

January 14, 2021

United States Securities and Exchange Commission
Division of Corporate Finance
Office of Life Sciences
Attention: Li Xiao
100 F Street, NE
Washington, D.C. 20549

**Re: Ionis Pharmaceuticals, Inc.
Form 10-K for the Fiscal Year Ended December 31, 2019
Filed March 2, 2020
File No. 000-19125**

Dear Ms. Xiao:

On behalf of Ionis Pharmaceuticals, Inc. (the “Company,” “Ionis” or “we”), enclosed for electronic filing via EDGAR pursuant to the Securities Act of 1933, please find responses to your comments in reference to the Company’s Form 10-K for the fiscal year ended December 31, 2019, File No. 000-19125.

As requested by the Staff in your letter, please find below our responses to your comments and our proposed disclosure to be included in future periodic reports.

Notes to Consolidated Financial Statements

1. Organization and Significant Accounting Policies

Inventory Valuation, page F-19

1. Your disclosure states that inventory is reflected at the lower of cost or market value under the first-in, first-out method. Please revise your future filings to clarify, if true, that your inventory is measured at the lower of cost or net realizable value consistent with ASC 330-10-35-1B.

We respectfully acknowledge the Staff’s comment and confirm that we measure our inventory at the lower of cost or net realizable value consistent with ASC 330-10-35-1B. We will revise our disclosure in future periodic reports beginning with our 2020 Form 10-K to clarify that our inventory is measured at the lower of cost or net realizable value under the first-in, first-out method.

2. Long-Term Obligations and Commitments

Convertible Notes and Call Spread, page F-26

2. We note your disclosure concerning the call spread transaction that was entered into in conjunction with the December 2019 note exchange. You indicate that the amounts paid/received for the note hedges/warrants was recorded in additional paid-in capital. Please tell us how you determined the appropriate accounting treatment for this transaction, including your consideration of whether these financial instruments meet the definition of a derivative. Please also revise your accounting policy disclosure accordingly in future filings.

We structured our response to this question using the following outline:

- I. Transaction Background
- II. Accounting Analysis
 - A. Evaluation of Freestanding Financial Instruments and Units of Accounting
 - i. Freestanding Financial Instruments
 - ii. Units of Accounting
 - B. Whether the note hedges and the warrants are liabilities under ASC 480
 - C. Whether the note hedges and the warrants meet the conditions to be classified in equity
 - i. Note Hedges
 - 1. Evaluation of Derivative Definition
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 - 1. Evaluation of Derivative Definition
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- III. Accounting Policy Disclosure

I. Transaction Background

In December 2019, we exchanged \$375.6 million of our existing 1% Notes for \$439.3 million of new 0.125% Notes. In addition, we issued \$109.5 million of the 0.125% Notes to new investors. Together, we will refer to these transactions as the “Exchange Transaction.” We completed the Exchange Transaction to refinance a large portion of our existing 1% Notes with new convertible notes that had a lower interest rate, an extended maturity date and a higher conversion price.

In conjunction with the execution of the Exchange Transaction, we executed a call spread transaction, which was comprised of purchasing note hedges and selling warrants. We entered into the call spread to minimize the impact of potential economic dilution upon conversion of our 0.125% Notes by increasing the effective conversion price even further.

II. Accounting Analysis

A. Evaluation of Freestanding Financial Instruments and Units of Accounting

i. Freestanding Financial Instruments

We began our accounting analysis by first evaluating if the 0.125% Notes, note hedges and warrants are considered freestanding financial instruments using the guidance in ASC 480-10.

ASC 480-10 Freestanding Financial Instrument

A financial instrument that meets either of the following conditions:

- It is entered into separately and apart from any of the entity’s other financial instruments or equity transactions.

- **It is entered into in conjunction with some other transaction and is legally detachable and separately exercisable.**
 - Since the 0.125% Notes, note hedges and warrants are documented under separate contractual arrangements, which can be transferred independently of each other and are separately exercisable and legally detachable, we concluded each instrument should be treated as a freestanding financial instrument.

ii. Units of Accounting

Since the 0.125% Notes, note hedges and warrants (each of these is a “transaction” for purposes of this section) are separate freestanding financial instruments, we evaluated the appropriate units of accounting using the guidance in ASC 815-10-15-9.

