Service Codes (see instructions)	(c) Enter amount of indirect compensation
FIDELITY INVESTMENTS INSTITUTIONAL	60	0
(d) Enter name and EIN (address) of source of indirect compensation	(e) Describe the indirect compensation, including any formula used to determine the service provider's eligibility for or the amount of the indirect compensation.	
BLK RK MIDCAP GRTH IS - BNY MELLON 301 BELLEVUE PARKWAY WILMINGTON, DE 19809	0.25%	
(a) Enter service provider name as it appears on line 2	(b) Service Codes (see instructions)	(c) Enter amount of indirect compensation
FIDELITY INVESTMENTS INSTITUTIONAL	60	0
(d) Enter name and EIN (address) of source of indirect compensation	(e) Describe the indirect compensation, including any formula used to determine the service provider's eligibility for or the amount of the indirect compensation.	
C&S INST REALTY SHS - DST ASSET MA 430 W 7TH STREET STE 219432 KANSAS CITY, MO 64105	0.10%	

Part I Service Provider Information (continued)

3. If you reported on line 2 receipt of indirect compensation, other than eligible indirect compensation, by a service provider, and the service provider is a fiduciary or provides contract administrator, consulting, custodial, investment advisory, investment management, broker, or recordkeeping services, answer the following questions for (a) each source from whom the service provider received \$1,000 or more in indirect compensation and (b) each source for whom the service provider gave you a formula used to determine the indirect compensation instead of an amount or estimated amount of the indirect compensation. Complete as many entries as needed to report the required information for each source.

(a) Enter service provider name as it appears on line 2	(b) Service Codes (see instructions)	(c) Enter amount of indirect compensation
FIDELITY INVESTMENTS INSTITUTIONAL	60	0
(d) Enter name and EIN (address) of source of indirect compensation	(e) Describe the indirect compensation, including any formula used to determine the service provider's eligibility for or the amount of the indirect compensation.	
CBA APPR I - BNY MELLON INVESTMENT 301 BELLEVUE PARKWAY WILMINGTON, DE 19809	0.15%	
(a) Enter service provider name as it appears on line 2	(b) Service Codes (see instructions)	(c) Enter amount of indirect compensation
FIDELITY INVESTMENTS INSTITUTIONAL	60	0
(d) Enter name and EIN (address) of source of indirect compensation	(e) Describe the indirect compensation, including any formula used to determine the service provider's eligibility for or the amount of the indirect compensation.	
DAVIS FINANCIAL Y - DST ASSET MANA 430 W 7TH STREET STE 219432 KANSAS CITY, MO 64105	0.15%	
(a) Enter service provider name as it appears on line 2	(b) Service Codes (see instructions)	(c) Enter amount of indirect compensation
FIDELITY INVESTMENTS INSTITUTIONAL	60	0
(d) Enter name and EIN (address) of source of indirect compensation	(e) Describe the indirect compensation, including any formula used to determine the service provider's eligibility for or the amount of the indirect compensation.	
J H ENTERPRISE T - JANUS SERVICES 43-1804048	0.35%	

Part I Service Provider Information (continued)

3. If you reported on line 2 receipt of indirect compensation, other than eligible indirect compensation, by a service provider, and the service provider is a fiduciary or provides contract administrator, consulting, custodial, investment advisory, investment management, broker, or recordkeeping services, answer the following questions for (a) each source from whom the service provider received \$1,000 or more in indirect compensation and (b) each source for whom the service provider gave you a formula used to determine the indirect compensation instead of an amount or estimated amount of the indirect compensation. Complete as many entries as needed to report the required information for each source.

(a) Enter service provider name as it appears on line 2	(b) Service Codes (see instructions)	(c) Enter amount of indirect compensation
FIDELITY INVESTMENTS INSTITUTIONAL	60	0
(d) Enter name and EIN (address) of source of indirect compensation	(e) Describe the indirect compensation, including any formula used to determine the service provider's eligibility for or the amount of the indirect compensation.	
PIF EQUITY INC INST - PRINCIPAL SH 620 COOLIDGE DR FOLSOM, CA 95630-3183	0.10%	
(a) Enter service provider name as it appears on line 2	(b) Service Codes (see instructions)	(c) Enter amount of indirect compensation
FIDELITY INVESTMENTS INSTITUTIONAL	60	0
(d) Enter name and EIN (address) of source of indirect compensation	(e) Describe the indirect compensation, including any formula used to determine the service provider's eligibility for or the amount of the indirect compensation.	
PUTNAM STABLE VALUE 101 SEAPORT BOULEVARD, SUITE 500 BOSTON, MA 02210	0.25%	
(a) Enter service provider name as it appears on line 2	(b) Service Codes (see instructions)	(c) Enter amount of indirect compensation
FIDELITY INVESTMENTS INSTITUTIONAL	60	0
(d) Enter name and EIN (address) of source of indirect compensation	(e) Describe the indirect compensation, including any formula used to determine the service provider's eligibility for or the amount of the indirect compensation.	
PUTNAM STABLE VALUE 101 SEAPORT BOULEVARD, SUITE 500 BOSTON, MA 02210	0.10%	

Part I Service Provider Information (continued)

3. If you reported on line 2 receipt of indirect compensation, other than eligible indirect compensation, by a service provider, and the service provider is a fiduciary or provides contract administrator, consulting, custodial, investment advisory, investment management, broker, or recordkeeping services, answer the following questions for (a) each source from whom the service provider received \$1,000 or more in indirect compensation and (b) each source for whom the service provider gave you a formula used to determine the indirect compensation instead of an amount or estimated amount of the indirect compensation. Complete as many entries as needed to report the required information for each source.

(a) Enter service provider name as it appears on line 2	(b) Service Codes (see instructions)	(c) Enter amount of indirect compensation
FIDELITY INVESTMENTS INSTITUTIONAL	60	0
(d) Enter name and EIN (address) of source of indirect compensation	(e) Describe the indirect compensation, including any formula used to determine the service provider's eligibility for or the amount of the indirect compensation.	
VICTORY S ESTB VAL I - FIS INVESTO FAITH INVESTOR SERVICES, LLC 14785 PRESTON ROAD, SUITE 1000 DALLAS, TX 75254	0.10%	
(a) Enter service provider name as it appears on line 2	(b) Service Codes (see instructions)	(c) Enter amount of indirect compensation
FIDELITY INVESTMENTS INSTITUTIONAL	60	0
(d) Enter name and EIN (address) of source of indirect compensation	(e) Describe the indirect compensation, including any formula used to determine the service provider's eligibility for or the amount of the indirect compensation.	
ARTISAN DEVELOPING WORLD FD INVEST 875 EAST WISCONSIN AVENUE SUITE 800 MILWAUKEE, WI 53202	0.39%	
(a) Enter service provider name as it appears on line 2	(b) Service Codes (see instructions)	(c) Enter amount of indirect compensation
FIDELITY INVESTMENTS INSTITUTIONAL	60	0
(d) Enter name and EIN (address) of source of indirect compensation	(e) Describe the indirect compensation, including any formula used to determine the service provider's eligibility for or the amount of the indirect compensation.	
OSTERWEIS EMERGING OPPORTUNITY FUN 777 E. WISCONSIN AVE 4TH FL MILWAUKEE, WI 53202	0.10%	

Part II Service Providers Who Fail or Refuse to Provide Information

4 Provide, to the extent possible, the following information for each service provider who failed or refused to provide the information necessary to complete this Schedule.

