

SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

POST EFFECTIVE  
AMENDMENT NO. 1  
TO  
FORM S-3  
REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933

ISIS PHARMACEUTICALS, INC.  
(Exact name of Registrant as specified in its charter)

Delaware  
(State or other jurisdiction  
of incorporation or organization)

33-0336973  
(I.R.S. Employer  
Identification Number)

2292 Faraday Avenue  
Carlsbad, California 92008  
(760) 931-9200  
(Address, including zip code, and telephone number, include area code, of  
Registrant's principal executive offices)

B. Lynne Parshall, Esq.  
Executive Vice President and Chief Financial Officer  
ISIS PHARMACEUTICALS, INC.  
2292 Faraday Avenue  
Carlsbad, California 92008  
(760) 931-9200  
(Name, address, including zip code, and telephone number,  
including area code, of agent for service)

Copy to:

D. Bradley Peck, Esq.  
COOLEY GODWARD LLP  
4365 Executive Drive  
San Diego, CA 92121  
(619) 550-6000

This Post-Effective Amendment No. 1 is being filed to deregister 1,098,684 shares of Common Stock (the "Shares") of Isis Pharmaceuticals, Inc. covered by the Form S-3 Registration Statement No. 33-72124 (the "Registration Statement"). The Shares are no longer being offered by the holders thereof in registered resale transactions described in the prospectus filed as part of the Registration Statement.

## SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has duly caused this Post-Effective Amendment No. 1 to the Registration Statement to be signed on its behalf by the undersigned thereunto duly authorized, in the city of Carlsbad, County of San Diego, State of California, on the 22nd day of July 1997.

ISIS PHARMACEUTICALS, INC.

By: /s/ B. LYNNE PARSHALL

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B. Lynne Parshall  
Executive Vice President and  
Chief Financial Officer

Pursuant to the requirements of the Securities Act of 1933, this Post-Effective Amendment No. 1 to the Registration Statement has been signed below by the following persons in the capacities indicated and on the dates indicated.

SIGNATURE -----	TITLE -----	DATE ----
* ----- Stanley T. Crooke, M.D., Ph.D	Chairman of the Board and Chief Executive Officer (Principal executive officer)	July 22, 1997
/s/ B. LYNNE PARSHALL ----- B. Lynne Parshall	Executive Vice President and Chief Financial Officer (Principal financial and accounting officer)	July 22, 1997
* ----- Daniel L. Kisner, M.D.	President, Chief Operating Officer and Director	July 22, 1997
* ----- Burkhard Blank	Director	July 22, 1997
* ----- Christopher F.O. Gabrieli	Director	July 22, 1997
* ----- Alan C. Mendelson	Director	July 22, 1997
* ----- William R. Miller	Director	July 22, 1997
* ----- Mark B. Skaletsky	Director	July 22, 1997
* ----- Larry Soll, Ph.D.	Director	July 22, 1997
* ----- Joseph H. Wender	Director	July 22, 1997

\*By: /s/ B. LYNNE PARSHALL

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B. Lynne Parshall, Attorney-  
in-Fact

