# United States SECURITIES AND EXCHANGE COMMISSION

**WASHINGTON, D.C. 20549** 

# **SCHEDULE 13G**

Under the Securities Exchange Act of 1934 (Amendment No. 4)\*

ISIS PHARMACEUTICALS, INC.
(Name of Issuer)
Common Stock
(Title of Class of Securities)
464330109
(CUSIP Number)
December 31, 2014
(Date of Event Which Requires Filing This Statement)
Check the appropriate box to designate the rule pursuant to which this Schedule is filed:
☐ Rule 13d-1(b)
⊠ Rule 13d-1(c)

The remainder of this cover page shall be filled out for a reporting person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter the disclosures provided in a prior cover page.

☐ Rule 13d-1(d)

The information required in the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934 ("Act") or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act (however, see the Notes).

# CUSIP No. 464330109 Names of Reporting Persons **BB Biotech AG** Check the Appropriate Box if a Member of a Group (See Instructions) (a) 🗵 (b) □ 3. SEC Use Only Citizenship or Place of Organization **Switzerland** 5. Sole Voting Power Number of Shared Voting Power Shares Beneficially 5,976,526 Owned by Each Sole Dispositive Power Reporting Person with: Shared Dispositive Power 5,976,526 Aggregate Amount Beneficially Owned by Each Reporting Person 5,976,526 10. Check if the Aggregate Amount in Row (9) Excludes Certain Shares

11. Percent of Class Represented by amount in Row (9)

12. Type of Reporting Person (See Instructions)

**5.1%** 

HC,CO

### CUSIP No. 464330109

1.	. Names of Reporting Persons				
	Biotech Target N.V.				
	I.R.S. Identification Nos. of above persons (entities only):				
	N/A				
2. Check the Appropriate Box if a Member of a Group (See Instructions)  (a) ⊠ (b) □					
3.	3. SEC Use Only				
4.	. Citizenship or Place of Organization				
	Curac	ao			
		5.	Sole Voting Power		
Number of Shares Beneficially Owned by Each Reporting Person with:			0		
		6.	Shared Voting Power		
			5,976,526		
		7.	Sole Dispositive Power		
			0		
		8.	Shared Dispositive Power		
			5,976,526		
9.	9. Aggregate Amount Beneficially Owned by Each Reporting Person				
	5,976,526				
10.	. Check if the Aggregate Amount in Row (9) Excludes Certain Shares				
11.	1. Percent of Class Represented by amount in Row (9)				
	5.1%				
12.	2. Type of Reporting Person (See Instructions)				
	СО				

#### Item 4. Ownership

Provide the following information regarding the aggregate number and percentage of the class of securities of the issuer identified in Item 1.

- (a) Amount beneficially owned: <u>5,976,526</u>
- (b) Percent of class: 5.1%
- (c) Number of shares as to which the person has:
- (i) Sole power to vote or to direct the vote  $\underline{0}$
- (ii) Shared power to vote or to direct the vote <u>5,976,526</u>
- (iii) Sole power to dispose or to direct the disposition of  $\underline{0}$
- (iv) Shared power to dispose or to direct the disposition of <u>5,976,526</u>

#### **Item 10. Certification**

By signing below I certify that, to the best of my knowledge and belief, the securities referred to above were not acquired and are not held for the purpose of or with the effect of changing or influencing the control of the issuer of the securities and were not acquired and are not held in connection with or as a participant in any transaction having that purpose or effect.

#### **SIGNATURES**

After reasonable inquiry and the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

BB Biotech AG			
Date: <b>February 11, 2015</b>	By:	/s/ Michael Hutter	
		Signatory Authority	
	Name:	Michael Hutter	
	Title:	Signatory Authority	
Date: <b><u>February 11, 2015</u></b>	Ву:	/s/ Ivo Betschart	
		Signatory Authority	
	Name:	Ivo Betschart	
	Title:	Signatory Authority	
Biotech Target N.V.			
Date: <b>February 11, 2015</b>	Ву:	/s/ Michael Hutter	
	,	Signatory Authority	
	Name:	Michael Hutter	
	Title:	Signatory Authority	
Date: <b>February 11, 2015</b>	Ву:	/s/ Ivo Betschart	
		Signatory Authority	
	Name:	Ivo Betschart	
	Title:	Signatory Authority	

## **Exhibit Index**

Exhibit A: Agreement by and between BB Biotech AG and Biotech Target N.V. with respect to the filing of this disclosure statement.\*

\*Previously filed as an exhibit to BB Biotech AG and Biotech Target N.V.'s Schedule 13G filed with the Securities and Exchange Commission on July 20, 2011.