

SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549

SCHEDULE 13D  
(RULE 13d-101)

INFORMATION TO BE INCLUDED IN STATEMENTS FILED PURSUANT  
TO RULE 13d-1(a) AND AMENDMENTS THERETO FILED PURSUANT TO  
RULE 13d-2(a)

(AMENDMENT NO. 3)

ISIS PHARMACEUTICALS, INC.

-----  
(Name of Issuer)

COMMON STOCK, PAR VALUE \$0.001 PER SHARE

-----  
(Title of Class of Securities)

464330 10 9

-----  
(Cusip Number)

HANS-PETER MUELLER  
BOEHRINGER INGELHEIM INTERNATIONAL GMBH  
BINGER STRASSE 173  
D-55216 INGELHEIM AM RHEIN, GERMANY  
011-49-61-32-77-2414

AND

KLAUS H. JANDER, ESQ.  
CLIFFORD CHANCE ROGERS & WELLS LLP  
200 PARK AVENUE  
NEW YORK, NY 10166  
(212) 878-8000

-----  
(Name, Address and Telephone Number of Person  
Authorized to Receive Notices and Communications)

JUNE 5, 2000

-----  
(Date of Event Which Requires Filing of This Statement)

If the filing person has previously filed a statement on Schedule 13G to report the acquisition that is the subject of this Schedule 13D, and is filing this schedule because of Rule 13d-1(e), 13d-1(f) or 13d-1(g), check the following box / /

Note. Schedules filed in paper format should include a signed original and five copies of the schedule, including all exhibits. See Rule 13d-7(b) for the other parties to whom copies are to be sent.

(Continued on following pages)

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CUSIP NO. 464330 10 9  
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13D

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PAGE 2 OF 5 PAGES  
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1. NAMES OF REPORTING PERSONS  
S.S. OR I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Boehringer Ingelheim International GmbH

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2. CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP

(a) / /  
(b) / /

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3. SEC USE ONLY

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4. SOURCES OF FUNDS

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5. CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM  
2(d) OR 2(e)

/ /

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6. CITIZENSHIP OR PLACE OF ORGANIZATION

Federal Republic of Germany

	7. SOLE VOTING POWER
	2,030,107
NUMBER OF	-----
UNITS	8. SHARED VOTING POWER
BENEFICIALLY	0
OWNED BY	-----
EACH REPORTING	9. SOLE DISPOSITIVE POWER
PERSON	2,030,107
WITH	-----
	10. SHARED DISPOSITIVE POWER
	0

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11. AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

2,030,107

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12. CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES

/ /

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13. PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)

5.5%

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14. TYPE OF REPORTING PERSON

CO

SCHEDULE 13D  
 FILED PURSUANT TO RULE 13d-1  
 OF THE GENERAL RULES AND REGULATIONS UNDER  
 THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

This Amendment No. 3, which relates to shares of the common stock, par value \$0.001 per share (the "Common Stock") of Isis Pharmaceuticals, Inc. (the "Issuer") and is being filed by Boehringer Ingelheim International GmbH ("Boehringer"), supplements and amends the statement on Schedule 13D, originally filed with the Commission on July 28, 1995, as amended by Amendment No. 1, filed with the Commission on December 23, 1996 and Amendment No. 2, filed with the Commission on September 2, 1999.

ITEM 5. INTEREST IN THE SECURITIES OF THE ISSUER.

Item 5 is hereby amended to read in its entirety as follows:

- (a) Beneficial Ownership: 2,030,107  
 Percentage Ownership: 5.5%
- (b) Sole Voting Power: 2,030,107  
 Shared Voting Power: -0-  
 Sole Dispositive Power: 2,030,107  
 Shared Dispositive Power: -0-
- (c) Recent Transactions: The following table sets forth sales of shares of Common Stock by Boehringer since September 2, 1999. Such sales were effected on the open market over the Nasdaq Stock Market by a broker.

DATE	AMOUNT OF SHARES	APPROXIMATE PRICE PER SHARE (exclusive of commissions)
3/23/00	10,000	\$18.0688
3/29/00	20,000	\$13.9263
3/30/00	20,000	\$13.6075
4/3/00	20,000	\$14.0000
4/5/00	20,000	\$12.5125
4/5/00	20,000	\$11.3388
4/6/00	40,000	\$14.7729
4/7/00	21,600	\$15.6079
4/11/00	3,800	\$14.0000
4/12/00	20,000	\$13.0000
5/2/00	20,000	\$12.0775
5/3/00	20,000	\$11.1016
5/4/00	9,600	\$11.5078
5/5/00	20,000	\$11.5000
5/15/00	20,000	\$10.0109
5/16/00	20,000	\$10.2538
5/18/00	20,000	\$10.5141
5/19/00	6,600	\$10.5000
5/22/00	1,900	\$10.6140
6/2/00	20,000	\$10.0863
6/5/00	9,000	\$11.2688
6/5/00	20,000	\$10.2500

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(d) Right to Receive Dividends: Not Applicable

(e) Ownership below 5%: Not Applicable

## SIGNATURES

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.

Dated: June 8, 2000

BOEHRINGER INGELHEIM INTERNATIONAL GmbH

By: /s/ Mueller  
Name: Mr. Mueller  
Title: Authorized Signatory

By: /s/ Joos  
Name: Mr. Joos  
Title: Authorized Signatory