

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D. C. 20549

FORM 8-K
RELATING TO ADOPTION OF A RIGHTS PLAN

PURSUANT TO SECTION 13 OR 15(d) OF THE
SECURITIES EXCHANGE ACT OF 1934

Date of Report (Date of earliest event reported): December 8, 2000

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

DELAWARE
(State or other jurisdiction of incorporation)

000-19125
(Commission File No.)

330336973
(IRS Employer Identification No.)

2292 FARADAY AVENUE
CARLSBAD, CA 92008
(Address of principal executive offices and zip code)

Registrant's telephone number, including area code: (760) 931-9200

ITEM 5. OTHER EVENTS.

On December 8, 2000, the Board of Directors of Isis Pharmaceuticals, Inc. (the "Company") approved the adoption of a Preferred Share Purchase Rights Plan (the "Plan"). Terms of the Plan provide for a dividend distribution of one preferred share purchase right (a "Right") for each outstanding share of common stock, par value \$0.001 per share (the "Common Shares"), of the Company. The dividend is payable on January 10, 2001 (the "Record Date") to the stockholders of record on that date. Each Right entitles the registered holder to purchase from the Company one one-hundredth of a share of Series C Junior Participating Preferred Stock, par value \$0.001 per share (the "Preferred Shares"), at a price of \$85 per one one-hundredth of a Preferred Share (the "Purchase Price"), subject to adjustment. Each one one-hundredth of a share of Preferred Shares has designations and powers, preferences and rights, and the qualifications, limitations and restrictions which make its value approximately equal to the value of a Common Share. The description and terms of the Rights are set forth in a Rights Agreement (the "Rights Agreement"), dated as of December 8, 2000, entered into between the Company and American Stock Transfer & Trust Company, as rights agent (the "Rights Agent").

Initially, the Rights will be evidenced by the stock certificates representing the Common Shares then outstanding, and no separate Right Certificates, as defined, will be distributed. Until the earlier to occur of (i) the date of a public announcement that a person, entity or group of affiliated or associated persons have acquired beneficial ownership of 20% or more of the outstanding Common Shares after the date of the adoption of the Rights Agreement, subject to certain exceptions set forth in the Rights Agreement (an "Acquiring Person"), or (ii) 10 business days (or such later date as may be determined by action of the Board of Directors prior to such time as any person or entity becomes an Acquiring Person) following the commencement of, or announcement of an intention to commence, a tender offer or exchange offer the consummation of which would result in any person or entity becoming an Acquiring Person (the earlier of such dates being called the "Distribution Date"), the Rights will be evidenced, with respect to any of the Common Share certificates outstanding as of the Record Date, by such Common Share certificate with or without a copy of the Summary of Rights, which is included in the Rights Agreement as Exhibit C thereof (the "Summary of Rights").

Until the Distribution Date, the Rights will be transferable with and only with the Common Shares. Until the Distribution Date (or earlier redemption or expiration of the Rights), new Common Share certificates issued after the Record Date, upon transfer or new issuance of Common Shares, will contain a notation incorporating the Rights Agreement by reference. Until the Distribution Date (or earlier redemption or expiration of the Rights), the surrender or transfer of any certificates for Common Shares outstanding as of the Record Date, even without such notation or a copy of the Summary of Rights being attached thereto, will also constitute the transfer of the Rights associated with the Common Shares represented by such certificate. As soon as practicable following the Distribution Date, separate certificates evidencing the Rights ("Right Certificates") will be mailed to holders of record of the Common Shares as of the close of business on the Distribution Date and such separate Right Certificates alone will evidence the Rights.

The Rights are not exercisable until the Distribution Date. The Rights will expire on December 7, 2010 (the "Final Expiration Date"), unless the Rights are earlier redeemed or exchanged by the Company, in each case, as described below.

The Purchase Price payable, and the number of Preferred Shares or other securities or other property issuable upon exercise of the Rights are subject to adjustment from time to time to prevent dilution (i) in the event of a stock dividend on, or a subdivision, combination or reclassification of, the Preferred Shares, (ii) upon the grant to holders of the Preferred Shares of certain rights or warrants to subscribe for or purchase Preferred Shares at a price, or securities convertible into Preferred Shares with a conversion price, less than the then current market price of the Preferred Shares or (iii) upon the distribution to holders of the Preferred Shares of evidences of indebtedness or assets (excluding regular periodic cash dividends paid out of earnings or retained earnings or dividends payable in Preferred Shares) or of subscription rights or warrants (other than those referred to above). The exercise of Rights for Preferred Shares is at all times subject to the availability of a sufficient number of authorized but unissued Preferred Shares.

The number of outstanding Rights and the number of one one-hundredths of a Preferred Share issuable upon exercise of each Right are also subject to adjustment in the event of a stock split of the Common Shares or a stock dividend on the Common Shares payable in Common Shares or subdivisions, consolidation or combinations of the Common Shares occurring, in any case, prior to the Distribution Date.

Preferred Shares purchasable upon exercise of the Rights will not be redeemable. Each Preferred Share will be entitled to a minimum preferential quarterly dividend payment of \$1.00, but will be entitled to an aggregate dividend of 100 times the dividend declared per Common Share. In the event of liquidation, the holders of the Preferred Shares would be entitled to a minimum preferential liquidation payment of \$100 per share, but would be entitled to receive an aggregate payment equal to 100 times the payment made per Common Share. Each Preferred Share will have 100 votes, voting together with the Common Shares. Finally, in the event of any merger, consolidation or other transaction in which Common Shares are exchanged, each Preferred Share will be entitled to receive 100 times the amount of consideration received per Common Share. These rights are protected by customary anti-dilution provisions. Because of the nature of the Preferred Shares' dividend and liquidation rights, the value of one one-hundredth of a Preferred Share should approximate the value of one Common Share. The Preferred Shares rank junior to any other series of the Company's preferred stock.

In the event that any person or group of affiliated or associated persons becomes an Acquiring Person, proper provision shall be made so that each holder of a Right, other than Rights beneficially owned by the Acquiring Person and its associates and affiliates (which will thereafter be void), will for a 60-day period (or such longer period as necessary to register the Company's securities) have the right to receive upon exercise that number of Common Shares having a market value of two times the exercise price of the Right (or, if such number of shares is not and cannot be authorized, the Company may issue cash, debt, other securities or a combination thereof in exchange for the Rights). This right will terminate 60 days after the date on which the Rights become nonredeemable (as described below), unless there is an injunction or similar obstacle to exercise of the Rights, in which event this right will terminate 60 days after the date on which the Rights again become exercisable (or such longer period as set forth in the Rights Agreement).

Generally, under the Plan, an "Acquiring Person" shall not be deemed to include (i) the Company, (ii) any subsidiary of the Company, (iii) any employee benefit or compensation plan of the Company or any subsidiary of the Company, (iv) any entity holding Common Shares for or pursuant to the terms of any such employee benefit or compensation plan or (v) any person, together with all affiliates and associates of such person, who is the beneficial owner of 20% or more of the Common Shares outstanding as of the date of the Rights Agreement until such time after the date of the Rights Agreement that such person, together with all affiliates and associates of such Person, shall become the beneficial owner of 25% or more of the Common Shares outstanding without the prior written consent of the Company. In addition, except under limited circumstances, no person or entity shall become an Acquiring Person as the result of the acquisition of Common Shares by the Company which, by reducing the number of shares outstanding, increases the proportionate number of shares beneficially owned by such person or entity to 20%, or in the case of (v) above, to 25% or more, of the Common Shares then outstanding. Further, except under certain circumstances, no person shall become an Acquiring Person due to the acquisition of Common Shares directly from the Company.

In the event that the Company is acquired in a merger or other business combination transaction or 50% or more of its consolidated assets or earning power are sold to an Acquiring Person, its associates or affiliates or certain other persons in which such persons have an interest, proper provision will be made so that each holder of a Right will thereafter have the right to receive, upon the exercise thereof at the then current exercise price of the Right, that number of shares of common stock of the acquiring company which at the time of such transaction will have a market value of two times the exercise price of the Right.