The following indicators should be considered in the aggregate and, if present, cause separate transactions to be accounted for as one unit:

- **The transactions were entered into contemporaneously and in contemplation of each other**
 - We executed the 0.125% Notes, note hedges and warrants contemporaneously and in contemplation of each other.
- **The transactions were executed with the same counterparty (or structured through an intermediary)**
 - The numerous institutional investors who are the holders of 0.125% Notes are not the counterparties of the note hedges and warrants.
 - The note hedges and warrants have the same counterparties (i.e., three financial institutions).
- **The transactions relate to the same risk**
 - The 0.125% Notes and the warrants do not relate to the same risk. The 0.125% Notes contain both interest rate and equity risks while the warrants have only equity risk.
 - The value of the note hedges fluctuates based on option pricing inputs.
- **There is no apparent economic need, nor substantive business purpose, for structuring the transactions separately that could not also have been accomplished in a single transaction**
 - We had a substantive business reason to execute the 0.125% Notes, note hedges and warrants separately:
 - o We issued the 0.125% Notes to refinance our existing convertible notes with new convertible notes that had a lower interest rate and an extended maturity date.
 - o Without the issuance of the 0.125% Notes, we wouldn’t have entered into the note hedges and warrants. However, there were substantive business reasons to structure the note hedges and warrants separately from the 0.125% Notes and from each other:

- We issued the note hedges to synthetically raise the conversion price of the 0.125% Notes.
- We integrated the premiums we paid for the warrants with the proceeds we received from the 0.125% Notes for tax purposes and used the premium we received from the warrants to finance the purchase of the note hedges.

Since each of the instruments relate to different risks, had unique business purposes and different counterparties, we concluded that each of the instruments should be accounted for separately.

B. Whether the note hedges and warrants are liabilities under ASC 480

The next part of our accounting analysis was to determine whether the note hedges and/or warrants are liabilities. We evaluated the note hedges and warrants using the guidance in ASC 480-10, which requires that an issuer classify a freestanding financial instrument that is within its scope as a liability (or an asset).

The following instruments are classified as liabilities pursuant to ASC 480-10:

- **ASC 480-10-25-4** **A mandatorily redeemable financial instrument, issued in the form of shares, embodied by an unconditional obligation requiring the issuer to redeem the instrument by transferring its assets at a specified or determinable date (or dates) or upon an event certain to occur shall be classified as a liability unless the redemption is required to occur only upon the liquidation or termination of the reporting entity.**
 - ASC 480-10-25-4 is not applicable because the note hedges and warrants are not in the form of outstanding shares.
- **ASC 480-10-25-8** **Any financial instrument, other than an outstanding share, that, at inception, has both of the following characteristics:**
 - **It embodies an obligation to repurchase the issuer's equity shares or is indexed to such an obligation.**
 - **It requires or may require the issuer to settle the obligation by transferring assets.**
 - The criteria for ASC 480-10-25-8 are not applicable because:
 - The warrants do not embody an obligation of Ionis to repurchase its shares by transferring assets pursuant to ASC 480-10-25-8 because:
 - The counterparties to the warrants cannot put the warrants back to Ionis.
 - The underlying shares that Ionis would be required to issue under the warrants are not redeemable.
 - These criteria are not applicable for the note hedges because the note hedges represent a right for Ionis to receive cash or shares, not an obligation to issue or repurchase shares.

- **ASC 480-10-25-14** **A financial instrument that embodies an unconditional obligation outside of the Company’s control, or a financial instrument other than an outstanding share that embodies a conditional obligation, that the issuer must or may settle by issuing a variable number of its equity shares shall be classified as a liability (or an asset in some circumstances) if, at inception, the monetary value of the obligation is based solely or predominantly on any one of the following:**
 - **A fixed monetary amount known at inception (for example, a payable settleable with a variable number of the issuer’s equity shares)**
 - **Variations in something other than the fair value of the issuer’s equity shares (for example, a financial instrument indexed to the Standard and Poor’s S&P 500 Index and settleable with a variable number of the issuer’s equity shares)**
 - **Variations inversely related to changes in the fair value of the issuer’s equity shares.**
- The criteria for ASC 480-10-25-14 are not applicable because:
 - Although Ionis is contingently obligated to issue a variable number of shares to net settle the warrants, Ionis’ obligation is:
 - Not predominately fixed;
 - Directly related to the value of Ionis’ stock price (i.e., as Ionis’ stock price increases, the monetary value of the obligation and the number of shares to deliver increases); and
 - Not inversely related to the underlying stock price or based on something other than Ionis’ stock price.
 - These criteria are not applicable for the note hedges because the note hedges represent a right for Ionis to receive cash or shares, not an obligation to issue or repurchase shares.