(a) Enter name and EIN or address of service provider (see instructions)	(b) Nature of Service Code(s)	(c) Describe the information that the service provider failed or refused to provide
(a) Enter name and EIN or address of service provider (see instructions)	(b) Nature of Service Code(s)	(c) Describe the information that the service provider failed or refused to provide
(a) Enter name and EIN or address of service provider (see instructions)	(b) Nature of Service Code(s)	(c) Describe the information that the service provider failed or refused to provide
(a) Enter name and EIN or address of service provider (see instructions)	(b) Nature of Service Code(s)	(c) Describe the information that the service provider failed or refused to provide
(a) Enter name and EIN or address of service provider (see instructions)	(b) Nature of Service Code(s)	(c) Describe the information that the service provider failed or refused to provide
(a) Enter name and EIN or address of service provider (see instructions)	(b) Nature of Service Code(s)	(c) Describe the information that the service provider failed or refused to provide

Part III Termination Information on Accountants and Enrolled Actuaries (see instructions)
(complete as many entries as needed)

a Name:	b EIN:
c Position:	
d Address:	e Telephone:

Explanation:

a Name:	b EIN:
c Position:	
d Address:	e Telephone:

Explanation:

a Name:	b EIN:
c Position:	
d Address:	e Telephone:

Explanation:

a Name:	b EIN:
c Position:	
d Address:	e Telephone:

Explanation:

a Name:	b EIN:
c Position:	
d Address:	e Telephone:

Explanation:

SCHEDULE D (Form 5500) Department of the Treasury Internal Revenue Service Department of Labor Employee Benefits Security Administration		DFE/Participating Plan Information This schedule is required to be filed under section 104 of the Employee Retirement Income Security Act of 1974 (ERISA). ▶ File as an attachment to Form 5500.		OMB No. 1210-0110 2021 This Form is Open to Public Inspection.	
For calendar plan year 2021 or fiscal plan year beginning 01/01/2021 and ending 12/31/2021					
A Name of plan IONIS PHARMACEUTICALS 401(K) PLAN				B Three-digit plan number (PN) ▶ 001	
C Plan or DFE sponsor's name as shown on line 2a of Form 5500 IONIS PHARMACEUTICALS, INC.				D Employer Identification Number (EIN) 33-0336973	
Part I Information on interests in MTIAs, CCTs, PSAs, and 103-12 IEs (to be completed by plans and DFEs) (Complete as many entries as needed to report all interests in DFEs)					
a Name of MTIA, CCT, PSA, or 103-12 IE: PUTNAM STABLE VALUE					
b Name of sponsor of entity listed in (a): PUTNAM FIDUCIARY TRUST COMPANY					
c EIN-PN 04-3159710-202		d Entity code C		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions) 12777530	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT, PSA, or 103-12 IE at end of year (see instructions)	
a Name of MTIA, CCT, PSA, or 103-12 IE:					
b Name of sponsor of entity listed in (a):					
c EIN-PN		d Entity code		e Dollar value of interest in MTIA, CCT,	

a Name of MTIA, CCT, PSA, or 103-12 IE:**b** Name of sponsor of entity listed in (a):**c** EIN-PN**d** Entity
code**e** Dollar value of interest in MTIA, CCT, PSA, or
103-12 IE at end of year (see instructions)**a** Name of MTIA, CCT, PSA, or 103-12 IE:**b** Name of sponsor of entity listed in (a):**c** EIN-PN**d** Entity
code**e** Dollar value of interest in MTIA, CCT, PSA, or
103-12 IE at end of year (see instructions)**a** Name of MTIA, CCT, PSA, or 103-12 IE:**b** Name of sponsor of entity listed in (a):**c** EIN-PN**d** Entity
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103-12 IE at end of year (see instructions)**a** Name of MTIA, CCT, PSA, or 103-12 IE:**b** Name of sponsor of entity listed in (a):**c** EIN-PN**d** Entity
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103-12 IE at end of year (see instructions)**a** Name of MTIA, CCT, PSA, or 103-12 IE:**b** Name of sponsor of entity listed in (a):**c** EIN-PN**d** Entity
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103-12 IE at end of year (see instructions)**a** Name of MTIA, CCT, PSA, or 103-12 IE:**b** Name of sponsor of entity listed in (a):**c** EIN-PN**d** Entity
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103-12 IE at end of year (see instructions)**a** Name of MTIA, CCT, PSA, or 103-12 IE:**b** Name of sponsor of entity listed in (a):**c** EIN-PN**d** Entity
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103-12 IE at end of year (see instructions)**a** Name of MTIA, CCT, PSA, or 103-12 IE:**b** Name of sponsor of entity listed in (a):**c** EIN-PN**d** Entity
code**e** Dollar value of interest in MTIA, CCT, PSA, or
103-12 IE at end of year (see instructions)**a** Name of MTIA, CCT, PSA, or 103-12 IE:**b** Name of sponsor of entity listed in (a):**c** EIN-PN**d** Entity
code**e** Dollar value of interest in MTIA, CCT, PSA, or
103-12 IE at end of year (see instructions)**a** Name of MTIA, CCT, PSA, or 103-12 IE:**b** Name of sponsor of entity listed in (a):**c** EIN-PN**d** Entity
code**e** Dollar value of interest in MTIA, CCT, PSA, or
103-12 IE at end of year (see instructions)

Part II Information on Participating Plans (to be completed by DFEs)

(Complete as many entries as needed to report all participating plans)

a Plan name**b** Name of
plan sponsor**c** EIN-PN**a** Plan name**b** Name of
plan sponsor**c** EIN-PN**a** Plan name**b** Name of
plan sponsor**c** EIN-PN**a** Plan name**b** Name of
plan sponsor**c** EIN-PN**a** Plan name**b** Name of
plan sponsor**c** EIN-PN**a** Plan name**b** Name of
plan sponsor**c** EIN-PN**a** Plan name**b** Name of
plan sponsor**c** EIN-PN**a** Plan name**b** Name of
plan sponsor**c** EIN-PN**a** Plan name**b** Name of
plan sponsor**c** EIN-PN**a** Plan name**b** Name of
plan sponsor**c** EIN-PN**a** Plan name**b** Name of
plan sponsor**c** EIN-PN**a** Plan name**b** Name of
plan sponsor**c** EIN-PN

SCHEDULE H (Form 5500) Department of the Treasury Internal Revenue Service Department of Labor Employee Benefits Security Administration Pension Benefit Guaranty Corporation	Financial Information This schedule is required to be filed under section 104 of the Employee Retirement Income Security Act of 1974 (ERISA), and section 6058(a) of the Internal Revenue Code (the Code). ► File as an attachment to Form 5500.	OMB No. 1210-0110 2021 This Form is Open to Public Inspection
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For calendar plan year 2021 or fiscal plan year beginning <u>01/01/2021</u> and ending <u>12/31/2021</u>		
A Name of plan <u>IONIS PHARMACEUTICALS 401(K) PLAN</u>	B Three-digit plan number (PN) ►	<u>001</u>
C Plan sponsor's name as shown on line 2a of Form 5500 <u>IONIS PHARMACEUTICALS, INC.</u>	D Employer Identification Number (EIN) <u>33-0336973</u>	

Part I	Asset and Liability Statement
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1 Current value of plan assets and liabilities at the beginning and end of the plan year. Combine the value of plan assets held in more than one trust. Report the value of the plan's interest in a commingled fund containing the assets of more than one plan on a line-by-line basis unless the value is reportable on lines 1c(9) through 1c(14). Do not enter the value of that portion of an insurance contract which guarantees, during this plan year, to pay a specific dollar benefit at a future date. **Round off amounts to the nearest dollar.** MTIAs, CCTs, PSAs, and 103-12 IEs do not complete lines 1b(1), 1b(2), 1c(8), 1g, 1h, and 1i. CCTs, PSAs, and 103-12 IEs also do not complete lines 1d and 1e. See instructions.

Assets		(a) Beginning of Year	(b) End of Year
a Total noninterest-bearing cash.....	1a	1132	0
b Receivables (less allowance for doubtful accounts):			
(1) Employer contributions	1b(1)	617907	610603
(2) Participant contributions.....	1b(2)	0	0
(3) Other	1b(3)	0	0
c General investments:			
(1) Interest-bearing cash (include money market accounts & certificates of deposit)	1c(1)	98924	164975
(2) U.S. Government securities	1c(2)	0	0
(3) Corporate debt instruments (other than employer securities):			
(A) Preferred	1c(3)(A)	0	0
(B) All other	1c(3)(B)	0	0
(4) Corporate stocks (other than employer securities):			
(A) Preferred	1c(4)(A)	0	13144
(B) Common	1c(4)(B)	1236468	2128616
(5) Partnership/joint venture interests	1c(5)	0	0
(6) Real estate (other than employer real property)	1c(6)	0	0
(7) Loans (other than to participants)	1c(7)	0	0
(8) Participant loans	1c(8)	753313	809978
(9) Value of interest in common/collective trusts	1c(9)	13253039	12777530
(10) Value of interest in pooled separate accounts	1c(10)	0	0
(11) Value of interest in master trust investment accounts	1c(11)	0	0
(12) Value of interest in 103-12 investment entities	1c(12)	0	0
(13) Value of interest in registered investment companies (e.g., mutual funds)	1c(13)	175382008	218036234
(14) Value of funds held in insurance company general account (unallocated contracts).....	1c(14)	0	0
(15) Other.....	1c(15)	0	0

		(a) Beginning of Year	(b) End of Year
1d	Employer-related investments:		
(1)	Employer securities.....	1d(1) 0	0
(2)	Employer real property.....	1d(2) 0	0
e	Buildings and other property used in plan operation	1e 0	0
f	Total assets (add all amounts in lines 1a through 1e)	1f 191342791	234541080
Liabilities			
g	Benefit claims payable	1g 0	0
h	Operating payables	1h 0	0
i	Acquisition indebtedness.....	1i 0	0
j	Other liabilities.....	1j 0	0
k	Total liabilities (add all amounts in lines 1g through 1j)	1k 0	0
Net Assets			
l	Net assets (subtract line 1k from line 1f)	1l 191342791	234541080

Part II Income and Expense Statement

2 Plan income, expenses, and changes in net assets for the year. Include all income and expenses of the plan, including any trust(s) or separately maintained fund(s) and any payments/receipts to/from insurance carriers. Round off amounts to the nearest dollar. MTIAs, CCTs, PSAs, and 103-12 IEs do not complete lines 2a, 2b(1)(E), 2e, 2f, and 2g.