At any time after an Acquiring Person becomes an Acquiring Person and prior to the acquisition by such Acquiring Person of 50% or more of the outstanding Common Shares, the Board of Directors of the Company may exchange the Rights (other than Rights owned by such person or group which have become void), in whole or in part, at an exchange ratio of one Common Share per Right (or, at the election of the Company, the Company may issue cash, debt, stock or a combination thereof in exchange for the Rights), subject to adjustment.

With certain exceptions, no adjustment in the Purchase Price will be required until cumulative adjustments require an adjustment of at least 1% in such Purchase Price. No fractional Preferred Shares will be issued (other than fractions which are integral multiples of the number of one one-hundredths of a Preferred Share issuable upon the exercise of one Right, which may, at the election of the Company, be evidenced by depository receipts), and in lieu thereof, an adjustment in cash will be made based on the market price of the Preferred Shares on the last trading day prior to the date of exercise.

At any time prior to the earliest of (i) the day that a person has become an Acquiring Person or (ii) the Final Expiration Date, the Board of Directors of the Company may redeem the Rights in whole, but not in part, at a price of \$0.001 per Right (the "Redemption Price"). Following the expiration of the above periods, the Rights become nonredeemable, except that after the expiration of the period during which the Rights are exercisable for Common Stock, then the Board of Directors of the Company may redeem the Rights in whole, but not in part, at the Redemption Price in connection with a sale or merger of the Company or its assets to a party which is unrelated to the Acquiring Person. Immediately upon any redemption of the Rights, the right to exercise the Rights will terminate and the only right of the holders of Rights will be to receive the Redemption Price.

The terms of the Rights may be amended by the Board of Directors of the Company without the consent of the holders of the Rights, except that from and after such time as the

rights are distributed no such amendment may adversely affect the interest of the holders of the Rights, excluding the interests of an Acquiring Person.

Until a Right is exercised, the holder thereof, as such, will have no rights as a stockholder of the Company, including, without limitation, the right to vote or to receive dividends.

The Rights have certain anti-takeover effects. The Rights will cause substantial dilution to a person or group that attempts to acquire the Company on terms not approved by the Company's Board of Directors. The Rights should not interfere with any merger or other business combination approved by the Board of Directors, since the Rights may be amended to permit such acquisition or may be redeemed by the Company at \$0.001 per Right, as set forth above.

ITEM 7. EXHIBITS.

- 4.1 Restated Certificate of Incorporation. (1)
- 4.2 Certificate of Designation of Series C Junior Participating Preferred Stock.
- 99.1 Press Release, dated as of December 8, 2000, entitled "Isis Pharmaceuticals, Inc. Adopts Stockholder Rights Plan."
- 99.2 Rights Agreement dated as of December 8, 2000 between Isis Pharmaceuticals, Inc. and American Stock Transfer & Trust Company.
- 99.3 Form of Right Certificate.

(1) Filed as an exhibit to the Registration Statement on Form S-1 (No. 33-39649) or amendments thereto and incorporated herein by reference.

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

ISIS PHARMACEUTICALS, INC.

Dated: December 12, 2000

By: /s/ B. LYNNE PARSHALL

B. LYNNE PARSHALL
Executive Vice President,
Chief Financial Officer and Secretary

INDEX TO EXHIBITS

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CERTIFICATE OF DESIGNATION

OF

SERIES C JUNIOR PARTICIPATING PREFERRED STOCK

(PURSUANT TO SECTION 151 OF THE
DELAWARE GENERAL CORPORATION LAW)

ISIS PHARMACEUTICALS, INC., a corporation organized and existing under the General Corporation Law of the State of Delaware (hereinafter called the "Company"), hereby certifies that the following resolution was adopted by the Board of Directors of the Corporation as required by Section 151 of the General Corporation Law at a meeting duly called and held on December 8, 2000:

RESOLVED, that pursuant to the authority granted to and vested in the Board of Directors of the Company in accordance with the provisions of its Restated Certificate of Incorporation, the Board of Directors hereby creates a series of Preferred Stock, par value \$.001 per share, of the Company and hereby states the designation and number of shares, and fixes the relative designations and the powers, preferences and rights, and the qualifications, limitations and restrictions thereof (in addition to the provisions set forth in the Restated Certificate of Incorporation of the Company, which are applicable to the Preferred Stock of all classes and series), as follows:

Series C Junior Participating Preferred Stock:

SECTION 1. DESIGNATION AND AMOUNT. One million (1,000,000) shares of Preferred Stock, \$.001 par value, are designated "Series C Junior Participating Preferred Stock" with the designations and the powers, preferences and rights, and the qualifications, limitations and restrictions specified herein (the "Junior Preferred Stock"). Such number of shares may be increased or decreased by resolution of the Board of Directors; PROVIDED, that no decrease shall reduce the number of shares of Junior Preferred Stock to a number less than the number of shares then outstanding plus the number of shares reserved for issuance upon the exercise of outstanding options, rights or warrants or upon the conversion of any outstanding securities issued by the Company convertible into Junior Preferred Stock.

SECTION 2. DIVIDENDS AND DISTRIBUTIONS.

(A) Subject to the rights of the holders of any shares of any series of Preferred Stock (or any similar stock) ranking prior and superior to the Junior Preferred Stock with respect

to dividends, the holders of shares of Junior Preferred Stock, in preference to the holders of Common Stock, par value \$.001 per share (the "Common Stock"), of the Company, and of any other junior stock, shall be entitled to receive, when, as and if declared by the Board of Directors out of funds legally available for the purpose, quarterly dividends payable in cash on the first day of April, July, October and January in each year (each such date being referred to herein as a "Quarterly Dividend Payment Date"), commencing on the first Quarterly Dividend Payment Date after the first issuance of a share or fraction of a share of Junior Preferred Stock, in an amount per share (rounded to the nearest cent) equal to the greater of (a) \$1.00 or (b) subject to the provision for adjustment hereinafter set forth, 100 times the aggregate per share amount of all cash dividends, and 100 times the aggregate per share amount (payable in kind) of all non-cash dividends or other distributions, other than a dividend payable in shares of Common Stock or a subdivision of the outstanding shares of Common Stock (by reclassification or otherwise), declared on the Common Stock since the immediately preceding Quarterly Dividend Payment Date or, with respect to the first Quarterly Dividend Payment Date, since the first issuance of any share or fraction of a share of Junior Preferred Stock. In the event the Company shall at any time declare or pay any dividend on the Common Stock payable in shares of Common Stock, or effect a subdivision or combination or consolidation of the outstanding shares of Common Stock (by reclassification or otherwise than by payment of a dividend in shares of Common Stock) into a greater or lesser number of shares of Common Stock, then in each such case the amount to which holders of shares of Junior Preferred Stock were entitled immediately prior to such event under clause (b) of the preceding sentence shall be adjusted by multiplying such amount by a fraction, the numerator of which is the number of shares of Common Stock outstanding immediately after such event and the denominator of which is the number of shares of Common Stock that were outstanding immediately prior to such event.

(B) The Company shall declare a dividend or distribution on the Junior Preferred Stock as provided in paragraph (A) of this Section immediately after it declares a dividend or distribution on the Common Stock (other than a dividend payable in shares of Common Stock); PROVIDED, that in the event no dividend or distribution shall have been declared on the Common Stock during the period between any Quarterly Dividend Payment Date and the next subsequent Quarterly Dividend Payment Date, a dividend of \$1.00 per share on the Junior Preferred Stock shall nevertheless be payable on such subsequent Quarterly Dividend Payment Date.

(C) Dividends shall begin to accrue and be cumulative on outstanding shares of Junior Preferred Stock from the Quarterly Dividend Payment Date next preceding the date of issue of such shares, unless the date of issue of such shares is prior to the record date for the first Quarterly Dividend Payment Date, in which case dividends on such shares shall begin to accrue from the date of issue of such shares, or unless the date of issue is a Quarterly Dividend Payment Date or is a date after the record date for the determination of holders of shares of Junior Preferred Stock entitled to receive a quarterly dividend and before such Quarterly Dividend Payment Date, in either of which events such dividends shall begin to accrue and be cumulative from such Quarterly Dividend Payment Date. Accrued but unpaid dividends shall not bear interest. Dividends paid on the shares of Junior Preferred Stock in an amount less than the total amount of such dividends at the time accrued and payable on such shares shall be allocated pro rata on a share-by-share basis among all such shares at the time outstanding. The Board of Directors may fix a record date for the determination of holders of shares of Junior Preferred

Stock entitled to receive payment of a dividend or distribution declared thereon, which record date shall be not more than 60 days prior to the date fixed for the payment thereof.

