

SCHEDULE 13G

Amendment No. 8  
ISIS PHARMACEUTICALS  
COMMON STOCK

Cusip #464330109

Check the appropriate box to designate the rule pursuant to which this  
Schedule is filed:

- Rule 13d-1(b)
- Rule 13d-1(c)
- Rule 13d-1(d)

Cusip #464330109

Item 1: Reporting Person - FMR LLC

Item 2: (a)

(b)

Item 4: Delaware

Item 5: 1,641,200

Item 6: 0

Item 7: 17,892,555

Item 8: 0

Item 9: 17,892,555

Item 11: 15.098%

Item 12: HC

Cusip #464330109

Item 1: Reporting Person - Edward C. Johnson 3d

Item 2: (a)

(b)

Item 4: United States of America

Item 5: 0

Item 6: 0

Item 7: 17,892,555

Item 8: 0

Item 9: 17,892,555

Item 11: 15.098%

Item 12: IN

Cusip #464330109

Item 1: Reporting Person - Abigail P. Johnson

Item 2: (a)

(b)

Item 4: United States of America

Item 5: 0

Item 6: 0

Item 7: 17,892,555

Item 8: 0

Item 9: 17,892,555

Item 11: 15.098%

Item 12: IN

Cusip #464330109

Item 1: Reporting Person - Fidelity Growth Company Fund

Item 2: (a)

(b)

Item 4: Massachusetts

Item 5: 8,412,397

Item 6: 0

Item 7: 0

Item 8: 0

Item 9: 8,412,397

Item 11: 7.098%

Item 12: IV

Item 1(a). Name of Issuer:

ISIS PHARMACEUTICALS

Item 1(b). Address of Issuer's Principal Executive Offices:

1896 Rutherford Road  
Carlsbad, CA 92008

Item 2(a). Name of Person Filing:

FMR LLC

Item 2(b). Address or Principal Business Office or, if None,  
Residence:

245 Summer Street, Boston, Massachusetts 02210

Item 2(c). Citizenship:

Not applicable

Item 2(d). Title of Class of Securities:

COMMON STOCK

Item 2(e). CUSIP Number:

464330109

Item 3. This statement is filed pursuant to Rule 13d-1(b) or 13d-2(b) or (c) and the person filing, FMR LLC, is a parent holding company in accordance with Section 240.13d-1(b)(1)(ii)(G). (Note: See Exhibit A).

Item 4. Ownership

(a) Amount Beneficially Owned: 17,892,555

(b) Percent of Class: 15.098%

(c) Number of shares as to which such person has:

(i) sole power to vote or to direct the vote:

1,641,200

(ii) shared power to vote or to direct the vote: 0

(iii) sole power to dispose or to direct the

disposition of: 17,892,555

(iv) shared power to dispose or to direct the

disposition of: 0

Item 5. Ownership of Five Percent or Less of a Class.

Not applicable.

Item 6. Ownership of More than Five Percent on Behalf of Another Person.

Not applicable.

Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on By the Parent Holding Company.

See attached Exhibit A.

Item 8. Identification and Classification of Members of the Group.

Not applicable.

Item 9. Notice of Dissolution of Group.

Not applicable.

Item 10. Certifications.

By signing below I certify that, to the best of my knowledge and belief, the securities referred to above were acquired and are held in the ordinary course of business and 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.

Signature

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

February 13, 2015  
Date

/s/ Scott C. Goebel  
Signature

Scott C. Goebel

Duly authorized under Power of Attorney effective as of June 1, 2008,  
by and on behalf of FMR LLC and its direct and indirect subsidiaries\*

\* This power of attorney is incorporated herein by reference to Exhibit B  
to the Schedule 13G filed by FMR LLC on June 10, 2014, accession number:  
0000315066-14-003512.

Exhibit A

Pursuant to the instructions in Item 7 of Schedule 13G,  
the following table lists the identity and Item 3 classification, if  
applicable, of each relevant entity that beneficially owns shares of the  
security class being reported on this Schedule 13G.

Entity	ITEM 3 Classification
FMR CO., INC *	IA
PYRAMIS GLOBAL ADVISORS TRUST COMPANY	BK

\* Entity beneficially owns 5% or greater of the outstanding shares of the  
security class being reported on this Schedule 13G.

Edward C. Johnson 3d is a Director and the Chairman of FMR  
LLC and Abigail P. Johnson is a Director, the Vice Chairman, the Chief  
Executive Officer and the President of FMR LLC.

Members of the family of Edward C. Johnson 3d, including  
Abigail P. Johnson, are the predominant owners, directly or through trusts,  
of Series B voting common shares of FMR LLC, representing 49% of the voting  
power of FMR LLC. The Johnson family group and all other Series B  
shareholders have entered into a shareholders' voting agreement under which  
all Series B voting common shares will be voted in accordance with the  
majority vote of Series B voting common shares. Accordingly, through their  
ownership of voting common shares and the execution of the shareholders'  
voting agreement, members of the Johnson family may be deemed, under the  
Investment Company Act of 1940, to form a controlling group with respect to  
FMR LLC.

Neither FMR LLC nor Edward C. Johnson 3d nor Abigail P.  
Johnson has the sole power to vote or direct the voting of the shares owned  
directly by the various investment companies registered under the  
Investment Company Act ("Fidelity Funds") advised by Fidelity Management &  
Research Company ("FMR Co"), a wholly owned subsidiary of FMR LLC, which  
power resides with the Fidelity Funds' Boards of Trustees. Fidelity  
Management & Research Company carries out the voting of the shares under  
written guidelines established by the Fidelity Funds' Boards of Trustees.

This filing reflects the securities beneficially owned, or  
that may be deemed to be beneficially owned, by FMR LLC, certain of its  
subsidiaries and affiliates, and other companies (collectively, the "FMR  
Reporters"). This filing does not reflect securities, if any, beneficially  
owned by certain other companies whose beneficial ownership of securities  
is disaggregated from that of the FMR Reporters in accordance with  
Securities and Exchange Commission Release No. 34-39538 (January 12, 1998).

RULE 13d-1(k)(1) AGREEMENT

The undersigned persons, on February 13, 2015, agree and  
consent to the joint filing on their behalf of this Schedule 13G in  
connection with their beneficial ownership of the COMMON STOCK of ISIS  
PHARMACEUTICALS at December 31, 2014.

FMR LLC

By /s/ Scott C. Goebel  
Scott C. Goebel  
Duly authorized under Power of Attorney effective as of June 1, 2008, by  
and on behalf of FMR LLC and its direct and indirect subsidiaries\*

Edward C. Johnson 3d

By /s/ Scott C. Goebel  
Scott C. Goebel  
Duly authorized under Power of Attorney effective as of June 1, 2008, by  
and on behalf of Edward C. Johnson 3d\*

Abigail P. Johnson

By /s/ Scott C. Goebel  
Scott C. Goebel  
Duly authorized under Power of Attorney effective as of April 24, 2014,  
by and on behalf of Abigail P. Johnson\*

Fidelity Growth Company Fund

By /s/ Scott C. Goebel  
Scott C. Goebel  
Secretary

\* This power of attorney is incorporated herein by reference to Exhibit B  
to the Schedule 13G filed by FMR LLC on June 10, 2014, accession number:  
0000315066-14-003512.