		(a) Amount	(b) Total
Income			
a	Contributions:		
(1)	Received or receivable in cash from: (A) Employers	2a(1)(A) 5777854	
	(B) Participants	2a(1)(B) 12242536	
	(C) Others (including rollovers).....	2a(1)(C) 4460958	
(2)	Noncash contributions.....	2a(2) 0	22481348
(3)	Total contributions. Add lines 2a(1)(A), (B), (C), and line 2a(2)	2a(3)	
b	Earnings on investments:		
(1)	Interest:		
	(A) Interest-bearing cash (including money market accounts and certificates of deposit).....	2b(1)(A) 25	
	(B) U.S. Government securities	2b(1)(B) 0	
	(C) Corporate debt instruments	2b(1)(C) 0	
	(D) Loans (other than to participants)	2b(1)(D) 0	
	(E) Participant loans.....	2b(1)(E) 30701	
	(F) Other	2b(1)(F) 0	
	(G) Total interest. Add lines 2b(1)(A) through (F).....	2b(1)(G)	30726
(2)	Dividends: (A) Preferred stock.....	2b(2)(A) 386	
	(B) Common stock	2b(2)(B) 6766	
	(C) Registered investment company shares (e.g. mutual funds).....	2b(2)(C) 12518975	
	(D) Total dividends. Add lines 2b(2)(A), (B), and (C)	2b(2)(D)	12526127
(3)	Rents	2b(3)	0
(4)	Net gain (loss) on sale of assets: (A) Aggregate proceeds	2b(4)(A) 6645196	
	(B) Aggregate carrying amount (see instructions).....	2b(4)(B) 6543774	
	(C) Subtract line 2b(4)(B) from line 2b(4)(A) and enter result	2b(4)(C)	
(5)	Unrealized appreciation (depreciation) of assets: (A) Real estate	2b(5)(A) 0	
	(B) Other	2b(5)(B) -15137	
	(C) Total unrealized appreciation of assets. Add lines 2b(5)(A) and (B)	2b(5)(C)	

		(a) Amount	(b) Total
(6) Net investment gain (loss) from common/collective trusts.....	2b(6)		265015
(7) Net investment gain (loss) from pooled separate accounts.....	2b(7)		0
(8) Net investment gain (loss) from master trust investment accounts.....	2b(8)		0
(9) Net investment gain (loss) from 103-12 investment entities.....	2b(9)		0
(10) Net investment gain (loss) from registered investment companies (e.g., mutual funds).....	2b(10)		25587165
c Other income.....	2c		0
d Total income. Add all income amounts in column (b) and enter total.....	2d		60976666
Expenses			
e Benefit payment and payments to provide benefits:			
(1) Directly to participants or beneficiaries, including direct rollovers.....	2e(1)	17682301	
(2) To insurance carriers for the provision of benefits.....	2e(2)	0	
(3) Other.....	2e(3)	0	
(4) Total benefit payments. Add lines 2e(1) through (3).....	2e(4)		17682301
f Corrective distributions (see instructions).....	2f		2291
g Certain deemed distributions of participant loans (see instructions).....	2g		20972
h Interest expense.....	2h		0
i Administrative expenses: (1) Professional fees.....	2i(1)	0	
(2) Contract administrator fees.....	2i(2)	0	
(3) Investment advisory and management fees.....	2i(3)	0	
(4) Other.....	2i(4)	72813	
(5) Total administrative expenses. Add lines 2i(1) through (4).....	2i(5)		72813
j Total expenses. Add all expense amounts in column (b) and enter total.....	2j		17778377
Net Income and Reconciliation			
k Net income (loss). Subtract line 2j from line 2d.....	2k		43198289
l Transfers of assets:			
(1) To this plan.....	2l(1)		0
(2) From this plan.....	2l(2)		0

Part III Accountant's Opinion

3 Complete lines 3a through 3c if the opinion of an independent qualified public accountant is attached to this Form 5500. Complete line 3d if an opinion is not attached.

a The attached opinion of an independent qualified public accountant for this plan is (see instructions):

(1) ☒ Unmodified (2) ☐ Qualified (3) ☐ Disclaimer (4) ☐ Adverse

b Check the appropriate box(es) to indicate whether the IQPA performed an ERISA section 103(a)(3)(C) audit. Check both boxes (1) and (2) if the audit was performed pursuant to both 29 CFR 2520.103-8 and 29 CFR 2520.103-12(d). Check box (3) if pursuant to neither.

(1) ☒ DOL Regulation 2520.103-8 (2) ☐ DOL Regulation 2520.103-12(d) (3) ☐ neither DOL Regulation 2520.103-8 nor DOL Regulation 2520.103-12(d).

c Enter the name and EIN of the accountant (or accounting firm) below:

(1) Name: JGD & ASSOCIATES LLP

(2) EIN: 95-3132551

d The opinion of an independent qualified public accountant is **not attached** because:

(1) ☐ This form is filed for a CCT, PSA, or MTIA. (2) ☐ It will be attached to the next Form 5500 pursuant to 29 CFR 2520.104-50.

Part IV Compliance Questions

4 CCTs and PSAs do not complete Part IV. MTIAs, 103-12 IEs, and GIAs do not complete lines 4a, 4e, 4f, 4g, 4h, 4k, 4m, 4n, or 5. 103-12 IEs also do not complete lines 4j and 4l. MTIAs also do not complete line 4l.

During the plan year:

a Was there a failure to transmit to the plan any participant contributions within the time period described in 29 CFR 2510.3-102? Continue to answer "Yes" for any prior year failures until fully corrected. (See instructions and DOL's Voluntary Fiduciary Correction Program.).....

	Yes	No	Amount
4a		X	

	Yes	No	Amount
b Were any loans by the plan or fixed income obligations due the plan in default as of the close of the plan year or classified during the year as uncollectible? Disregard participant loans secured by participant's account balance. (Attach Schedule G (Form 5500) Part I if "Yes" is checked.)			
4b		X	
c Were any leases to which the plan was a party in default or classified during the year as uncollectible? (Attach Schedule G (Form 5500) Part II if "Yes" is checked.)			
4c		X	
d Were there any nonexempt transactions with any party-in-interest? (Do not include transactions reported on line 4a. Attach Schedule G (Form 5500) Part III if "Yes" is checked.)			
4d		X	
e Was this plan covered by a fidelity bond?	X		500000
f Did the plan have a loss, whether or not reimbursed by the plan's fidelity bond, that was caused by fraud or dishonesty?		X	
4f		X	
g Did the plan hold any assets whose current value was neither readily determinable on an established market nor set by an independent third party appraiser?			
4g		X	
h Did the plan receive any noncash contributions whose value was neither readily determinable on an established market nor set by an independent third party appraiser?			
4h		X	
i Did the plan have assets held for investment? (Attach schedule(s) of assets if "Yes" is checked, and see instructions for format requirements.)	X		
4i	X		
j Were any plan transactions or series of transactions in excess of 5% of the current value of plan assets? (Attach schedule of transactions if "Yes" is checked and see instructions for format requirements.)			
4j		X	
k Were all the plan assets either distributed to participants or beneficiaries, transferred to another plan, or brought under the control of the PBGC?			
4k		X	
l Has the plan failed to provide any benefit when due under the plan?			
4l		X	
m If this is an individual account plan, was there a blackout period? (See instructions and 29 CFR 2520.101-3.)			
4m		X	
n If 4m was answered "Yes," check the "Yes" box if you either provided the required notice or one of the exceptions to providing the notice applied under 29 CFR 2520.101-3.			
4n		X	

5a Has a resolution to terminate the plan been adopted during the plan year or any prior plan year? ☐ Yes ☒ No
If "Yes," enter the amount of any plan assets that reverted to the employer this year _____.