SECTION 3. VOTING RIGHTS. The holders of shares of Junior Preferred Stock shall have the following voting rights:

(A) Subject to the provision for adjustment hereinafter set forth, each share of Junior Preferred Stock shall entitle the holder thereof to 100 votes on all matters submitted to a vote of the stockholders of the Company. In the event the Company shall at any time declare or pay any dividend on the Common Stock payable in shares of Common Stock, or effect a subdivision or combination or consolidation of the outstanding shares of Common Stock (by reclassification or otherwise than by payment of a dividend in shares of Common Stock) into a greater or lesser number of shares of Common Stock, then in each such case the number of votes per share to which holders of shares of Junior Preferred Stock were entitled immediately prior to such event shall be adjusted by multiplying such number by a fraction, the numerator of which is the number of shares of Common Stock outstanding immediately after such event and the denominator of which is the number of shares of Common Stock that were outstanding immediately prior to such event.

(B) Except as otherwise provided herein, in any other Certificate of Designation creating a series of Preferred Stock or any similar stock, or by law, the holders of shares of Junior Preferred Stock and the holders of shares of Common Stock and any other capital stock of the Company having general voting rights shall vote together as one class on all matters submitted to a vote of stockholders of the Company.

(C) Except as set forth herein, or as otherwise provided by law, holders of Junior Preferred Stock shall have no special voting rights and their consent shall not be required (except to the extent they are entitled to vote with holders of Common Stock as set forth herein) for taking any corporate action.

SECTION 4. CERTAIN RESTRICTIONS.

(A) Whenever quarterly dividends or other dividends or distributions payable on the Junior Preferred Stock as provided in Section 2 are in arrears, thereafter and until all accrued and unpaid dividends and distributions, whether or not declared, on shares of Junior Preferred Stock outstanding shall have been paid in full, the Company shall not:

(i) declare or pay dividends, or make any other distributions, on any shares of stock ranking junior (either as to dividends or upon liquidation, dissolution or winding up) to the Junior Preferred Stock;

(ii) declare or pay dividends, or make any other distributions, on any shares of stock ranking on a parity (either as to dividends or upon liquidation, dissolution or winding up) with the Junior Preferred Stock, except dividends paid ratably on the Junior Preferred Stock and all such parity stock on which dividends are payable or in arrears in proportion to the total amounts to which the holders of all such shares are then entitled;

(iii) redeem or purchase or otherwise acquire for consideration shares of any stock ranking junior (either as to dividends or upon liquidation, dissolution or winding up) to the Junior Preferred Stock, provided that the Company may at any time redeem, purchase or otherwise acquire shares of any such junior stock in exchange for shares of any stock of the Company ranking junior (either as to dividends or upon dissolution, liquidation or winding up) to the Junior Preferred Stock; or

(iv) redeem or purchase or otherwise acquire for consideration any shares of Junior Preferred Stock, or any shares of stock ranking on a parity (either as to dividends or upon liquidation, dissolution or winding up) with the Junior Preferred Stock, except in accordance with a purchase offer made in writing or by publication (as determined by the Board of Directors) to all holders of such shares upon such terms as the Board of Directors, after consideration of the respective annual dividend rates and other relative rights and preferences of the respective series and classes, shall determine in good faith will result in fair and equitable treatment among the respective series or classes.

(B) The Company shall not permit any subsidiary of the Company to purchase or otherwise acquire for consideration any shares of stock of the Company unless the Company could, under paragraph (A) of this Section 4, purchase or otherwise acquire such shares at such time and in such manner.

SECTION 5. REACQUIRED SHARES. Any shares of Junior Preferred Stock purchased or otherwise acquired by the Company in any manner whatsoever shall be retired and cancelled promptly after the acquisition thereof. All such shares shall upon their cancellation become authorized but unissued shares of Preferred Stock and may be reissued as part of a new series of Preferred Stock subject to the conditions and restrictions on issuance set forth herein, in the Restated Certificate of Incorporation, or in any other Certificate of Designation creating a series of Preferred Stock or any similar stock or as otherwise required by law.

SECTION 6. LIQUIDATION, DISSOLUTION OR WINDING UP. Upon any liquidation, dissolution or winding up of the Company, no distribution shall be made (1) to the holders of shares of stock ranking junior (either as to dividends or upon liquidation, dissolution or winding up) to the Junior Preferred Stock unless, prior thereto, the holders of shares of Junior Preferred Stock shall have received \$100 per share, plus an amount equal to accrued and unpaid dividends and distributions thereon, whether or not declared, to the date of such payment, or if greater, the holders of shares of Junior Preferred Stock shall be entitled to receive an aggregate amount per share, subject to the provision for adjustment hereinafter set forth, equal to 100 times the aggregate amount to be distributed per share to holders of shares of Common Stock; or (2) to the holders of shares of stock ranking on a parity (either as to dividends or upon liquidation, dissolution or winding up) with the Junior Preferred Stock, except distributions made ratably on the Junior Preferred Stock and all such parity stock in proportion to the total amounts to which the holders of all such shares are entitled upon such liquidation, dissolution or winding up. In the event the Company shall at any time declare or pay any dividend on the Common Stock payable in shares of Common Stock, or effect a subdivision or combination or consolidation of the outstanding shares of Common Stock (by reclassification or otherwise than by payment of a dividend in shares of Common Stock) into a greater or lesser number of shares of Common Stock, then in each such case the aggregate amount to which holders of shares of Junior

Preferred Stock were entitled immediately prior to such event under the proviso in clause (1) of the preceding sentence shall be adjusted by multiplying such amount by a fraction the numerator of which is the number of shares of Common Stock outstanding immediately after such event and the denominator of which is the number of shares of Common Stock that were outstanding immediately prior to such event.

SECTION 7. CONSOLIDATION, MERGER, ETC. In case the Company shall enter into any consolidation, merger, combination or other transaction in which the shares of Common Stock are exchanged for or changed into other stock or securities, cash and/or any other property, then in any such case each share of Junior Preferred Stock shall at the same time be similarly exchanged or changed into an amount per share, subject to the provision for adjustment hereinafter set forth, equal to 100 times the aggregate amount of stock, securities, cash and/or any other property (payable in kind), as the case may be, into which or for which each share of Common Stock is changed or exchanged. In the event the Company shall at any time declare or pay any dividend on the Common Stock payable in shares of Common Stock, or effect a subdivision or combination or consolidation of the outstanding shares of Common Stock (by reclassification or otherwise than by payment of a dividend in shares of Common Stock) into a greater or lesser number of shares of Common Stock, then in each such case the amount set forth in the preceding sentence with respect to the exchange or change of shares of Junior Preferred Stock shall be adjusted by multiplying such amount by a fraction, the numerator of which is the number of shares of Common Stock outstanding immediately after such event and the denominator of which is the number of shares of Common Stock that were outstanding immediately prior to such event.

SECTION 8. NO REDEMPTION. The shares of Junior Preferred Stock shall not be redeemable.

SECTION 9. RANK. The Junior Preferred Stock shall rank, with respect to the payment of dividends and the distribution of assets, junior to all series of any other class of the Company's Preferred Stock.

SECTION 10. AMENDMENT. The Restated Certificate of Incorporation of the Company shall not be amended in any manner which would materially alter or change the powers, preferences or special rights of the Junior Preferred Stock so as to affect them adversely without the affirmative vote of the holders of at least two-thirds of the outstanding shares of Junior Preferred Stock, voting together as a single class.

IN WITNESS WHEREOF, the undersigned have executed this certificate as of December 12, 2000.