Based on the above criteria, we concluded that the note hedges and warrants are not in the scope of ASC 480 and should not be classified as liabilities (or assets) under that guidance. The next step in our accounting analysis was to evaluate the note hedges and warrants using the guidance in ASC 815.

C. Whether the note hedges and the warrants meet the conditions to be classified in equity.

i. Note Hedges

1. Evaluation of Derivative Definition

The next part of the accounting analysis for the note hedges required us to determine if the note hedges met the definition of a derivative. We used the guidance in ASC 815-10-15-83, which defines a derivative instrument as a financial instrument or other contract with all of the following characteristics:

- **Underlying, notional amount, payment provision. The contract has both of the following terms, which determine the amount of the settlement or settlements, and, in some cases, whether or not a settlement is required:**
 - **One or more underlyings**
 - **One or more notional amounts or payment provisions or both.**
- The note hedges met this criterion because:
 - The underlying of the note hedges is Ionis’ common stock.

- o The notional of the note hedges is a specified number of shares of Ionis' common stock and/or cash we would receive from the counterparties to the note hedges.
- **Initial net investment. The contract requires no initial net investment or an initial net investment that is smaller than would be required for other types of contracts that would be expected to have a similar response to changes in market factors.**
 - The note hedges met this criterion because the premium we paid for the note hedges was less by more than a nominal amount than investing in the underlying shares. As such, the premium we paid for the note hedges represented a minimal initial net investment.
- **Net settlement. The contract can be settled net by any of the following means:**
 - **Its terms implicitly or explicitly require or permit net settlement.**
 - **It can readily be settled net by a means outside the contract.**
 - **It provides for delivery of an asset that puts the recipient in a position not substantially different from net settlement.**
 - The note hedges met these criteria because the note hedges are net share settleable by contract.

Based on the above criteria, we concluded that the note hedges met the definition of a derivative.

2. Evaluation of Derivative Scope Exception

We next evaluated if the note hedges met the requirements for a derivative scope exception using the guidance in ASC 815-10-15-74(a):

Notwithstanding the conditions of ASC 815-10-15-13 through 15-139, the reporting entity shall not consider the following contracts to be derivative instruments for purposes of this Subtopic. Contracts issued or held by that reporting entity that are both: (i) indexed to its own stock and (ii) classified in stockholders' equity in its statement of financial position:

i. Indexed to its own stock

To evaluate whether an instrument is considered indexed to an entity's own stock, we used the guidance in ASC 815-40-15-7:

An entity shall evaluate whether an equity-linked financial instrument (or embedded feature), as discussed in ASC 815-40-15-5 through 15-8 is considered indexed to its own stock within the meaning of this Subtopic and ASC 815-10-15-74(a) using the following two-step approach:

1. Step 1: Evaluate the instrument's contingent exercise provisions, if any.

ASC 815-40-15-7A states that an exercise contingency shall not preclude an instrument (or embedded feature) from being considered indexed to an entity's own stock provided that it is not based on either of the following:

- **An observable market, other than the market for the issuer's stock (if applicable).**
 - **An observable index, other than an index calculated or measured solely by reference to the issuer's own operations (for example, sales revenue of the issuer; earnings before interest, taxes, depreciation, and amortization of the issuer; net income of the issuer; or total equity of the issuer).**
- We concluded that Step 1 of this evaluation did not preclude the note hedges from being considered indexed to Ionis' stock because the contingent exercise provisions of the note hedges are not based on an observable market or index that is not based on Ionis' stock or operations.