5b If, during this plan year, any assets or liabilities were transferred from this plan to another plan(s), identify the plan(s) to which assets or liabilities were transferred. (See instructions.)

5b(1) Name of plan(s)	5b(2) EIN(s)	5b(3) PN(s)

5c Was the plan a defined benefit plan covered under the PBGC insurance program at any time during this plan year? (See ERISA section 4021 and instructions.) ☐ Yes ☐ No ☐ Not determined
If "Yes" is checked, enter the My PAA confirmation number from the PBGC premium filing for this plan year _____.

SCHEDULE R (Form 5500) Department of the Treasury Internal Revenue Service Department of Labor Employee Benefits Security Administration Pension Benefit Guaranty Corporation	Retirement Plan Information This schedule is required to be filed under sections 104 and 4065 of the Employee Retirement Income Security Act of 1974 (ERISA) and section 6058(a) of the Internal Revenue Code (the Code). ► File as an attachment to Form 5500.	OMB No. 1210-0110 2021 This Form is Open to Public Inspection.
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For calendar plan year 2021 or fiscal plan year beginning 01/01/2021 and ending 12/31/2021

A Name of plan IONIS PHARMACEUTICALS 401(K) PLAN	B Three-digit plan number (PN) ► 001
C Plan sponsor's name as shown on line 2a of Form 5500 IONIS PHARMACEUTICALS, INC.	D Employer Identification Number (EIN) 33-0336973

Part I	Distributions
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All references to distributions relate only to payments of benefits during the plan year.

1 Total value of distributions paid in property other than in cash or the forms of property specified in the instructions.....	1
2 Enter the EIN(s) of payor(s) who paid benefits on behalf of the plan to participants or beneficiaries during the year (if more than two, enter EINs of the two payors who paid the greatest dollar amounts of benefits): EIN(s): 04-6568107 Profit-sharing plans, ESOPs, and stock bonus plans, skip line 3.	
3 Number of participants (living or deceased) whose benefits were distributed in a single sum, during the plan year	3

Part II	Funding Information (If the plan is not subject to the minimum funding requirements of section 412 of the Internal Revenue Code or ERISA section 302, skip this Part.)
---------	--

4 Is the plan administrator making an election under Code section 412(d)(2) or ERISA section 302(d)(2)? If the plan is a defined benefit plan, go to line 8.	☐ Yes ☐ No ☐ N/A
5 If a waiver of the minimum funding standard for a prior year is being amortized in this plan year, see instructions and enter the date of the ruling letter granting the waiver. Date: Month _____ Day _____ Year _____ If you completed line 5, complete lines 3, 9, and 10 of Schedule MB and do not complete the remainder of this schedule.	
6 a Enter the minimum required contribution for this plan year (include any prior year accumulated funding deficiency not waived)	6a
b Enter the amount contributed by the employer to the plan for this plan year	6b
c Subtract the amount in line 6b from the amount in line 6a. Enter the result (enter a minus sign to the left of a negative amount).....	6c
If you completed line 6c, skip lines 8 and 9.	
7 Will the minimum funding amount reported on line 6c be met by the funding deadline?	☐ Yes ☐ No ☐ N/A
8 If a change in actuarial cost method was made for this plan year pursuant to a revenue procedure or other authority providing automatic approval for the change or a class ruling letter, does the plan sponsor or plan administrator agree with the change?	☐ Yes ☐ No ☐ N/A

Part III	Amendments
----------	------------

9 If this is a defined benefit pension plan, were any amendments adopted during this plan year that increased or decreased the value of benefits? If yes, check the appropriate box. If no, check the "No" box.....	☐ Increase ☐ Decrease ☐ Both ☐ No
--	--

Part IV	ESOPs (see instructions). If this is not a plan described under section 409(a) or 4975(e)(7) of the Internal Revenue Code, skip this Part.
---------	--

10 Were unallocated employer securities or proceeds from the sale of unallocated securities used to repay any exempt loan?	☐ Yes ☐ No
11 a Does the ESOP hold any preferred stock?	☐ Yes ☐ No
b If the ESOP has an outstanding exempt loan with the employer as lender, is such loan part of a "back-to-back" loan? (See instructions for definition of "back-to-back" loan.)	☐ Yes ☐ No
12 Does the ESOP hold any stock that is not readily tradable on an established securities market?	☐ Yes ☐ No

For Paperwork Reduction Act Notice, see the Instructions for Form 5500.

Schedule R (Form 5500) 2021
v. 201209

Part V Additional Information for Multiemployer Defined Benefit Pension Plans

13 Enter the following information for each employer that contributed more than 5% of total contributions to the plan during the plan year (measured in dollars). See instructions. *Complete as many entries as needed to report all applicable employers.*

a Name of contributing employer

b EIN

c Dollar amount contributed by employer

d Date collective bargaining agreement expires (If employer contributes under more than one collective bargaining agreement, check box ☐ and see instructions regarding required attachment. Otherwise, enter the applicable date.) Month _____ Day _____ Year _____

e Contribution rate information (If more than one rate applies, check this box ☐ and see instructions regarding required attachment. Otherwise, complete lines 13e(1) and 13e(2).)

(1) Contribution rate (in dollars and cents) _____

(2) Base unit measure: ☐ Hourly ☐ Weekly ☐ Unit of production ☐ Other (specify): _____

a Name of contributing employer

b EIN

c Dollar amount contributed by employer

d Date collective bargaining agreement expires (If employer contributes under more than one collective bargaining agreement, check box ☐ and see instructions regarding required attachment. Otherwise, enter the applicable date.) Month _____ Day _____ Year _____

e Contribution rate information (If more than one rate applies, check this box ☐ and see instructions regarding required attachment. Otherwise, complete lines 13e(1) and 13e(2).)

(1) Contribution rate (in dollars and cents) _____

(2) Base unit measure: ☐ Hourly ☐ Weekly ☐ Unit of production ☐ Other (specify): _____

a Name of contributing employer

b EIN

c Dollar amount contributed by employer

d Date collective bargaining agreement expires (If employer contributes under more than one collective bargaining agreement, check box ☐ and see instructions regarding required attachment. Otherwise, enter the applicable date.) Month _____ Day _____ Year _____

e Contribution rate information (If more than one rate applies, check this box ☐ and see instructions regarding required attachment. Otherwise, complete lines 13e(1) and 13e(2).)

(1) Contribution rate (in dollars and cents) _____

(2) Base unit measure: ☐ Hourly ☐ Weekly ☐ Unit of production ☐ Other (specify): _____

a Name of contributing employer

b EIN

c Dollar amount contributed by employer

d Date collective bargaining agreement expires (If employer contributes under more than one collective bargaining agreement, check box ☐ and see instructions regarding required attachment. Otherwise, enter the applicable date.) Month _____ Day _____ Year _____

e Contribution rate information (If more than one rate applies, check this box ☐ and see instructions regarding required attachment. Otherwise, complete lines 13e(1) and 13e(2).)

(1) Contribution rate (in dollars and cents) _____

(2) Base unit measure: ☐ Hourly ☐ Weekly ☐ Unit of production ☐ Other (specify): _____

a Name of contributing employer

b EIN

c Dollar amount contributed by employer

d Date collective bargaining agreement expires (If employer contributes under more than one collective bargaining agreement, check box ☐ and see instructions regarding required attachment. Otherwise, enter the applicable date.) Month _____ Day _____ Year _____

e Contribution rate information (If more than one rate applies, check this box ☐ and see instructions regarding required attachment. Otherwise, complete lines 13e(1) and 13e(2).)

(1) Contribution rate (in dollars and cents) _____

(2) Base unit measure: ☐ Hourly ☐ Weekly ☐ Unit of production ☐ Other (specify): _____

a Name of contributing employer

b EIN

c Dollar amount contributed by employer

d Date collective bargaining agreement expires (If employer contributes under more than one collective bargaining agreement, check box ☐ and see instructions regarding required attachment. Otherwise, enter the applicable date.) Month _____ Day _____ Year _____

e Contribution rate information (If more than one rate applies, check this box ☐ and see instructions regarding required attachment. Otherwise, complete lines 13e(1) and 13e(2).)