By: /s/ B. LYNNE PARSHALL

Print Name: B. LYNNE PARSHALL
Executive Vice President,
Chief Financial Officer and Secretary

CONTACT:
Kristina Peterson
Isis Pharmaceuticals, Inc.
760-603-2521

EXHIBIT 99.1

FOR IMMEDIATE RELEASE

ISIS PHARMACEUTICALS ADOPTS STOCKHOLDER RIGHTS PLAN

Carlsbad, CA - December 8, 2000 - Isis Pharmaceuticals, Inc. (NASDAQ: ISIP) announced that its Board of Directors approved the adoption of a Stockholder Rights Plan under which all stockholders of record as of January 10, 2001 will receive rights to purchase shares of a new series of Preferred Stock.

The Rights Plan is designed to enable all Isis stockholders to realize the full value of their investment and to provide for fair and equal treatment for all stockholders in the event that an unsolicited attempt is made to acquire Isis. The adoption of the Rights Plan is intended as a means to guard against abusive takeover tactics and is not in response to any particular proposal.

The rights will be distributed as a non-taxable dividend and will expire December 7, 2010. The rights will be exercisable only if a person or group acquires 20% or more of the Isis Pharmaceuticals, Inc. Common Stock or announces a tender offer for twenty percent or more of the company's Common Stock. If a person or group acquires 20% or more of the company's Common Stock, all rightsholders except the acquiror will be entitled to acquire the company's Common Stock at a discount. The effect will be to discourage acquisitions of more than 20% of the Common Stock of Isis without first negotiating with the company's Board.

The rights will trade with the company's Common Stock, unless and until they are separated upon the occurrence of certain future events. The rights distribution is not taxable to the stockholders. The company's Board of Directors may terminate the Rights Plan at any time or redeem the rights prior to the time a person acquires more than 20% of the company's Common Stock. Additional details regarding the Rights Plan will be outlined in a summary to be mailed to all stockholders following the record date.

Isis Pharmaceuticals, Inc. is exploiting its expertise in RNA to discover and develop novel human therapeutic drugs. The company has commercialized its first product, Vitravene-TM- (formivirsen), to treat CMV-induced retinitis in patients with AIDS. In addition, Isis has 11 products in its development pipeline, with two in late-stage development and four in Phase II human clinical trials. ISIS 3521, an inhibitor of PKC-alpha, is in Phase III trials for non-small cell lung cancer. Isis is preparing to initiate a Phase III program for ISIS 2302, an ICAM-1 inhibitor, in Crohn's disease. Isis has a broad and proprietary patent estate of nearly 700 issued and allowed patents worldwide. Isis' GeneTrove-TM- division uses antisense to assist pharmaceutical industry partners in validating and prioritizing potential gene targets through customized services and access to an extensive gene function database. Isis Therapeutics-TM- is a division focused on the discovery of small molecule drugs that bind to RNA.

This press release contains forward-looking statements concerning Isis and its prospects. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics. Actual results could differ materially from those projected in this release. As a result, the reader is cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' research and development programs are described in additional detail in Isis' Quarterly Report on Form 10-Q for the quarter ended September 30, 2000, which is on file with the U.S. Securities and Exchange Commission, copies of which are available from the company.

Vitravene-TM- is a trademark of Novartis AG. GeneTrove-TM- and Ibis Therapeutics-TM- are trademarks of Isis Pharmaceuticals, Inc.

ISIS PHARMACEUTICALS, INC.
CARLSBAD RESEARCH CENTER, 2292 FARADAY AVENUE, CARLSBAD, CA 92008
VOICE: 760.931.9200

ISIS PHARMACEUTICALS, INC.

AND

AMERICAN STOCK TRANSFER & TRUST COMPANY

AS RIGHTS AGENT

RIGHTS AGREEMENT

DATED AS OF DECEMBER 8, 2000

RIGHTS AGREEMENT

THIS RIGHTS AGREEMENT ("Agreement"), dated as of December 8, 2000, between ISIS PHARMACEUTICALS, INC., a Delaware corporation (the "Company"), and AMERICAN STOCK TRANSFER & TRUST COMPANY ("Rights Agent").

WHEREAS, the Board of Directors of the Company (the "Board of Directors") has authorized and declared a dividend of one preferred share purchase right (a "Right") for each Common Share (as such term is hereinafter defined) outstanding at the close of business on January 10, 2001 (the "Record Date"), each Right representing the right to purchase one one-hundredth of a Preferred Share (as such term is hereinafter defined), upon the terms and subject to the conditions herein set forth, and has further authorized and directed the issuance of one Right with respect to each Common Share that shall become outstanding between the Record Date and the earliest to occur of the Distribution Date, the Redemption Date and the Final Expiration Date (as such terms are hereinafter defined); PROVIDED, HOWEVER, that Rights may be issued with respect to Common Shares that shall become outstanding after the Distribution Date and prior to the earlier of the Redemption Date and the Final Expiration Date in accordance with the provisions of Section 22 hereof; and

WHEREAS, the Board of Directors has approved and authorized the appointment of the Rights Agent, and the Rights Agent desires to accept such appointment.

NOW THEREFORE, in consideration of the premises and the mutual agreements herein set forth, the parties hereby agree as follows:

SECTION 1. CERTAIN DEFINITIONS. For purposes of this Agreement, the following terms have the meanings indicated:

(a) "ACQUIRING PERSON" shall mean any Person (as such term is hereinafter defined) who or which, together with all Affiliates and Associates (as such terms are hereinafter defined) of such Person, shall be the Beneficial Owner (as such term is hereinafter defined) of 20% or more of the Common Shares then outstanding. Notwithstanding the foregoing, (A) the term Acquiring Person shall not include (i) the Company, (ii) any Subsidiary (as such term is hereinafter defined) of the Company, (iii) any employee benefit or compensation plan of the Company or any Subsidiary of the Company, (iv) any entity holding Common Shares for or pursuant to the terms of any such employee benefit or compensation plan or (v) any Person, together with all Affiliates and Associates of such Person, who is the Beneficial Owner of 20% or more of the Common Shares outstanding as of the date of this Agreement until such time after the date of this Agreement that such Person, together with all Affiliates and Associates of such Person, shall become the Beneficial Owner of 25% or more of the Common Shares outstanding without the prior written consent of the Company, and (B) no Person shall become an "Acquiring Person" (x) as the result of an acquisition of Common Shares by the Company which, by reducing the number of shares outstanding, increases the proportionate number of shares beneficially owned by such Person to 20% or more, or 25% or more for the purpose of (A)(v) above, of the Common Shares then outstanding; PROVIDED, HOWEVER, that if a Person shall become the Beneficial Owner of 20% or more, or 25% or more for the purpose of (A)(v) above, of the

Common Shares then outstanding by reason of share purchases by the Company and shall, following written notice from, or public disclosure by the Company of such share purchases by the Company, become the Beneficial Owner of any additional Common Shares without the prior consent of the Company and shall then Beneficially Own 20% or more, or 25% or more for the purpose of (A)(v) above, of the Common Shares then outstanding, then such Person shall be deemed to be an "Acquiring Person," (y) as the result of the acquisition of Common Shares directly from the Company, PROVIDED HOWEVER that if a Person shall become the Beneficial Owner of 20% or more of the Common Shares then outstanding by reason of the purchase of securities directly from the Company and shall, after that date, become Beneficial Owner of any additional Common Shares without the prior written consent of the Company and shall then Beneficially Own 20% or more of the Common Shares then outstanding, then such Person shall be deemed to be an "Acquiring Person", or (z) if the Board of Directors determines in good faith that a Person who would otherwise be an "Acquiring Person," as defined pursuant to the foregoing provisions of this paragraph (a), has become such inadvertently, and without any intention of changing or influencing control of the Company, and such Person promptly enters into an irrevocable written commitment in favor of the Company to divest, and thereafter divests (without retaining any power, including voting with respect to such Common Shares), as promptly as practicable (as determined in good faith by the Board of Directors), following receipt of written notice from the Company of such event, of Beneficial Ownership of a sufficient number of Common Shares so that such Person would no longer be an Acquiring Person, as defined pursuant to the foregoing provisions of this paragraph (a), then such Person shall not be deemed to be an "Acquiring Person" for any purposes of this Agreement; PROVIDED, HOWEVER, that if such Person shall again become the Beneficial Owner of 20% or more, or 25% or more for the purpose of (A)(v) above, of the Common Shares then outstanding, such Person shall be deemed an "Acquiring Person," subject to the exceptions set forth in this Section 1(a).