2. Step 2: Evaluation of Settlement Provisions. ASC 815-40-15-7C states an instrument (or embedded feature) shall be considered indexed to an entity's own stock if its settlement amount will equal the difference between the following:

- **The fair value of a fixed number of the entity's equity shares.**
 - **A fixed monetary amount or a fixed amount of a debt instrument issued by the entity.**
- We concluded the note hedges met the Step 2 criteria to be indexed to Ionis' stock because we can exercise the note hedges on a net-share basis for a fixed number of shares for a fixed amount. However, the note hedges allow for adjustments to the settlement amount in certain instances to protect the parties to the note hedges from dilution and other extraordinary events. These adjustments are appropriately designed in a commercially reasonable manner to maintain the fair value of the note hedges both before and after such events and to allow the counterparties to the note hedges to maintain a standard hedge position. There are no adjustment provisions that provide down round or other inappropriate price protections.

We concluded that the note hedges were indexed to Ionis' stock.

ii. Classified in stockholders' equity in its statement of financial position

Contracts shall be initially classified as equity in both of the following situations:

- **Contracts that require physical settlement or net share settlement**
- **Contracts that give the entity a choice of net cash settlement or settlement in its own shares (physical settlement or net share settlement), assuming that all the criteria set forth in paragraphs 815-40-25-7 through 25-35 have been met.**

- o Ionis has the ability to elect net cash settlement or net settlement in shares for the note hedges. Therefore, we evaluated the criteria in ASC 815-40-25-7 through 25-43:
 - **The contracts cannot include any provisions that could require net-cash settlement, other than if the cash payment is only required upon the final liquidation of the Company. [ASC 815-40-25-7 through 10].**
 - The default contractual settlement method for the note hedges is net share settlement. The company has the option in certain cases to require settlement in cash, but the counterparties cannot require cash settlement.
 - **The contract must permit the Company to settle in unregistered shares. [ASC 815-40-25-11 through 16]**
 - This is not applicable for the note hedges because Ionis will never be required to deliver shares to the counterparties.
 - **The Company must have sufficient authorized and unissued shares available to settle the contract after considering all other commitments that may require the issuance of stock during the maximum period the derivative contract could remain outstanding. [ASC 815-40-25-19 through 24]**
 - This is not applicable for the note hedges because Ionis will never be required to deliver shares to the counterparties.
 - **The contract contains an explicit limit on the number of shares to be delivered in a share settlement. [ASC 815-40-25-26 through 28]**
 - This is not applicable for the note hedges because Ionis will never be required to deliver shares to the counterparties.
 - **There are no required cash payments to the counterparty in the event the Company fails to make timely filings with the SEC. [ASC 815-40-25-29]**
 - This is not applicable to the note hedges because there is no such provision in the note hedges.

- **There are no required cash payments to the counterparty if the shares initially delivered upon settlement are subsequently sold by the counterparty and the sales proceeds are insufficient to provide the counterparty with full return of the amount due (that is, there are no cash settled "top-off" or "make-whole" provisions). [ASC 815-40-25-30]**
 - This is not applicable for the note hedges because the note hedges do not contain this term.
- **There are no provisions in the contract that indicate that the counterparty has rights that rank higher than those of a shareholder of the stock underlying the contract. [ASC 815-40-25-31 through 34]**
 - This is not applicable for the note hedges because the note hedges do not contain this or similar terms.
- **There is no requirement in the contract to post collateral at any point or for any reason. [ASC 815-40-25-35]**
 - The note hedges explicitly state that Ionis is not required to post any collateral.

Based on the above facts, we concluded that the note hedges met the criteria for classification in stockholders' equity.

3. Accounting Treatment Conclusion

Since we concluded that the note hedges met the above qualifications for a derivative scope exception (i.e., the note hedges were indexed to Ionis' stock and met the criteria for classification in stockholders' equity), we classified the amount we paid as additional paid in capital.

ii. Warrants

1. Evaluation of Derivative Definition

The next part of the analysis for the warrants required us to determine if the warrants met the definition of a derivative. We used the guidance in ASC 815-10-15-83, which defines a derivative instrument as a financial instrument or other contract with all of the following characteristics:

- **Underlying, notional amount, payment provision. The contract has both of the following terms, which determine the amount of the settlement or settlements, and, in some cases, whether or not a settlement is required:**
 - **One or more underlyings**
 - **One or more notional amounts or payment provisions or both.**
- The warrants met this criterion because:
 - The underlying of the warrants is Ionis' common stock.
 - The notional of the warrants is a specified number of shares of Ionis' common stock we would issue to the counterparties to the warrants.