(1) Contribution rate (in dollars and cents) _____

(2) Base unit measure: ☐ Hourly ☐ Weekly ☐ Unit of production ☐ Other (specify): _____

- 14** Enter the number of deferred vested and retired participants (inactive participants), as of the beginning of the plan year, whose contributing employer is no longer making contributions to the plan for:

a The current plan year. Check the box to indicate the counting method used to determine the number of inactive participants: ☐ last contributing employer ☐ alternative ☐ reasonable approximation (see instructions for required attachment).....

14a

b The plan year immediately preceding the current plan year. ☐ Check the box if the number reported is a change from what was previously reported (see instructions for required attachment).....

14b

c The second preceding plan year. ☐ Check the box if the number reported is a change from what was previously reported (see instructions for required attachment).....

14c

- 15** Enter the ratio of the number of participants under the plan on whose behalf no employer had an obligation to make an employer contribution during the current plan year to:

a The corresponding number for the plan year immediately preceding the current plan year.....

15a

b The corresponding number for the second preceding plan year.....

15b

- 16** Information with respect to any employers who withdrew from the plan during the preceding plan year:

a Enter the number of employers who withdrew during the preceding plan year.....

16a

b If line 16a is greater than 0, enter the aggregate amount of withdrawal liability assessed or estimated to be assessed against such withdrawn employers.....

16b

- 17** If assets and liabilities from another plan have been transferred to or merged with this plan during the plan year, check box and see instructions regarding supplemental information to be included as an attachment..... ☐

Part VI Additional Information for Single-Employer and Multiemployer Defined Benefit Pension Plans

- 18** If any liabilities to participants or their beneficiaries under the plan as of the end of the plan year consist (in whole or in part) of liabilities to such participants and beneficiaries under two or more pension plans as of immediately before such plan year, check box and see instructions regarding supplemental information to be included as an attachment..... ☐

- 19** If the total number of participants is 1,000 or more, complete lines (a) through (c)

a Enter the percentage of plan assets held as:

Stock: _____% Investment-Grade Debt: _____% High-Yield Debt: _____% Real Estate: _____% Other: _____%

b Provide the average duration of the combined investment-grade and high-yield debt:

☐ 0-3 years ☐ 3-6 years ☐ 6-9 years ☐ 9-12 years ☐ 12-15 years ☐ 15-18 years ☐ 18-21 years ☐ 21 years or more

c What duration measure was used to calculate line 19(b)?

☐ Effective duration ☐ Macaulay duration ☐ Modified duration ☐ Other (specify): _____

- 20 PBGC missed contribution reporting requirements.** If this is a multiemployer plan or a single-employer plan that is not covered by PBGC, skip line 20.

a Is the amount of unpaid minimum required contributions for all years from Schedule SB (Form 5500) line 40 greater than zero? ☐ Yes ☐ No

b If line 20a is "Yes," has PBGC been notified as required by ERISA sections 4043(c)(5) and/or 303(k)(4)? Check the applicable box:

☐ Yes.

☐ No. Reporting was waived under 29 CFR 4043.25(c)(2) because contributions equal to or exceeding the unpaid minimum required contribution were made by the 30th day after the due date.

☐ No. The 30-day period referenced in 29 CFR 4043.25(c)(2) has not yet ended, and the sponsor intends to make a contribution equal to or exceeding the unpaid minimum required contribution by the 30th day after the due date.

☐ No. Other. Provide explanation _____

IONIS PHARMACEUTICALS 401(K) PLAN

FINANCIAL REPORT

DECEMBER 31, 2021 AND 2020

IONIS PHARMACEUTICALS 401(K) PLAN

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All other schedules required by the Department of Labor's Rules and Regulations for Reporting and Disclosure under the Employee Retirement Income Security Act of 1974 are omitted because of the absence of conditions under which they are required.

INDEPENDENT AUDITOR'S REPORT

To the 401(k) Fiduciary Committee of the
Ionis Pharmaceuticals 401(k) Plan
Carlsbad, California

Scope and Nature of the ERISA Section 103(a)(3)(C) Audit for the 2021 Financial Statements

We have performed an audit of the financial statements of Ionis Pharmaceuticals 401(k) Plan, an employee benefit plan subject to the Employee Retirement Income Security Act of 1974 (ERISA), as permitted by ERISA Section 103(a)(3)(C) (ERISA Section 103(a)(3)(C) audit). The financial statements comprise the statement of net assets available for benefits as of December 31, 2021, and the related statement of changes in net assets available for benefits for the year then ended, and the related notes to the financial statements (2021 financial statements).

Management, having determined it is permissible in the circumstances, has elected to have the audit of the 2021 financial statements performed in accordance with ERISA Section 103(a)(3)(C) pursuant to 29 CFR 2520.103-8 of the Department of Labor's Rules and Regulations for Reporting and Disclosure under ERISA. As permitted by ERISA Section 103(a)(3)(C), our audit need not extend to any statements or information related to assets held for investment of the plan (investment information) by a bank or similar institution or insurance carrier that is regulated, supervised, and subject to periodic examination by a state or federal agency, provided that the statements or information regarding assets so held are prepared and certified to by the bank or similar institution or insurance carrier in accordance with 29 CFR 2520.103-5 of the Department of Labor's Rules and Regulations for Reporting and Disclosure under ERISA (qualified institution).

Management has obtained a certification from a qualified institution as of and for the year ended December 31, 2021, stating that the certified investment information, as described in Note 3 to the financial statements, is complete and accurate.

Opinion on the 2021 Financial Statements

In our opinion, based on our audit and on the procedures performed as described in the Auditor's Responsibilities for the Audit of the 2021 Financial Statements section of our report

- the amounts and disclosures in the accompanying 2021 financial statements, other than those agreed to or derived from the certified investment information, are presented fairly, in all material respects, in accordance with accounting principles generally accepted in the United States of America.
- the information in the accompanying 2021 financial statements related to assets held by and certified to by a qualified institution agrees to, or is derived from, in all material respects, the information prepared and certified by an institution that management determined meets the requirements of ERISA Section 103(a)(3)(C).

Basis for Opinion on the 2021 Financial Statements

We conducted our audit in accordance with auditing standards generally accepted in the United States of America. Our responsibilities under those standards are further described in the Auditor's Responsibilities for the Audit of the Financial Statements section of our report. We are required to be independent of Ionis Pharmaceuticals 401(k) Plan and to meet our other ethical responsibilities in accordance with the relevant ethical requirements relating to our audit. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our ERISA Section 103(a)(3)(C) audit opinion.

Responsibilities of Management for the 2021 Financial Statements

Management is responsible for the preparation and fair presentation of the financial statements in accordance with accounting principles generally accepted in the United States of America, and for the design, implementation, and maintenance of internal control relevant to the preparation and fair presentation of financial statements that are free from material misstatement, whether due to fraud or error. Management's election of the ERISA Section 103(a)(3)(C) audit does not affect management's responsibility for the financial statements.

In preparing the financial statements, management is required to evaluate whether there are conditions or events, considered in the aggregate, that raise substantial doubt about Ionis Pharmaceuticals 401(k) Plan's ability to continue as a going concern within one year after the date that the financial statements are issued or available to be issued.

Management is also responsible for maintaining a current plan instrument, including all plan amendments, administering the plan, and determining that the plan's transactions that are presented and disclosed in the financial statements are in conformity with the plan's provisions, including maintaining sufficient records with respect to each of the participants, to determine the benefits due or which may become due to such participants.

Auditor's Responsibilities for the Audit of the 2021 Financial Statements

Except as described in the Scope and Nature of the ERISA Section 103(a)(3)(C) Audit of the 2021 Financial Statements section of our report, our objectives are to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditor's report that includes our opinion. Reasonable assurance is a high level of assurance but is not absolute assurance and therefore is not a guarantee that an audit conducted in accordance with GAAS will always detect a material misstatement when it exists. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control. Misstatements are considered material if, there is a substantial likelihood that, individually or in the aggregate, they would influence the judgment made by a reasonable user based on the financial statements.

In performing an audit in accordance with GAAS, we:

- Exercise professional judgment and maintain professional skepticism throughout the audit.
- Identify and assess the risks of material misstatement of the financial statements, whether due to fraud or error, and design and perform audit procedures responsive to those risks. Such procedures include examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements.
- Obtain an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of Ionis Pharmaceuticals 401(k) Plan's internal control. Accordingly, no such opinion is expressed.
- Evaluate the appropriateness of accounting policies used and the reasonableness of significant accounting estimates made by management, as well as evaluate the overall presentation of the financial statements.
- Conclude whether, in our judgment, there are conditions or events, considered in the aggregate, that raise substantial doubt about Ionis Pharmaceuticals 401(k) Plan's ability to continue as a going concern for a reasonable period of time.