(b) "AFFILIATE" and "ASSOCIATE" shall have the respective meanings ascribed to such terms in Rule 12b-2 of the General Rules and Regulations under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), as in effect on the date of this Agreement.

(c) A Person shall be deemed the "BENEFICIAL OWNER" or to have "BENEFICIAL OWNERSHIP" of and shall be deemed to "beneficially own" any securities:

(i) which such Person or any of such Person's Affiliates or Associates is deemed to beneficially own, within the meaning of Rule 13d-3 of the General Rules and Regulations under the Exchange Act as in effect on the date of this Agreement;

(ii) which such Person or any of such Person's Affiliates or Associates has (A) the right to acquire (whether such right is exercisable immediately or only after the passage of time or the occurrence or fulfillment of a condition) pursuant to any agreement, arrangement or understanding (other than customary agreements with and between underwriters and selling group members with respect to a bona fide public offering of securities and other than agreements between the Company and any Person to which the right or obligation to purchase securities is conditioned upon the achievement of research and development milestones which have not been achieved), or upon the exercise of conversion rights, exchange rights, rights (other than these Rights), warrants or options, or otherwise; PROVIDED, HOWEVER, that a Person shall not be deemed the Beneficial Owner of, or to beneficially own, securities tendered pursuant to

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tender or exchange offer made by or on behalf of such Person or any of such Person's Affiliates or Associates until such tendered securities are accepted for purchase or exchange; or (B) the right to vote pursuant to any agreement, arrangement or understanding; PROVIDED, HOWEVER, that a Person shall not be deemed the Beneficial Owner of, or to beneficially own, any security if the agreement, arrangement or understanding to vote such security (1) arises solely from a revocable proxy or consent given to such Person in response to a public proxy or consent solicitation made pursuant to, and in accordance with, the applicable rules and regulations promulgated under the Exchange Act and (2) is not also then reportable on Schedule 13D under the Exchange Act (or any comparable or successor report); or

(iii) which are beneficially owned, directly or indirectly, by any other Person with which such Person or any of such Person's Affiliates or Associates has any agreement, arrangement or understanding (other than customary agreements with and between underwriters and selling group members with respect to a bona fide public offering of securities) for the purpose of acquiring, holding, voting (except to the extent contemplated by the proviso to Section 1(c)(ii)(B) hereof) or disposing of any securities of the Company; PROVIDED, HOWEVER, an agreement, arrangement or understanding for purposes of this Section 1(c)(iii) shall not be deemed to include actions (including any agreement, arrangement or understanding) or statements by (1) any member of the Company's Board of Directors (as it is comprised on the date of this Agreement) (the "Existing Directors"), (2) any subsequent directors of the Company who have been nominated by a majority of the Existing Directors (the "Successor Directors"), or (3) any subsequent directors of the Company who have been nominated by a majority of the Existing Directors and the Successor Directors as a group.

Notwithstanding anything in this definition of Beneficial Ownership to the contrary, the phrase, "then outstanding," when used with reference to a Person's Beneficial Ownership of securities of the Company, shall mean the number of such securities then issued and outstanding together with the number of such securities not then actually issued and outstanding which such Person would be deemed to beneficially own hereunder.

(d) "BUSINESS DAY" shall mean any day other than a Saturday, a Sunday, or a day on which banking institutions in the State of New York are authorized or obligated by law or executive order to close.

(e) "CLOSE OF BUSINESS" on any given date shall mean 5:00 p.m., New York Time, on such date; PROVIDED, HOWEVER, that if such date is not a Business Day it shall mean 5:00 p.m., New York Time, on the next succeeding Business Day.

(f) "COMMON SHARES" shall mean the shares of common stock, par value \$.001 per share, of the Company; PROVIDED, HOWEVER, that, "Common Shares," when used in this Agreement in connection with a specific reference to any Person other than the Company, shall mean the capital stock (or equity interest) with the greatest voting power of such other Person or, if such other Person is a Subsidiary of another Person, the Person or Persons which ultimately control such first-mentioned Person.

(g) "DISTRIBUTION DATE" shall have the meaning set forth in Section 3(a) hereof.

(h) "FINAL EXPIRATION DATE" shall have the meaning set forth in Section 7 hereof.

(i) "INTERESTED STOCKHOLDER" shall mean any Acquiring Person or any Affiliate or Associate of an Acquiring Person or any other Person in which any such Acquiring Person, Affiliate or Associate has an interest, or any other Person acting directly or indirectly on behalf of or in concert with any such Acquiring Person, Affiliate or Associate.

(j) "PERSON" shall mean any individual, firm, corporation or other entity, and shall include any successor (by merger or otherwise) of such entity.

(k) "PREFERRED SHARES" shall mean shares of Series C Junior Participating Preferred Stock, par value \$.001 per share, of the Company having the designations and the powers, preferences and rights, and the qualifications, limitations and restrictions set forth in the Form of Certificate of Designation attached to this Agreement as EXHIBIT A.

(l) "PRINCIPAL PARTY" shall have the meaning set forth in Section 13(b) hereof.

(m) "PURCHASE PRICE" shall have the meaning set forth in Section 7(b) hereof.

(n) "REDEMPTION DATE" shall have the meaning set forth in Section 7(a) hereof.

(o) "SHARES ACQUISITION DATE" shall mean the first date of public announcement by the Company or an Acquiring Person that an Acquiring Person has become such provided, however that, if such Person is determined not to have become an Acquiring Person pursuant to clause (z) of Subsection 1(a)(B) hereof, then no Shares Acquisition Date shall be deemed to have occurred.

(p) "SUBSIDIARY" of any Person shall mean any corporation or other entity of which a majority of the voting power of the voting equity securities or equity interest is owned, directly or indirectly, by such Person.

(q) "TRANSACTION" shall mean any merger, consolidation or sale of assets described in Section 13(a) hereof or any acquisition of Common Shares which would result in a Person becoming an Acquiring Person or a Principal Party.

(r) "TRANSACTION PERSON" with respect to a Transaction shall mean (i) any Person who (x) is or will become an Acquiring Person or a Principal Party if the Transaction were to be consummated and (y) directly or indirectly proposed or nominated a director of the Company which director is in office at the time of consideration of the Transaction, or (ii) an Affiliate or Associate of such a Person.

SECTION 2. APPOINTMENT OF RIGHTS AGENT The Company hereby appoints the Rights Agent to act as agent for the Company in accordance with the terms and conditions hereof, and the Rights Agent hereby accepts such appointment. The Company may from time to time appoint such co-Rights Agents as it may deem necessary or desirable.

SECTION 3. ISSUE OF RIGHT CERTIFICATES.

(a) Until the earlier of the Close of Business on (i) the Shares Acquisition Date or (ii) the tenth Business Day (or such later date as may be determined by action of the Board of Directors prior to such time as any Person becomes an Acquiring Person) after the date of the commencement (determined in accordance with Rule 14d-2 under the Exchange Act) by any Person (other than the Company, any Subsidiary of the Company, any employee benefit plan of the Company or of any Subsidiary of the Company or any entity holding Common Shares for or pursuant to the terms of any such plan) of, or of the first public announcement of the intention of any Person (other than the Company, any Subsidiary of the Company, any employee benefit plan of the Company or of any Subsidiary of the Company or any entity holding Common Shares for or pursuant to the terms of any such plan) to commence, a tender or exchange offer (which intention to commence remains in effect for five Business Days after such announcement), the consummation of which would result in any Person becoming an Acquiring Person (including any such date which is after the date of this Agreement and prior to the issuance of the Rights, the earlier of such dates being herein referred to as the "DISTRIBUTION DATE"), (x) the Rights will be evidenced by the certificates for Common Shares registered in the names of the holders thereof (which certificates shall also be deemed to be Right Certificates) and not by separate Right Certificates, and (y) the Rights (and the right to receive Right Certificates therefor) will be transferable only in connection with the transfer of Common Shares. As soon as practicable after the Distribution Date, the Company will prepare and execute, the Rights Agent will countersign, and the Company will send or cause to be sent (and the Rights Agent will, if requested, send) by first-class, insured, postage-prepaid mail, to each record holder of Common Shares as of the Close of Business on the Distribution Date, at the address of such holder shown on the records of the Company, a Right Certificate, in substantially the form of EXHIBIT B hereto (a "Right Certificate"), evidencing one Right for each Common Share so held, subject to the adjustment provisions of Section 11 of this Agreement. As of the Distribution Date, the Rights will be evidenced solely by such Right Certificates.

