

The Securities and Exchange Commission has not necessarily reviewed the information in this filing and has not determined if it is accurate and complete.

The reader should not assume that the information is accurate and complete.

**UNITED STATES SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549  
**FORM D**

| OMB APPROVAL                                    |           |
|---|-----------|
| OMB Number:                                     | 3235-0076 |
| Estimated average burden<br>hours per response: | 4.00      |

**Notice of Exempt Offering of Securities**

**1. Issuer's Identity**

|  |                |  |  |
|--|----------------|--|--|
| CIK (Filer ID Number)  | Previous Names | <input checked="" type="checkbox"/> None | Entity Type  |
| <a href="#">0000874015</a>                                     |                |  | <input checked="" type="checkbox"/> Corporation    |
| Name of Issuer   |                |  | <input type="checkbox"/> Limited Partnership       |
| <a href="#">ISIS PHARMACEUTICALS INC</a>                       |                |  | <input type="checkbox"/> Limited Liability Company |
| Jurisdiction of Incorporation/Organization                     |                |  | <input type="checkbox"/> General Partnership       |
| <a href="#">DELAWARE</a>                                       |                |  | <input type="checkbox"/> Business Trust            |
| Year of Incorporation/Organization                             |                |  | <input type="checkbox"/> Other (Specify)           |
| <input checked="" type="checkbox"/> Over Five Years Ago        |                |  |  |
| <input type="checkbox"/> Within Last Five Years (Specify Year) |                |  |  |
| <input type="checkbox"/> Yet to Be Formed                      |                |  |  |

**2. Principal Place of Business and Contact Information**

|  |                            |                       |                            |
|--|----------------------------|-----------------------|----------------------------|
| Name of Issuer                           |                            |                       |                            |
| <a href="#">ISIS PHARMACEUTICALS INC</a> |                            |                       |                            |
| Street Address 1                         | Street Address 2           |                       |                            |
| <a href="#">2855 GAZELLE COURT</a>       |                            |                       |                            |
| City                                     | State/Province/Country     | ZIP/PostalCode        | Phone Number of Issuer     |
| <a href="#">CARLSBAD</a>                 | <a href="#">CALIFORNIA</a> | <a href="#">92010</a> | <a href="#">7609319200</a> |

**3. Related Persons**

|  |                            |                       |
|--|----------------------------|-----------------------|
| Last Name  | First Name                 | Middle Name           |
| <a href="#">CROOKE</a>   | <a href="#">STANLEY</a>    | <a href="#">T</a>     |
| Street Address 1   | Street Address 2           |                       |
| <a href="#">2855 GAZELLE COURT</a>   |                            |                       |
| City   | State/Province/Country     | ZIP/PostalCode        |
| <a href="#">CARLSBAD</a>   | <a href="#">CALIFORNIA</a> | <a href="#">92010</a> |
| Relationship: <input checked="" type="checkbox"/> Executive Officer <input checked="" type="checkbox"/> Director <input type="checkbox"/> Promoter |                            |                       |

Clarification of Response (if Necessary):

|   |                                    |                       |
|---|------------------------------------|-----------------------|
| Last Name   | First Name                         | Middle Name           |
| <a href="#">BERTHELSEN</a>  | <a href="#">SPENCER</a>            | <a href="#">R</a>     |
| Street Address 1  | Street Address 2                   |                       |
| <a href="#">C/O ISIS PHARMACEUTICALS, INC.</a>  | <a href="#">2855 GAZELLE COURT</a> |                       |
| City  | State/Province/Country             | ZIP/PostalCode        |
| <a href="#">CARLSBAD</a>  | <a href="#">CALIFORNIA</a>         | <a href="#">92010</a> |
| Relationship: <input type="checkbox"/> Executive Officer <input checked="" type="checkbox"/> Director <input type="checkbox"/> Promoter |                                    |                       |

Clarification of Response (if Necessary):

|  |                                    |             |
|--|------------------------------------|-------------|
| Last Name                                      | First Name                         | Middle Name |
| <a href="#">KLEIN III</a>                      | <a href="#">JOSEPH</a>             |             |
| Street Address 1                               | Street Address 2                   |             |
| <a href="#">C/O ISIS PHARMACEUTICALS, INC.</a> | <a href="#">2855 GAZELLE COURT</a> |             |

City State/Province/Country ZIP/PostalCode  
CARLSBAD CALIFORNIA 92010

Relationship:  Executive Officer  Director  Promoter

Clarification of Response (if Necessary):

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Last Name First Name Middle Name  
MUTO FREDERICK T  
Street Address 1 Street Address 2  
4401 EASTGATE MALL  
City State/Province/Country ZIP/PostalCode  
SAN DIEGO CALIFORNIA 92121

Relationship:  Executive Officer  Director  Promoter

Clarification of Response (if Necessary):