Our audit did not extend to the certified investment information, except for obtaining and reading the certification, comparing the certified investment information with the related information presented and disclosed in the 2021 financial statements, and reading the disclosures relating to the certified investment information to assess whether they are in accordance with the presentation and disclosure requirements of accounting principles generally accepted in the United States of America.

Accordingly, the objective of an ERISA Section 103(a)(3)(C) audit is not to express an opinion about whether the financial statements as a whole are presented fairly, in all material respects, in accordance with accounting principles generally accepted in the United States of America.

We are required to communicate with those charged with governance regarding, among other matters, the planned scope and timing of the audit, significant audit findings, and certain internal control-related matters that we identified during the audit.

Other Matter - 2021 Supplemental Schedule Required by ERISA

The supplemental schedule of Schedule H, line 4i – Schedule of Assets (Held at End of Year) for December 31, 2021 is presented for purposes of additional analysis and is not a required part of the financial statements but is supplementary information required by the Department of Labor's Rules and Regulations for Reporting and Disclosure under ERISA. Such information is the responsibility of management and was derived from and relates directly to the underlying accounting and other records used to prepare the financial statements. The information included in the supplemental schedule, other than that agreed to or derived from the certified investment information, has been subjected to auditing procedures applied in the audit of the financial statements and certain additional procedures, including comparing and reconciling such information directly to the underlying accounting and other records used to prepare the financial statements or to the financial statements themselves, and other additional procedures in accordance with GAAS. For information included in the supplemental schedule that agreed to or is derived from the certified investment information, we compared such information to the related certified investment information.

In forming our opinion on the supplemental schedule, we evaluated whether the supplemental schedule, other than the information agreed to or derived from the certified investment information, including its form and content, is

presented in conformity with the Department of Labor's Rules and Regulations for Reporting and Disclosure under ERISA.

In our opinion

- the form and content of the supplemental schedule, other than the information in the supplemental schedule that agreed to or is derived from the certified investment information, are presented, in all material respects, in conformity with the Department of Labor's Rules and Regulations for Reporting and Disclosure under ERISA.
- the information in the supplemental schedule related to assets held by and certified to by a qualified institution agrees to, or is derived from, in all material respects, the information prepared and certified by an institution that management determined meets the requirements of ERISA Section 103(a)(3)(C).

Other Matter - Auditor's Report on the 2020 Financial Statements

We were engaged to audit the 2020 financial statements of Ionis Pharmaceuticals 401(k) Plan. As permitted by 29 CFR 2520.103-8 of the Department of Labor's Rules and Regulations for Reporting and Disclosure under ERISA, the plan administrator instructed us not to perform and we did not perform any auditing procedures with respect to the information certified by a qualified institution. In our report dated October 13, 2021, we indicated that (a) because of the significance of the information that we did not audit, we were not able to obtain sufficient appropriate audit evidence to provide a basis for an audit opinion and accordingly, we did not express an opinion on the 2020 financial statements, and (b) the form and content of the information included in the 2020 financial statements other than that derived from the certified information were presented in compliance with the Department of Labor's Rules and Regulations for Reporting and Disclosure under ERISA.

 JGD & Associates, LLP

San Diego, California
October 4, 2022

Ionis Pharmaceuticals 401(k) Plan
STATEMENTS OF NET ASSETS AVAILABLE FOR BENEFITS
December 31, 2021 and 2020

	<u>2021</u>	<u>2020</u>
<u>ASSETS</u>		
INVESTMENTS, AT FAIR VALUE (Notes 2 and 4)		
Mutual funds	\$ 217,806,962	\$ 174,576,023
Common/collective trust	12,777,530	13,253,039
Self-directed brokerage account	<u>2,536,007</u>	<u>2,142,509</u>
Total investments, at fair value	<u>233,120,499</u>	<u>189,971,571</u>
RECEIVABLES		
Employer contribution receivable	610,603	617,907
Notes receivable from participants	<u>809,978</u>	<u>753,313</u>
Total receivables	<u>1,420,581</u>	<u>1,371,220</u>
Total assets	<u>234,541,080</u>	<u>191,342,791</u>
NET ASSETS AVAILABLE FOR BENEFITS	<u>\$ 234,541,080</u>	<u>\$ 191,342,791</u>

The accompanying notes are an integral part of these financial statements.

Ionis Pharmaceuticals 401(k) Plan
STATEMENT OF CHANGES IN NET ASSETS AVAILABLE FOR BENEFITS
Year ended December 31, 2021

ADDITIONS TO NET ASSETS ATTRIBUTED TO

Investment income (Note 2)

Net appreciation in fair value of investments	\$ 25,573,922
Dividends	12,622,504
Interest income on investments	<u>268,191</u>
Net investment income	<u>38,464,617</u>

Interest income on notes receivable from participants	<u>30,701</u>
---	---------------

Contributions

Employer's match	5,777,854
Participants'	12,242,536
Participant rollovers	<u>4,460,958</u>
Total contributions	<u>22,481,348</u>
Total additions	<u>60,976,666</u>

DEDUCTIONS FROM NET ASSETS ATTRIBUTED TO

Benefits paid to participants	17,705,564
Administrative expenses	<u>72,813</u>
Total deductions	<u>17,778,377</u>
Net increase	43,198,289

NET ASSETS AVAILABLE FOR BENEFITS

Beginning of year	<u>191,342,791</u>
End of year	<u><u>\$ 234,541,080</u></u>

The accompanying notes are an integral part of these financial statements.

Ionis Pharmaceuticals 401(k) Plan
NOTES TO THE FINANCIAL STATEMENTS
December 31, 2021 and 2020

NOTE 1--DESCRIPTION OF PLAN

The following description of the Ionis Pharmaceuticals 401(k) Plan (the Plan) provides only general information. Participants should refer to the plan agreement for a more complete description of the Plan's provisions.

General : The Plan, which was adopted on January 1, 1991 and last amended on October 1, 2020, is a defined contribution plan covering substantially all employees of Isis Pharmaceuticals, Inc. and its wholly owned subsidiaries (the Company). The Plan is subject to the provisions of the Employee Retirement Income Security Act of 1974 (ERISA). The Fiduciary Committee is responsible for oversight of the Plan and determines the appropriateness and monitors performance of the Plan's investment offerings.

Contributions : Participant salary reduction contributions: Each year, participants may contribute up to 100% of pretax annual compensation, as defined by the Plan. Participants who have attained age 50 before the end of the plan year are eligible to make catch-up contributions. Such contributions are 100% vested and non-forfeitable. The Plan includes an auto enrollment provision whereby all newly eligible employees are automatically enrolled in the Plan unless they affirmatively elect not to participate. Automatically enrolled participants have their deferral rate set at 5% of eligible compensation and their contributions invested in a designated fund until changed by the participant. As defined by the Plan, participants are permitted to designate a portion or all of the deferral contributions they are otherwise eligible to make under the Plan as Roth deferral contributions. Participant contributions are subject to certain Internal Revenue Service (IRS) limitations.

Employer non-discretionary matching contributions: The Company makes a discretionary nonelective contributions in an amount equal to 100% of a participant's salary reduction contribution subject to a maximum of 5% of the employee's eligible compensation contributed to the Plan each year. These employer non-discretionary matching contributions are subject to overall employer contribution limits and additions to individual participant account limits. Each participant is 100% vested in his or her employer contributions. For the year ended December 31, 2021, the Company made employer non-discretionary matching contributions totaling \$5,777,854.

Employer discretionary matching contributions: The Company may make an employer discretionary matching contribution on behalf of each eligible participant in an amount equal to a percentage determined annually based on the salary reduction contributions made by each participant during the year. For the year ended December 31, 2021, the Company elected to not make employer discretionary matching contributions.

Participant rollover contributions: Participants may also contribute amounts representing distributions from other qualified defined contribution or defined benefit plans (rollover). Such contributions are 100% vested and non for non-forfeitable.

NOTE 1--DESCRIPTION OF PLAN (Continued)

Qualified non-elective employer contributions: The Company may make qualified non-elective contributions in the same proportion that each eligible participant's compensation for such plan year bears to the total compensation of all eligible participants for such plan year. These qualified non-elective employer contributions are subject to overall employer contribution limits and additions to individual participant account limits. Participants must have been eligible at any time during the plan year and must be non-highly compensated employees to be eligible to share in the employer qualified non-elective contribution. Qualified non-elective employer contributions are 100% vested and non-forfeitable. The Company elected to not make qualified non-elective employer contributions to the Plan during the year ended December 31, 2021.