(b) On the Record Date, or as soon as practicable thereafter, the Company will send (directly or through the Rights Agent or its transfer agent) a copy of a Summary of Rights to Purchase Preferred Shares, in substantially the form of EXHIBIT C hereto (the "Summary of Rights"), by first-class, postage-prepaid mail, to each record holder of Common Shares as of the Close of Business on the Record Date, at the address of such holder shown on the records of the Company. With respect to certificates for Common Shares outstanding as of the Record Date, until the Distribution Date, the Rights will be evidenced by such certificates registered in the names of the holders thereof. Until the Distribution Date (or the earlier of the Redemption Date and the Final Expiration Date), the surrender for transfer of any certificate for Common Shares outstanding on the Record Date shall also constitute the transfer of the Rights associated with the Common Shares represented thereby.

(c) Certificates for Common Shares which become outstanding (including, without limitation, reacquired Common Shares referred to in the last sentence of this subsection (c)) after the Record Date but prior to the earliest of the Distribution Date, the Redemption Date or the Final Expiration Date shall have impressed on, printed on, written on or otherwise affixed to them the following legend:

This certificate also evidences and entitles the holder hereof to certain rights as set forth in a Rights Agreement between Isis Pharmaceuticals, Inc. (the

"Company") and American Stock Transfer & Trust Company as Rights Agent (the "Rights Agent"), dated as of December 8, 2000, as amended from time to time (the "Rights Agreement"), the terms of which are hereby incorporated herein by reference and a copy of which is on file at the principal executive offices of the Company. Under certain circumstances, as set forth in the Rights Agreement, such Rights will be evidenced by separate certificates and will no longer be evidenced by this certificate. The Company will mail to the holder of this certificate a copy of the Rights Agreement without charge after receipt of a written request therefor. As described in the Rights Agreement, Rights issued to any Person who becomes an Acquiring Person or an Affiliate or Associate thereof (as defined in the Rights Agreement) and certain related persons, whether currently held by or on behalf of such Person or by any subsequent holder, shall become null and void.

With respect to such certificates containing the foregoing legend, until the Distribution Date (or the earlier of the Redemption Date or the Final Expiration Date), the Rights associated with the Common Shares represented by such certificates shall be evidenced by such certificates alone, and the surrender for transfer of any such certificate shall also constitute the transfer of the Rights associated with the Common Shares represented thereby. In the event that the Company purchases or acquires any Common Shares after the Record Date but prior to the Distribution Date, any Rights associated with such Common Shares shall be deemed canceled and retired so that the Company shall not be entitled to exercise any Rights associated with the Common Shares which are no longer outstanding. Notwithstanding this Section 3(c), the omission of a legend shall not affect the enforceability of any part of this Agreement or the rights of any holder of the Rights.

SECTION 4. FORM OF RIGHT CERTIFICATES.

(a) The Right Certificates (and the form of election to purchase Preferred Shares, the form of assignment and the form of certification to be printed on the reverse thereof) shall be substantially the same as EXHIBIT B hereto and may have such marks of identification or designation and such legends, summaries or endorsements printed thereon as the Company may deem appropriate and as are not inconsistent with the provisions of this Agreement, or as may be required to comply with any applicable law or with any rule or regulation made pursuant thereto or with any rule or regulation of any stock exchange or quotation system on which the Rights may from time to time be listed, or to conform to usage. Subject to the provisions of Sections 7, 11 and 22 hereof, the Right Certificates shall entitle the holders thereof to purchase such number of one one-hundredths of a Preferred Share as shall be set forth therein at the Purchase Price (as define in Section 7(b)), but the number of such one one-hundredths of a Preferred Share and the Purchase Price shall be subject to adjustment as provided herein.

(b) Any Right Certificate issued pursuant to Section 3(a) or Section 22 hereof that represents Rights which are null and void pursuant to the second paragraph of Section 11(a)(ii) hereof and any Right Certificate issued pursuant to Section 6 or Section 11 hereof upon transfer, exchange, replacement or adjustment of any other Right Certificate referred to in this sentence, shall contain (to the extent feasible) the following legend:

The Rights represented by this Right Certificate are or were beneficially owned by a Person who was or became an Acquiring Person or an Affiliate or Associate of an Acquiring Person (as such terms are defined in the Agreement). Accordingly, this Right Certificate and the Rights represented hereby are null and void.

The provisions of Section 11(a)(ii) hereof shall be operative whether or not the foregoing legend is contained on any such Right Certificate.

SECTION 5. COUNTERSIGNATURE AND REGISTRATION. The Right Certificates shall be executed on behalf of the Company by its Chairman of the Board, its Chief Executive Officer, its President, its Vice Chairman of the Board, its Chief Financial Officer, or any of its Vice Presidents, either manually or by facsimile signature, shall have affixed thereto the Company's seal or a facsimile thereof, and shall be attested by the Secretary or an Assistant Secretary of the Company, either manually or by facsimile signature. The Right Certificates shall be manually countersigned by the Rights Agent and shall not be valid for any purpose unless countersigned. In case any officer of the Company who shall have signed any of the Right Certificates shall cease to be such officer of the Company before countersignature by the Rights Agent and issuance and delivery by the Company, such Right Certificates, nevertheless, may be countersigned by the Rights Agent and issued and delivered by the Company with the same force and effect as though the person who signed such Right Certificates had not ceased to be such officer of the Company; and any Right Certificate may be signed on behalf of the Company by any person who, at the actual date of the execution of such Right Certificate, shall be a proper officer of the Company to sign such Right Certificate, although at the date of the execution of this Agreement any such person was not such an officer.

Following the Distribution Date, the Rights Agent will keep or cause to be kept, at its office designated for such purpose, books for registration and transfer of the Right Certificates issued hereunder. Such books shall show the names and addresses of the respective holders of the Right Certificates, the number of Rights evidenced on its face by each of the Right Certificates and the date of each of the Right Certificates.

SECTION 6. TRANSFER, SPLIT UP, COMBINATION AND EXCHANGE OF RIGHT CERTIFICATES; MUTILATED, DESTROYED, LOST OR STOLEN RIGHT CERTIFICATES. Subject to the provisions of Section 11(a)(ii), Section 14 and Section 24 hereof, at any time after the Close of Business on the Distribution Date, and at or prior to the Close of Business on the earlier of the Redemption Date or the Final Expiration Date, any Right Certificate or Right Certificates may be transferred, split up, combined or exchanged for another Right Certificate or Right Certificates, entitling the registered holder to purchase a like number of one one-hundredths of a Preferred Share as the Right Certificate or Right Certificates surrendered then entitled such holder to purchase. Any registered holder desiring to transfer, split up, combine or exchange any Right Certificate or Right Certificates shall make such request in writing delivered to the Rights Agent, and shall surrender the Right Certificate or Right Certificates to be transferred, split up, combined or exchanged at the office of the Rights Agent designated for such purpose. Neither the Rights Agent nor the Company shall be obligated to take any action whatsoever with respect to the transfer of any such surrendered Right Certificate until the registered holder shall have completed and signed the certificate contained in the form of assignment on the reverse side of such Right Certificate and shall have provided such additional evidence of the identity of the

Beneficial Owner (or former Beneficial Owner) or Affiliates or Associates thereof as the Company shall reasonably request. Thereupon the Rights Agent shall, subject to Section 11(a)(ii), Section 14 and Section 24 hereof, countersign and deliver to the person entitled thereto a Right Certificate or Right Certificates, as the case may be, as so requested. The Company may require payment of a sum sufficient to cover any tax or governmental charge that may be imposed in connection with any transfer, split up, combination or exchange of Right Certificates.