- **Initial net investment.** The contract requires no initial net investment or an initial net investment that is smaller than would be required for other types of contracts that would be expected to have a similar response to changes in market factors.
 - The warrants met this criterion because the premium the counterparties paid for the warrants was less by more than a nominal amount than investing in the underlying shares. As such, the premium the counterparties paid for the warrants represented a minimal initial net investment.
- **Net settlement.** The contract can be settled net by any of the following means:
 - Its terms implicitly or explicitly require or permit net settlement.
 - It can readily be settled net by a means outside the contract.
 - It provides for delivery of an asset that puts the recipient in a position not substantially different from net settlement.
 - The warrants met these criteria because the warrants are net share settleable by contract.

Based on the above criteria, we concluded that the warrants met the definition of a derivative.

2. Evaluation of Derivative Scope Exception

We next evaluated if the warrants met the requirements for a derivative scope exception using the guidance in ASC 815-10-15-74(a):

Notwithstanding the conditions of paragraphs 815-10-15-13 through 15-139, the reporting entity shall not consider the following contracts to be derivative instruments for purposes of this Subtopic. Contracts issued or held by that reporting entity that are both: (i) indexed to its own stock and (ii) classified in stockholders' equity in its statement of financial position:

i. Indexed to its own stock

To evaluate whether an instrument is considered indexed to an entity's own stock, we used the guidance in ASC 815-40-15-7:

An entity shall evaluate whether an equity-linked financial instrument (or embedded feature), as discussed in ASC 815-40-15-5 through 15-8 is considered indexed to its own stock within the meaning of this Subtopic and ASC 815-10-15-74(a) using the following two-step approach:

1. Step 1: Evaluate the instrument's contingent exercise provisions, if any.

ASC 815-40-15-7C states that an exercise contingency shall not preclude an instrument (or embedded feature) from being considered indexed to an entity's own stock provided that it is not based on either of the following:

- An observable market, other than the market for the issuer's stock (if applicable).
- An observable index, other than an index calculated or measured solely by reference to the issuer's own operations (for example, sales revenue of the issuer; earnings before interest, taxes, depreciation, and amortization of the issuer; net income of the issuer; or total equity of the issuer).

We concluded that Step 1 of this evaluation did not preclude the warrants from being considered indexed to Ionis' stock because the contingent exercise provisions of the warrants are not based on an observable market or index that is not based on Ionis' stock or operations.

2. Step 2: Evaluation of Settlement Provisions. ASC 815-40-15-7C states an instrument (or embedded feature) shall be considered indexed to an entity's own stock if its settlement amount will equal the difference between the following:

- **The fair value of a fixed number of the entity's equity shares.**
- **A fixed monetary amount or a fixed amount of a debt instrument issued by the entity.**
 - o We concluded the warrants met the Step 2 criteria to be indexed to Ionis' stock because the counterparties can exercise the warrants on a net-share basis for a fixed number of shares for a fixed amount. However, the warrants allow for adjustments to the settlement amount in certain instances to protect the parties to the warrants from dilution and other extraordinary events. These adjustments are appropriately designed in a commercially reasonable manner to maintain the fair value of the warrants both before and after such events and to allow the counterparties to the warrants to maintain a standard hedge position. There are not adjustment provisions that provide down round or other inappropriate price protections.