Participant rollover contributions: Participants may also contribute amounts representing distributions from other qualified defined contribution or defined benefit plans (rollover to the Plan).

- COVID-19 : In 2020, the Plan adopted the following provisions provided by the Coronavirus Aid, Relief, and Economic Security Act (CARES Act): (1) Qualified individuals may request penalty-free distributions of up to \$100,000 and allows for qualified loans of up to the lesser of \$100,000 or 100 percent of a participant's vested balance for coronavirus-related reasons. (2) Temporary waiver of any required minimum distributions.
- Eligibility to participate : Employees who have reached age eighteen are eligible to participate in the Plan immediately upon hire. All eligible employees are automatically enrolled in the Plan after thirty days of being hired, unless affirmatively elected otherwise.
- ERISA account : The Plan held an expense reimbursement account as of December 31, 2021 and 2020 Expense reimbursement balances were \$3,191 and \$1,939, respectively. During the year ended December 31, 2021, \$1,196 were used to reduce fees.
- Forfeitures : At December 31, 2021 and 2020, forfeited nonvested accounts held by the Plan totaled \$140 and \$35,031. These accounts will be used to reduce future employer contributions. During 2021, forfeited nonvested accounts totaling \$315,470 were used to reduce employer matching contributions.
- Notes receivable from participants : Participants may borrow from their fund accounts a minimum of \$1,000 up to a maximum equal to the lesser of \$50,000 or 50% of their account balance. The loans are secured by the balance in the participant's account. The loan interest rate is set at the prime rate of the loan.
- Participant accounts : Participants direct the investment of their contributions into various investment options offered by the Plan. If a participant has not elected investment options, contributions will be directed to the default investments as determined by the plan administrator. Individual accounts are maintained for each plan participant. Each participant's account is credited with the participant's salary reduction and rollover contributions, employer non-discretionary matching contributions, qualified non-elective employer contributions, and plan earnings. Participant accounts are charged with an allocation of administrative expenses that are paid by the Plan. Allocations are based on participant earnings, account balances, or

NOTE 1--DESCRIPTION OF PLAN (Continued)

specific participant transactions, as defined. The benefit to which a participant is entitled is the benefit that can be provided from the participant's vested account.

Payment of benefits : On termination of service due to death, disability, or retirement, a participant may elect to receive a lump sum amount equal to the value of the participant's vested interest in his or her account, or annual installments. For termination of service for other reasons, a participant may receive the value of the vested interest in his or her account as a lump sum distribution. The distribution shall be made to the participant or beneficiary in accordance with the election of the participant. Participants may defer receiving these benefits until their normal retirement age if their vested account balance exceeds \$1,000.

Participants may also elect to withdraw in cash certain vested amounts within his or her contribution account to the extent necessary to meet a financial hardship, in accordance with the regulations and rulings of the Internal Revenue Code (IRC).

Vesting : Participants are vested immediately in their participant salary reduction, employer non-discretionary matching contributions, employer discretionary matching contributions and rollover contributions plus actual earnings thereon.

NOTE 2--SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of accounting : The financial statements of the Plan are presented on the accrual basis of accounting.

Administrative expenses : Certain expenses of maintaining the Plan are paid directly by the Company and are excluded from these financial statements. Fees related to the administration of notes receivable from participants and to distributions from participant accounts are charged directly to the participant's account and are included in administrative expenses. Investment related expenses are included in net appreciation (depreciation) of fair value of investments.

Investment valuation and income recognition : Investments are reported at fair value. Fair value is the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. See Note 4 for discussion of fair value measurements.

Purchases and sales of securities are recorded on a trade-date basis. Interest income is recorded on the accrual basis. Dividends are recorded on the ex-dividend date. Net appreciation (depreciation) includes the Plan's gains and losses on investments bought and sold as well as held during the year.

NOTE 2--SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (Continued)

Notes receivable from participants	:	Notes receivable from participants are measured at their unpaid principal balance plus any accrued but unpaid interest. Interest income is recorded on the accrual basis. Related fees are recorded as administrative expenses and are expensed when incurred. No allowance for credit losses have been recorded as of December 31, 2021 and 2020. If a participant ceases to make loan repayments and the plan administrator deems the participant loan to be in default, the participant loan balance is reduced and a benefit payment is recorded.
Payment of benefits	:	Benefits are recorded when paid.
Subsequent events	:	The Plan has evaluated subsequent events through October 4, 2022, the date the financial statements were available to be issued.
Use of estimates	:	The preparation of financial statements in accordance with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and changes therein, and disclosure of contingent assets and liabilities. Actual results could differ from those estimates.

NOTE 3--CERTIFIED INFORMATION

The plan administrator has elected the method of annual reporting compliance permitted by ERISA Section 103(a)(3)(C) pursuant to 29 CFR 2520.103-8 of the Department of Labor's Rules and Regulations for Reporting and Disclosure under ERISA. Accordingly, the Plan's custodian, a qualified institution, has certified that the following investment information included in the accompanying financial statements and ERISA-required supplemental schedule is complete and accurate:

- Investments and notes receivable as shown in the statements of net assets available for benefits as of December 31, 2021 and 2020.
- Investment income, interest income on notes receivable and administrative expenses as shown in the statement of changes in net assets available for benefits for the year ended December 31, 2021.
- Investment information included in Note 4 and the schedule of assets (held at end of year) as of December 31, 2021, as shown on the ERISA-required supplemental schedule.

At the request of the Plan administrator, the Plan's independent auditors did not perform auditing procedures with respect to this certified investment information, except for comparing such certified investment information to the related investment information included in the financial statements and ERISA-required supplemental schedule.

NOTE 4--FAIR VALUE MEASUREMENTS

The framework for measuring fair value provides a fair value hierarchy that prioritizes the inputs to valuation techniques used to measure fair value. The hierarchy gives the highest priority to unadjusted quoted prices in active markets for identical assets or liabilities (level 1 measurements) and the lowest priority to unobservable inputs (level 3 measurements). The asset's or liability's fair value measurement level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement. Valuation techniques used need to maximize the use of observable inputs and minimize the use of unobservable inputs. The three levels of the fair value hierarchy under FASB ASC 820 and a description of the valuation methodologies used for assets measured at fair value are described as follows:

NOTE 4--FAIR VALUE MEASUREMENTS (Continued)

Level 1 Fair Value Measurements

Inputs to the valuation methodology are unadjusted quoted prices for identical assets or liabilities in active markets that the Plan has the ability to access.

Mutual funds are valued at the daily closing price as reported by the fund. Mutual funds held by the Plan are open-end mutual funds that are registered with the Securities and Exchange Commission. These funds are

required to publish their daily net asset value (NAV) and to transact at that price. The mutual funds held by the Plan are deemed to be actively traded.

Level 2 Fair Value Measurements

Inputs to the valuation methodology include (a) quoted prices for similar assets or liabilities in active markets, (b) quoted prices for identical or similar assets or liabilities in inactive markets, (c) inputs other than quoted prices that are observable for the asset or liability or (d) inputs that are derived principally from or corroborated by observable market data by correlation or other means. If the asset or liability has a specified (contractual) term, the level 2 input must be observable for substantially the full term of the asset or liability.

The Plan held no level 2 assets as of December 31, 2021 and 2020.

Level 3 Fair Value Measurements

Inputs to the valuation methodology are unobservable and significant to the fair value measurement.

The Plan held no level 3 assets as of December 31, 2021 and 2020.

The methods described above may produce a fair value calculation that may not be indicative of net realizable value or reflective of future fair values. Furthermore, while plan management believes its valuation methods are appropriate and consistent with other market participants, the use of different methodologies or assumptions to determine the fair value of certain financial instruments could result in a different fair value measurement at the reporting date.