Upon receipt by the Company and the Rights Agent of evidence reasonably satisfactory to them of the loss, theft, destruction or mutilation of a Right Certificate, and, in case of loss, theft or destruction, of indemnity or security reasonably satisfactory to them, and, at the Company's request, reimbursement to the Company and the Rights Agent of all reasonable expenses incidental thereto, and upon surrender to the Rights Agent and cancellation of the Right Certificate if mutilated, the Company will issue, execute and deliver a new Right Certificate of like tenor to the Rights Agent for countersignature and delivery to the registered holder in lieu of the Right Certificate so lost, stolen, destroyed or mutilated.

Notwithstanding any other provisions hereof, the Company and the Rights Agent may amend this Agreement to provide for uncertificated Rights in addition to or in place of Rights evidenced by Rights Certificates.

SECTION 7. EXERCISE OF RIGHTS; PURCHASE PRICE; EXPIRATION DATE OF RIGHTS.

(a) The registered holder of any Right Certificate may exercise the Rights evidenced thereby (except as otherwise provided herein) in whole or in part at any time after the Distribution Date (upon effectiveness of the registration statement described in Section 9(d)(i) below) upon surrender of the Right Certificate, with the form of election to purchase on the reverse side thereof duly executed, to the Rights Agent at the office of the Rights Agent designated for such purpose, together with payment of the Purchase Price for each one one-hundredth of a Preferred Share (or such other number of shares or other securities) as to which the Rights are exercised, at or prior to the earliest of (i) the Close of Business on December 7, 2010 (the "FINAL EXPIRATION DATE"), (ii) the time at which the Rights are redeemed as provided in Section 23 hereof (the "REDEMPTION DATE"), or (iii) the time at which such Rights are exchanged as provided in Section 24 hereof.

(b) The purchase price (the "PURCHASE PRICE") for each one one-hundredth of a Preferred Share pursuant to the exercise of a Right shall initially be \$85 (the "PURCHASE PRICE") and shall be subject to adjustment from time to time as provided in Sections 11 and 13 hereof and shall be payable in lawful money of the United States of America in accordance with paragraph (c) below.

(c) Upon receipt of a Right Certificate representing exercisable Rights, with the form of election to purchase duly executed, accompanied by payment of the Purchase Price for the shares to be purchased and an amount equal to any applicable transfer tax required to be paid by the holder of such Right Certificate in accordance with Section 9 hereof by certified check, cashier's check, bank draft or money order payable to the order of the Company, the Rights Agent shall thereupon promptly (i) (A) requisition from any transfer agent for the Preferred

Shares certificates for the number of Preferred Shares to be purchased and the Company hereby irrevocably authorizes its transfer agent to comply with all such requests, or (B) if the Company, in its sole discretion, shall have elected to deposit the Preferred Shares issuable upon exercise of the Rights hereunder into a depository, requisition from the depository agent depository receipts representing such number of one one-hundredths of a Preferred Share as are to be purchased (in which case certificates for the Preferred Shares represented by such receipts shall be deposited by the transfer agent with the depository agent) and the Company hereby directs the depository agent to comply with such request, (ii) when appropriate, requisition from the Company the amount of cash to be paid in lieu of issuance of fractional shares in accordance with Section 14 hereof, (iii) after receipt of such certificates or depository receipts, cause the same to be delivered to or upon the order of the registered holder of such Right Certificate, registered in such name or names as may be designated by such holder, and (iv) when appropriate, after receipt, deliver such cash to or upon the order of the registered holder of such Right Certificate. In the event that the Company is obligated to issue securities of the Company other than Preferred Shares (including Common Shares) of the Company pursuant to Section 11(a) hereof, the Company will make all arrangements necessary so that such other securities are available for distribution by the Rights Agent, if and when appropriate.

In addition, in the case of an exercise of the Rights by a holder pursuant to Section 11(a)(ii) hereof, the Rights Agent shall return such Right Certificate to the registered holder thereof after imprinting, stamping or otherwise indicating thereon that the rights represented by such Right Certificate no longer include the rights provided by Section 11(a)(ii) hereof, and, if fewer than all the Rights represented by such Right Certificate were so exercised, the Rights Agent shall indicate on the Right Certificate the number of Rights represented thereby which continue to include the rights provided by Section 11(a)(ii) hereof.

(d) In case the registered holder of any Right Certificate shall exercise fewer than all the Rights evidenced thereby, a new Right Certificate evidencing Rights equivalent to the Rights remaining unexercised shall be issued by the Rights Agent to the registered holder of such Right Certificate or to his duly authorized assigns, subject to the provisions of Section 14 hereof.

(e) The Company covenants and agrees that it will cause to be reserved and kept available out of its authorized and unissued Preferred Shares or any Preferred Shares held in its treasury, the number of Preferred Shares that will be sufficient to permit the exercise in full of all outstanding Rights in accordance with this Section 7.

(f) Notwithstanding anything in this Agreement to the contrary, neither the Rights Agent nor the Company shall be obligated to undertake any action with respect to a registered holder upon the occurrence of any purported exercise as set forth in this Section 7 unless such registered holder shall have (i) completed and signed the certification following the form of election to purchase set forth on the reverse side of the Rights Certificate surrendered for such exercise and (ii) tendered the Purchase Price (and an amount equal to any applicable transfer tax required to be paid by the holder of such Right Certificate in accordance with Section 9) to the Company in the manner set forth in Section 7(c), and (iii) provided such additional evidence of the identity of the Beneficial Owner (or former Beneficial Owner) or Affiliates or Associates thereof as the Company shall reasonably request.

SECTION 8. CANCELLATION AND DESTRUCTION OF RIGHT CERTIFICATES. All Right Certificates surrendered for the purpose of exercise, transfer, split up, combination or exchange shall, if surrendered to the Company or to any of its agents, be delivered to the Rights Agent for cancellation or in canceled form, or, if delivered or surrendered to the Rights Agent, shall be canceled by it, and no Right Certificates shall be issued in lieu thereof except as expressly permitted by any of the provisions of this Agreement. The Company shall deliver to the Rights Agent for cancellation and retirement, and the Rights Agent shall so cancel and retire, any other Right Certificate purchased or acquired by the Company otherwise than upon the exercise thereof. The Rights Agent shall deliver all canceled Right Certificates to the Company approximately one and one-half years after the cancellation date, or shall, at the written request of the Company, destroy such canceled Right Certificates, and in such case shall deliver a certificate of destruction thereof to the Company.

SECTION 9. AVAILABILITY OF PREFERRED SHARES.

(a) The Company covenants and agrees that so long as the Preferred Shares (and, after the time a person becomes an Acquiring Person, Common Shares or any other securities) issuable upon the exercise of the Rights may be listed on any national securities exchange or quotation system, the Company shall use its best efforts to cause, from and after such time as the Rights become exercisable, all shares reserved for such issuance to be listed on such exchange or quotation system upon official notice of issuance upon such exercise.

(b) The Company covenants and agrees that it will take all such action as may be necessary to ensure that all Preferred Shares (or Common Shares and other securities, as the case may be) delivered upon exercise of Rights shall, at the time of delivery of the certificates for such Preferred Shares (subject to payment of the Purchase Price), be duly and validly authorized and issued and fully paid and nonassessable shares or other securities.

(c) The Company further covenants and agrees that it will pay when due and payable any and all federal and state transfer taxes and charges which may be payable in respect of the issuance or delivery of the Right Certificates or of any Preferred Shares upon the exercise of Rights. The Company shall not, HOWEVER, be required to pay any transfer tax which may be payable in respect of any transfer or delivery of Right Certificates to a Person other than, or the issuance or delivery of certificates or depositary receipts for the Preferred Shares in a name other than that of, the registered holder of the Right Certificate evidencing Rights surrendered for exercise or to issue or to deliver any certificates or depositary receipts for Preferred Shares upon the exercise of any Rights until any such tax shall have been paid (any such tax being payable by the holder of such Right Certificate at the time of surrender) or until it has been established to the Company's reasonable satisfaction that no such tax is due.