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Last Name First Name Middle Name  
PARSHALL B LYNNE  
Street Address 1 Street Address 2  
2855 GAZELLE COURT  
City State/Province/Country ZIP/PostalCode  
CARLSBAD CALIFORNIA 92010

Relationship:  Executive Officer  Director  Promoter

Clarification of Response (if Necessary):

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Last Name First Name Middle Name  
REED JOHN C  
Street Address 1 Street Address 2  
C/O ISIS PHARMACEUTICALS, INC. 2855 GAZELLE COURT  
City State/Province/Country ZIP/PostalCode  
CARLSBAD CALIFORNIA 92010

Relationship:  Executive Officer  Director  Promoter

Clarification of Response (if Necessary):

---

Last Name First Name Middle Name  
WENDER JOSEPH H  
Street Address 1 Street Address 2  
C/O ISIS PHARMACEUTICALS, INC. 2855 GAZELLE COURT  
City State/Province/Country ZIP/PostalCode  
CARLSBAD CALIFORNIA 92010

Relationship:  Executive Officer  Director  Promoter

Clarification of Response (if Necessary):

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Last Name First Name Middle Name  
BENNETT C FRANK  
Street Address 1 Street Address 2  
2855 GAZELLE COURT  
City State/Province/Country ZIP/PostalCode  
CARLSBAD CALIFORNIA 92010

Relationship:  Executive Officer  Director  Promoter

Clarification of Response (if Necessary):

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Last Name First Name Middle Name  
GEARY RICHARD S  
Street Address 1 Street Address 2

2855 GAZELLE COURT

City State/Province/Country ZIP/PostalCode  
CARLSBAD CALIFORNIA 92010

Relationship:  Executive Officer  Director  Promoter

Clarification of Response (if Necessary):

Last Name First Name Middle Name  
MONIA BRETT P  
Street Address 1 Street Address 2  
2855 GAZELLE COURT  
City State/Province/Country ZIP/PostalCode  
CARLSBAD CALIFORNIA 92010  
Relationship:  Executive Officer  Director  Promoter

Clarification of Response (if Necessary):

**4. Industry Group**

- Agriculture
- Banking & Financial Services
  - Commercial Banking
  - Insurance
  - Investing
  - Investment Banking
  - Pooled Investment Fund
- Is the issuer registered as an investment company under the Investment Company Act of 1940?
  - Yes  No
- Other Banking & Financial Services
- Business Services
  - Energy
    - Coal Mining
    - Electric Utilities
    - Energy Conservation
    - Environmental Services
    - Oil & Gas
    - Other Energy
- Health Care
  - Biotechnology
  - Health Insurance
  - Hospitals & Physicians
  - Pharmaceuticals
  - Other Health Care
- Manufacturing
- Real Estate
  - Commercial
  - Construction
  - REITS & Finance
  - Residential
  - Other Real Estate
- Retailing
- Restaurants
- Technology
  - Computers
  - Telecommunications
  - Other Technology
- Travel
  - Airlines & Airports
  - Lodging & Conventions
  - Tourism & Travel Services
  - Other Travel
- Other

**5. Issuer Size**

Revenue Range OR Aggregate Net Asset Value Range  
 No Revenues  No Aggregate Net Asset Value

- \$1 - \$1,000,000
- \$1,000,001 - \$5,000,000
- \$5,000,001 - \$25,000,000
- \$25,000,001 - \$100,000,000
- Over \$100,000,000
- Decline to Disclose
- Not Applicable

- \$1 - \$5,000,000
- \$5,000,001 - \$25,000,000
- \$25,000,001 - \$50,000,000
- \$50,000,001 - \$100,000,000
- Over \$100,000,000
- Decline to Disclose
- Not Applicable

**6. Federal Exemption(s) and Exclusion(s) Claimed (select all that apply)**

- Rule 504(b)(1) (not (i), (ii) or (iii))
- Rule 504 (b)(1)(i)
- Rule 504 (b)(1)(ii)
- Rule 504 (b)(1)(iii)
- Rule 505
- Rule 506
- Securities Act Section 4(5)
- Investment Company Act Section 3(c)
  - Section 3(c)(1)
  - Section 3(c)(2)
  - Section 3(c)(3)
  - Section 3(c)(4)
  - Section 3(c)(5)
  - Section 3(c)(6)
  - Section 3(c)(7)
  - Section 3(c)(9)
  - Section 3(c)(10)
  - Section 3(c)(11)
  - Section 3(c)(12)
  - Section 3(c)(13)
  - Section 3(c)(14)

**7. Type of Filing**

- New Notice Date of First Sale 2012-08-13  First Sale Yet to Occur
- Amendment

**8. Duration of Offering**

Does the Issuer intend this offering to last more than one year?  Yes  No

**9. Type(s) of Securities Offered (select all that apply)**

- Equity
- Debt
- Option, Warrant or Other Right to Acquire Another Security
- Security to be Acquired Upon Exercise of Option, Warrant or Other Right to Acquire Security
- Pooled Investment Fund Interests
- Tenant-in-Common Securities
- Mineral Property Securities
- Other (describe)