We concluded that the warrants were indexed to Ionis' stock.

iii. Classified in stockholders' equity in its statement of financial position

Contracts shall be initially classified as equity in both of the following situations:

- **Contracts that require physical settlement or net share settlement**
- **Contracts that give the entity a choice of net cash settlement or settlement in its own shares (physical settlement or net share settlement), assuming that all the criteria set forth in paragraphs 815-40-25-7 through 25-35 have been met.**

Ionis has the ability to elect net cash settlement or net settlement in shares for the warrants. Therefore, we evaluated the criteria in ASC 815-40-25-7 through 25-43:

- **The contracts cannot include any provisions that could require net-cash settlement, other than if the cash payment is only required upon the final liquidation of the Company. [ASC 815-40-25-7 through 10].**

- The default contractual settlement method for the warrants is net share settlement. Ionis has the option to settle in cash, but the counterparties cannot require cash settlement.
- **The contract must permit the Company to settle in unregistered shares. [ASC 815-40-25-11 through 16]**
 - The warrants allow Ionis to settle in unregistered shares.
- **The Company must have sufficient authorized and unissued shares available to settle the contract after considering all other commitments that may require the issuance of stock during the maximum period the derivative contract could remain outstanding. [ASC 815-40-25-19 through 24]**
 - Ionis has sufficient authorized and unissued shares available to settle the warrants. Prior to executing the transactions in December 2019, Ionis had 300 million shares of common stock authorized with 175 million shares of common stock that were outstanding or reserved for future issuance. The maximum number of shares of common stock Ionis would issue for the conversion of 0.125% Notes and the exercise of the warrants is approximately 22 million shares of common stock.
- **The contract contains an explicit limit on the number of shares to be delivered in a share settlement. [ASC 815-40-25-26 through 28]**
 - The warrants contain an explicit limit on the number of shares to be delivered.
- **There are no required cash payments to the counterparty in the event the Company fails to make timely filings with the SEC. [ASC 815-40-25-29]**
 - This is not applicable to the warrants because there is no such provision in the warrants.
- **There are no required cash payments to the counterparty if the shares initially delivered upon settlement are subsequently sold by the counterparty and the sales proceeds are insufficient to provide the counterparty with full return of the amount due (that is, there are no cash settled "top-off" or "make-whole" provisions). [ASC 815-40-25-30]**
 - This is not applicable to the warrants because the warrants do not contain this or similar terms.

- **There are no provisions in the contract that indicate that the counterparty has rights that rank higher than those of a shareholder of the stock underlying the contract. [ASC 815-40-25-31 through 34]**
 - This is not applicable to the warrants because the warrants do not contain this or similar terms.
- **There is no requirement in the contract to post collateral at any point or for any reason. [ASC 815-40-25-35]**
 - The warrants explicitly state that Ionis is not required to post any collateral.

Based on the above facts, we concluded that the warrants met the criterion for classification in stockholders' equity.

3. Accounting Treatment Conclusion

Since we concluded that the warrants met the above qualifications for a derivative scope exception (i.e., the warrants were indexed to Ionis' stock and met the criteria for classification in stockholders' equity), we classified the amount we received from the counterparties as additional paid in capital.

IV. Accounting Policy Disclosure

In response to the Staff's request, we will include the following accounting policy disclosure in future periodic reports:

Call Spread

In conjunction with the issuance of our 0.125% Notes, we entered into a call spread transaction, which was comprised of purchasing note hedges and selling warrants. We account for the note hedges and warrants as separate freestanding financial instruments and treat each instrument as a separate unit of accounting. We determined that the note hedges and warrants do not meet the definition of a liability using the guidance contained in ASC Topic 480, therefore we account for the note hedges and warrants using the Derivatives and Hedging – Contracts in Entity's Own Equity accounting guidance contained in ASC Topic 815. We determined that the note hedges and warrants meet the definition of a derivative, are indexed to our stock and meet the criteria to be classified in shareholders' equity. We recorded the aggregate amount paid for the note hedges and the aggregate amount received for the warrants as additional paid-in capital in our consolidated balance sheet. We reassess our ability to continue to classify the note hedges and warrants in shareholders' equity at each reporting period.

In connection with this response, we acknowledge the following:

- The company is responsible for the adequacy and accuracy of the disclosure in the filings;
- Staff comments or changes to disclosure in response to staff comments do not foreclose the Commission from taking any action with respect to the filings; and
- The company may not assert staff comments as a defense in any proceeding initiated by the Commission or any person under the federal securities laws of the United States.

Should you have any questions regarding our responses or require any additional information, please contact me at (760) 603-2492.

Sincerely,

/s/ Elizabeth L. Hougen

Elizabeth L. Hougen
Exec Vice President, Finance and CFO