The following tables set forth by level, within the fair value hierarchy, the Plan's assets at fair value as of December 31, 2021 and 2020:

<u>Assets at Fair Value as of December 31, 2021</u>				
	<u>Level 1</u>	<u>Level 2</u>	<u>Level 3</u>	<u>Total Fair Value</u>
Mutual funds	\$ 217,806,962	\$ 0	\$ 0	\$ 217,806,962
Self-directed brokerage account	<u>2,536,007</u>	<u>0</u>	<u>0</u>	<u>2,536,007</u>
Total assets in the fair value hierarchy	<u>\$ 220,342,969</u>	<u>\$ 0</u>	<u>\$ 0</u>	220,342,969
Investments measured at NAV				<u>12,777,530</u>
Total investments				<u>\$ 233,120,499</u>

NOTE 4--FAIR VALUE MEASUREMENTS (Continued)

<u>Assets at Fair Value as of December 31, 2020</u>				
	<u>Level 1</u>	<u>Level 2</u>	<u>Level 3</u>	<u>Total Fair Value</u>
Mutual funds	\$ 174,576,023	\$ 0	\$ 0	\$ 174,576,023
Self-directed brokerage account	<u>2,142,509</u>	<u>0</u>	<u>0</u>	<u>2,142,509</u>
Total assets in the fair value hierarchy	<u>\$ 176,718,532</u>	<u>\$ 0</u>	<u>\$ 0</u>	176,718,532
Investments measured at NAV				<u>13,253,039</u>
Total investments				<u>\$ 189,971,571</u>

Common/collective trusts are valued daily and have a daily redemption period. There are no unfunded commitments for the common collective trust held by the Plan as of December 31, 2021 and 2020. The total value of the common/collective trust is \$12,777,530 and \$13,253,039 at December 31, 2021 and 2020, respectively.

NOTE 5--PLAN TERMINATION

Although it has not expressed any intent to do so, the Company has the right under the Plan to discontinue its contributions at any time and to terminate the Plan subject to the provisions of ERISA. In the event of plan termination, participants will become 100% vested in their employer contributions.

NOTE 6--TAX STATUS

The Internal Revenue Service has determined and informed the Company by a letter dated June 30, 2020, that the Plan and related trust are designed in accordance with applicable sections of the Internal Revenue Code. Although the Plan has been amended since receiving the determination letter, the plan administrator and the Plan's tax counsel believe that the Plan is currently designed and being operated in compliance with the applicable requirements of the IRC and therefore believe that the Plan is qualified and the related trust is tax-exempt.

Accounting principles generally accepted in the United States of America require plan management to evaluate tax positions taken by the Plan and recognize a tax liability (or asset) if the Plan has taken an uncertain position that more likely than not would not be sustained upon examination by the U.S.

Department of Labor (DOL) Employee Benefits Security Administration (EBSA). Plan management has analyzed the tax positions taken by the Plan, and has concluded that as of December 31, 2021, there are no uncertain positions taken or expected to be taken that would require recognition of a liability (or asset) or disclosure in the financial statements. The Plan is subject to routine income tax examinations by taxing jurisdiction.

NOTE 7--PARTY-IN-INTEREST TRANSACTIONS

Certain plan investments are shares of mutual funds, a self-directed brokerage account, and a common/collective trust managed by Fidelity Management Trust Company. Fidelity Management Trust Company is the trustee as defined by the Plan and, therefore, these transactions qualify as party-in-interest transactions. Fees incurred by the Plan for the investment management services are included in net appreciation in fair value of the investment, as they are paid through revenue sharing, rather than a direct payment. The plan sponsor pays directly any other fees related to the Plan's operations.

NOTE 8--RISKS AND UNCERTAINTIES

The Plan invests in various investment securities. Investment securities are exposed to various risks such as interest rate, market, and credit risks. Due to the level of risk associated with certain investment securities, it is at least reasonably possible that changes in the values of investment securities will occur in the near term and that such changes could materially affect participants' account balances and the amounts reported in the Statements of Net Assets Available for Benefits.

SUPPLEMENTARY INFORMATION

Ionis Pharmaceuticals 401(k) Plan
(EIN # 33-0336973) (Plan #001)
Schedule H, Line 4i - SCHEDULE OF ASSETS (HELD AT END OF YEAR)
December 31, 2021

(a)	(b) Identity of issue, borrower, lessor, or similar party	(c) Description of investment including maturity date, rate of interest, collateral, par or maturity value	(d) Cost	(e) Current value
	Common/collective trust			
	Putnam Investments	Putnam Stable Value Fund	\$	\$ 12,777,530
	Mutual funds			
	Alliance Bernstein	AB Large Cap Growth Fund		29,942,948
	Cohen & Steers	C&S Institutional Realty Shares		1,709,765
	American Century Investments	American Century Global Growth Fund		4,224,686
	American Funds	American Funds 2010 Retirement Fund		105,196
	American Funds	American Funds 2015 Retirement Fund		1,253,506
	American Funds	American Funds 2020 Retirement Fund		2,699,943
	American Funds	American Funds 2025 Retirement Fund		5,413,863
	American Funds	American Funds 2030 Retirement Fund		8,390,178
	American Funds	American Funds 2035 Retirement Fund		9,873,440
	American Funds	American Funds 2040 Retirement Fund		9,029,564
	American Funds	American Funds 2045 Retirement Fund		6,812,070
	American Funds	American Funds 2050 Retirement Fund		6,209,075
	American Funds	American Funds 2055 Retirement Fund		2,050,242
	American Funds	American Funds 2060 Retirement Fund		655,693
	American Funds	American Funds New World Fund		3,156,038
	ClearBridge Investments	ClearBridge Appreciation Fund		1,771,662
	Davis Funds	Davis Financial Fund		13,044,425
*	Fidelity Investments	Fidelity Advisor Small Cap Growth Fund		8,680,317
*	Fidelity Investments	Fidelity Advisor Technology Fund		19,651,394
*	Fidelity Investments	Fidelity Advisors High Income Fund		1,013,750
*	Fidelity Investments	Fidelity Advisors Small Cap Value Fund		4,129,742
*	Fidelity Investments	Fidelity Emerging Markets Index Fund		564,498
*	Fidelity Investments	Fidelity International Index Fund		6,034,029
*	Fidelity Investments	Fidelity Government Money Market Fund		3,964

Ionis Pharmaceuticals 401(k) Plan
(EIN # 33-0336973) (Plan #001)
Schedule H, Line 4i - SCHEDULE OF ASSETS (HELD AT END OF YEAR) (Continued)
December 31, 2021

(a)	(b) Identity of issue, borrower, lessor, or similar party	(c) Description of investment including maturity date, rate of interest, collateral, par or maturity value	(d) Cost	(e) Current value
	Mutual funds (continued)			
*	Fidelity Investments	Fidelity Large Cap Growth Index Fund		1,550,569
*	Fidelity Investments	Fidelity Real Estate Index Fund		180,229
*	Fidelity Investments	Fidelity Spartan 500 Index Investment Fund		34,688,600
*	Fidelity Investments	Fidelity Spartan Inflation-Protected Bond Index Fund		1,619,823
*	Fidelity Investments	Fidelity Spartan Mid Cap Index Fund		3,783,107
*	Fidelity Investments	Fidelity Spartan Small Cap Index Fund		9,138,704
*	Fidelity Investments	Fidelity Total Market Index Fund		652,493
*	Fidelity Investments	Fidelity US Bond Index Fund		1,274,707
	Putnam Investments	PIF Equity Income Fund		11,248,207
	Victory Capital	Victory Sycamore Established Value Fund		7,250,535
	Self-directed brokerage account			
*	Various	Self-Directed - Fidelity	<u>0</u>	<u>2,536,007</u>
	Total investments, at fair value		0	233,120,499
*	Participant Loans	Interest rates range from 3.25% to 5.50% with maturity dates ranging from 2022 to 2026.	<u>0</u>	<u>809,978</u>
	Total		<u>\$ 0</u>	<u>\$ 233,930,477</u>

* Indicates party-in-interest

In accordance with ERISA section 404(c), cost information is not required when reporting investments of an individual account plan that is participant or beneficiary directed.

Ionis Pharmaceuticals 401(k) Plan
(EIN # 33-0336973) (Plan #001)
Schedule H, Line 4i - SCHEDULE OF ASSETS (HELD AT END OF YEAR)
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Ionis Pharmaceuticals 401(k) Plan
(EIN # 33-0336973) (Plan #001)
Schedule H, Line 4i - SCHEDULE OF ASSETS (HELD AT END OF YEAR) (Continued)
December 31, 2021

(a)	(b) Identity of issue, borrower, lessor, or similar party	(c) Description of investment including maturity date, rate of interest, collateral, par or maturity value	(d) Cost	(e) Current value
	Mutual funds (continued)			
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	Total		<u>\$ 0</u>	<u>\$ 233,930,477</u>

* Indicates party-in-interest

In accordance with ERISA section 404(c), cost information is not required when reporting investments of an individual account plan that is participant or beneficiary directed.