**10. Business Combination Transaction**

Is this offering being made in connection with a business combination transaction, such as a merger, acquisition or exchange offer?  Yes  No

Clarification of Response (if Necessary):

**11. Minimum Investment**

Minimum investment accepted from any outside investor \$0 USD

**12. Sales Compensation**

Recipient (Associated) Broker or Dealer  None  
 Recipient CRD Number  None  
 (Associated) Broker or Dealer CRD Number  None

Street Address 1

City

State(s) of Solicitation (select all that apply)  All States  
Check "All States" or check individual States

Street Address 2

State/Province/Country

Foreign/non-US

ZIP/Postal Code

### 13. Offering and Sales Amounts

Total Offering Amount \$201,250,000 USD or  Indefinite

Total Amount Sold \$201,250,000 USD

Total Remaining to be Sold \$0 USD or  Indefinite

Clarification of Response (if Necessary):

Represents the aggregate principal amount of 2-3/4% Convertible Senior Notes due 2019, which were sold to the initial purchasers at a 3% discount from the aggregate principal amount.

### 14. Investors

Select if securities in the offering have been or may be sold to persons who do not qualify as accredited investors, and enter the number of such non-accredited investors who already have invested in the offering.

Regardless of whether securities in the offering have been or may be sold to persons who do not qualify as accredited investors, enter the total number of investors who already have invested in the offering:

### 15. Sales Commissions & Finder's Fees Expenses

Provide separately the amounts of sales commissions and finders fees expenses, if any. If the amount of an expenditure is not known, provide an estimate and check the box next to the amount.

Sales Commissions \$0 USD  Estimate

Finders' Fees \$0 USD  Estimate

Clarification of Response (if Necessary):

### 16. Use of Proceeds

Provide the amount of the gross proceeds of the offering that has been or is proposed to be used for payments to any of the persons required to be named as executive officers, directors or promoters in response to Item 3 above. If the amount is unknown, provide an estimate and check the box next to the amount.

\$0 USD  Estimate

Clarification of Response (if Necessary):

### Signature and Submission

Please verify the information you have entered and review the Terms of Submission below before signing and clicking SUBMIT below to file this notice.

#### Terms of Submission

In submitting this notice, each issuer named above is:

- Notifying the SEC and/or each State in which this notice is filed of the offering of securities described and undertaking to furnish them, upon written request, in the accordance with applicable law, the information furnished to offerees.\*
- Irrevocably appointing each of the Secretary of the SEC and, the Securities Administrator or other legally designated officer of the State in which the issuer maintains its principal place of business and any State in which this notice is filed, as its agents for service of process, and agreeing that these persons may accept service on its behalf, of any notice, process or pleading, and further agreeing that such service may be made by registered or certified mail, in any Federal or state action, administrative proceeding, or arbitration brought against it in any place subject to the jurisdiction of the United States, if the action, proceeding or arbitration (a) arises out of any activity in connection with the offering of securities that is the subject of this notice, and (b) is founded, directly or indirectly, upon the provisions of: (i) the Securities Act of 1933, the Securities Exchange Act of 1934, the Trust Indenture Act of 1939, the Investment Company Act of 1940, or the Investment Advisers Act of 1940, or any rule or regulation under any of these statutes, or (ii) the laws of the State in which the issuer maintains its principal place of business or any State in which this notice is filed.
- Certifying that, if the issuer is claiming a Rule 505 exemption, the issuer is not disqualified from relying on Rule 505 for one of the reasons stated in Rule 505(b)(2)(iii).

Each Issuer identified above has read this notice, knows the contents to be true, and has duly caused this notice to be signed on its behalf by the

undersigned duly authorized person.

For signature, type in the signer's name or other letters or characters adopted or authorized as the signer's signature.

| Issuer                   | Signature             | Name of Signer    | Title                         | Date       |
|--------------------------|-----------------------|-------------------|-------------------------------|------------|
| ISIS PHARMACEUTICALS INC | /s/ Patrick R. O'Neil | Patrick R. O'Neil | VP, Legal and General Counsel | 2012-08-27 |

*Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB number.*

\* This undertaking does not affect any limits Section 102(a) of the National Securities Markets Improvement Act of 1996 ("NSMIA") [Pub. L. No. 104-290, 110 Stat. 3416 (Oct. 11, 1996)] imposes on the ability of States to require information. As a result, if the securities that are the subject of this Form D are "covered securities" for purposes of NSMIA, whether in all instances or due to the nature of the offering that is the subject of this Form D, States cannot routinely require offering materials under this undertaking or otherwise and can require offering materials only to the extent NSMIA permits them to do so under NSMIA's preservation of their anti-fraud authority.

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