

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

SCHEDULE 14A INFORMATION

Proxy Statement Pursuant to Section 14(a) of
the Securities Exchange Act of 1934 (Amendment No.)

Filed by the Registrant

Filed by a Party other than the Registrant

Check the appropriate box:

- Preliminary Proxy Statement
 Confidential, for Use of the Commission Only (as permitted by Rule 14a-6(e)(2))
 Definitive Proxy Statement
 Definitive Additional Materials
 Soliciting Material Pursuant to §240.14a-12

Isis Pharmaceuticals, Inc.

(Name of Registrant as Specified In Its Charter)

(Name of Person(s) Filing Proxy Statement, if other than the Registrant)

Payment of Filing Fee (Check the appropriate box):

- No fee required.
 Fee computed on table below per Exchange Act Rules 14a-6(i)(1) and 0-11.
- (1) Title of each class of securities to which transaction applies:

- (2) Aggregate number of securities to which transaction applies:

- (3) Per unit price or other underlying value of transaction computed pursuant to Exchange Act Rule 0-11 (set forth the amount on which the filing fee is calculated and state how it was determined):

- (4) Proposed maximum aggregate value of transaction:

- (5) Total fee paid:

- Fee paid previously with preliminary materials.
 Check box if any part of the fee is offset as provided by Exchange Act Rule 0-11(a)(2) and identify the filing for which the offsetting fee was paid previously. Identify the previous filing by registration statement number, or the Form or Schedule and the date of its filing.
- (1) Amount Previously Paid:

- (2) Form, Schedule or Registration Statement No.:

- (3) Filing Party:

- (4) Date Filed:

Important Notice Regarding the Availability of Proxy Materials for the Stockholder Meeting to be held on June 5, 2008.

This communication presents only an overview of the more complete proxy materials that are available to you on the Internet. We encourage you to access and review all of the important information contained in the proxy materials before voting.

The following materials are available for view:

Notice and Proxy Statement / 10K Wrap

To view this material, have the 12-digit Control #(s) available and visit: www.proxyvote.com

If you want to receive a paper or e-mail copy of the above listed documents you must request one. There is no charge to you for requesting a copy. To facilitate timely delivery please make the request as instructed below on or before May 21, 2008.

To request material: **Internet:** www.proxyvote.com

Telephone: 1-800-579-1639

****Email:** sendmaterial@proxyvote.com

If requesting material by e-mail please send a blank e-mail with the **12-digit Control# (located on the following page) in the subject line. Requests, instructions and other inquiries will NOT be forwarded to your investment advisor.



ISIS PHARMACEUTICALS, INC.
1896 RUTHERFORD ROAD
CARLSBAD, CA 92008

ISIS PHARMACEUTICALS, INC.

Vote In Person

Many stockholder meetings have attendance requirements including, but not limited to, the possession of an attendance ticket issued by the entity holding the meeting. Please check the meeting materials for any special requirements for meeting attendance. At the Meeting you will need to request a ballot to vote these stocks.

Vote By Internet

To vote **now** by Internet, go to **WWW.PROXYVOTE.COM**. Use the Internet to transmit your voting instructions and for electronic delivery of information up until 11:59 P.M. Eastern Time the day before the cut-off date or meeting date. Have your notice in hand when you access the web site and follow the instructions.

Meeting Location

The Annual Meeting for stockholders as of April 7, 2008 is to be held on June 5, 2008 at 3:00 p.m. PDT
at: 1896 Rutherford Road Carlsbad, California 92008

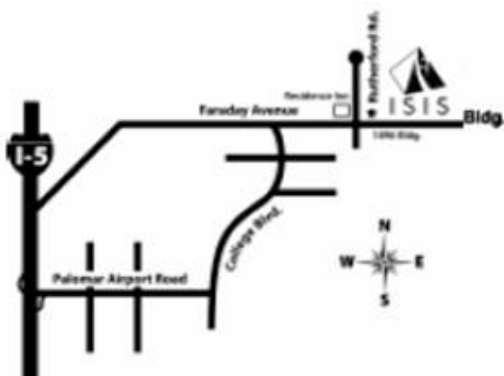
Directions

From Los Angeles and Points North:

- 1-5S exit at Cannon Road
- Turn left- Continue on Cannon Road to Faraday
- Turn right on Faraday (light)
- Pass College
- Turn left onto Rutherford (look for Isis' signs) 1896 is located at your immediate right, immediately after the Marriott Residence Inn

From San Diego Airport, Downtown and Points South:

- 1-5N exit Cannon Road, turn right
- Turn right on Faraday (light)
- Pass College
- Turn left onto Rutherford (look for Isis' signs) 1896 is located at your immediate right, immediately after the Marriott Residence Inn



Voting items

THE BOARD OF DIRECTORS RECOMMENDS A VOTE "FOR" ITEMS 1 through 4.

1. To elect as Directors of Isis Pharmaceuticals, Inc. the nominees listed below.

- 01) Spencer R. Berthelsen
- 02) B. Lynne Parshall

03) Joseph H. Wender

2. To approve an Amendment to the 2002 Non-Employee Directors' Stock Option Plan to increase the annual nondiscretionary stock option grant for our non-employee directors from 12,500 shares to 15,000 shares and the initial stock option grant from 20,000 shares to 30,000 shares.
 3. To approve an increase in shares reserved for issuance under the 1989 Stock Option Plan from 13,200,000 shares to 16,700,000 shares.
 4. To ratify the Audit Committee's selection of Ernst & Young LLP as independent auditors for our 2008 fiscal year.
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