(d) As soon as practicable after the Distribution Date, the Company shall use its best efforts to:

(i) prepare and file a registration statement under the Securities Act of 1933, as amended (the "Act"), with respect to the securities purchasable upon exercise of the Rights on an appropriate form, will use its best efforts to cause such registration statement to become effective as soon as practicable after such filing and will use its best efforts to cause such

registration statement to remain effective (with a prospectus at all times meeting the requirements of the Act) until the Final Expiration Date; and

(ii) use its best efforts to qualify or register the Rights and the securities purchasable upon exercise of the Rights under the blue sky laws of such jurisdictions as may be necessary or appropriate.

SECTION 10. PREFERRED SHARES RECORD DATE. Each person in whose name any certificate for Preferred Shares or other securities is issued upon the exercise of Rights shall for all purposes be deemed to have become the holder of record of the Preferred Shares or other securities represented thereby on, and such certificate shall be dated, the date upon which the Right Certificate evidencing such Rights was duly surrendered with the forms of election and certification duly executed and payment of the Purchase Price (and any applicable transfer taxes) was made; PROVIDED, HOWEVER, that if the date of such surrender and payment is a date upon which the Preferred Shares or other securities transfer books of the Company are closed, such person shall be deemed to have become the record holder of such shares on, and such certificate shall be dated, the next succeeding Business Day on which the Preferred Shares or other securities transfer books of the Company are open. Prior to the exercise of the Rights evidenced thereby, the holder of a Right Certificate, as such, shall not be entitled to any rights of a holder of Preferred Shares for which the Rights shall be exercisable, including, without limitation, the right to vote, to receive dividends or other distributions or to exercise any preemptive rights, and shall not be entitled to receive any notice of any proceedings of the Company, except as provided herein.

SECTION 11. ADJUSTMENT OF PURCHASE PRICE, NUMBER OF SHARES OR NUMBER OF RIGHTS. The Purchase Price, the number of Preferred Shares covered by each Right and the number of Rights outstanding are subject to adjustment from time to time as provided in this Section 11.

(a)

(i) In the event the Company shall at any time after the date of this Agreement (A) declare a dividend on the Preferred Shares payable in Preferred Shares, (B) subdivide the outstanding Preferred Shares, (C) combine the outstanding Preferred Shares into a smaller number of Preferred Shares, or (D) issue any shares of its capital stock in a reclassification of the Preferred Shares (including any such reclassification in connection with a consolidation or merger in which the Company is the continuing or surviving corporation), except as otherwise provided in this Section 11(a), the Purchase Price in effect at the time of the record date for such dividend or of the effective date of such subdivision, combination or reclassification, and the number and kind of shares of capital stock issuable on such date, shall be proportionately adjusted so that the holder of any Right exercised after such time shall be entitled to receive the aggregate number and kind of shares of capital stock which, if such Right had been exercised immediately prior to such date and at a time when the Preferred Shares transfer books of the Company were open, such holder would have owned upon such exercise and been entitled to receive by virtue of such dividend, subdivision, combination or reclassification; PROVIDED, HOWEVER, that in no event shall the consideration to be paid upon the exercise of one Right be less than the aggregate par value of the shares of capital stock of the Company issuable upon exercise

of one Right. If an event occurs which would require an adjustment under both Section 11(a)(i) and Section 11(a)(ii) hereof, the adjustment provided for in this Section 11(a)(i) shall be in addition to, and shall be made prior to any adjustment required pursuant to Section 11(a)(ii) hereof.

(ii) Subject to Section 24 hereof and the provisions of the next paragraph of this Section 11(a)(ii), in the event any Person shall become an Acquiring Person, each holder of a Right shall, for a period of 60 days after the later of such time any Person becomes an Acquiring Person or the effective date of an appropriate registration statement filed under the Act pursuant to Section 9 hereof (provided, however that, if at any time prior to the expiration or termination of the Rights there shall be a temporary restraining order, a preliminary injunction, an injunction, or temporary suspension by the Board of Directors, or similar obstacle to exercise of the Rights (the "Injunction") which prevents exercise of the Rights, a new 60-day period shall commence on the date the Injunction is removed), have a right to receive, upon exercise thereof at a price equal to the then current Purchase Price multiplied by the number of one one-hundredths of a Preferred Share for which a Right is then exercisable, in accordance with the terms of this Agreement and in lieu of Preferred Shares, such number of Common Shares as shall equal the result obtained by (A) multiplying the then current Purchase Price by the number of one one-hundredths of a Preferred Share for which a Right is then exercisable and dividing that product by (B) 50% of the then current per share market price of the Common Shares (determined pursuant to Section 11(d) hereof) on the date such Person became an Acquiring Person; PROVIDED, HOWEVER, that if the transaction that would otherwise give rise to the foregoing adjustment is also subject to the provisions of Section 13 hereof, then only the provisions of Section 13 hereof shall apply and no adjustment shall be made pursuant to this Section 11(a)(ii). In the event that any Person shall become an Acquiring Person and the Rights shall then be outstanding, the Company shall not take any action which would eliminate or diminish the benefits intended to be afforded by the Rights.

Notwithstanding anything in this Agreement to the contrary, from and after the time any Person becomes an Acquiring Person, any Rights beneficially owned by (i) such Acquiring Person or an Associate or Affiliate of such Acquiring Person, (ii) a transferee of such Acquiring Person (or of any such Associate or Affiliate) who becomes a transferee after the Acquiring Person became such, or (iii) a transferee of such Acquiring Person (or of any such Associate or Affiliate) who becomes a transferee prior to or concurrently with the Acquiring Person's becoming such and receives such Rights pursuant to either (A) a transfer (whether or not for consideration) from the Acquiring Person to holders of equity interests in such Acquiring Person or to any Person with whom the Acquiring Person has any continuing agreement, arrangement or understanding regarding the transferred Rights or (B) a transfer which the Board of Directors has determined is part of a plan, arrangement or understanding which has as a primary purpose or effect the avoidance of this Section 11(a)(ii), shall become null and void without any further action and no holder of such Rights shall have any rights whatsoever with respect to such Rights, whether under any provision of this Agreement or otherwise. The Company shall use all reasonable efforts to insure that the provisions of this Section 11(a)(ii) and Section 4(b) hereof are complied with, but shall have no liability to any holder of Right Certificates or other Person as a result of its failure to make any determinations with respect to an Acquiring Person or its Affiliates, Associates or transferees hereunder. No Right Certificate shall be issued at any time upon the transfer of any Rights to an Acquiring Person whose Rights would be void pursuant to

the preceding sentence or any Associate or Affiliate thereof or to any nominee of such Acquiring Person, Associate or Affiliate; and any Right Certificate delivered to the Rights Agent for transfer to an Acquiring Person whose Rights would be void pursuant to the preceding sentence shall be canceled.

(iii) In lieu of issuing Common Shares in accordance with Section 11(a)(ii) hereof, the Company may, if a majority of the Board of Directors then in office determines that such action is necessary or appropriate and not contrary to the interests of holders of Rights, elect to (and, in the event that the Board of Directors has not exercised the exchange right contained in Section 24(c) hereof and there are not sufficient treasury shares and authorized but unissued Common Shares to permit the exercise in full of the Rights in accordance with the foregoing subparagraph (ii), the Company shall) take all such action as may be necessary to authorize, issue or pay, upon the exercise of the Rights, cash (including by way of a reduction of the Purchase Price), property, Common Shares, other securities or any combination thereof having an aggregate value equal to the value of the Common Shares which otherwise would have been issuable pursuant to Section 11(a)(ii) hereof, which aggregate value shall be determined by a nationally recognized investment banking firm selected by a majority of the Board of Directors then in office. For purposes of the preceding sentence, the value of the Common Shares shall be determined pursuant to Section 11(d) hereof. Any such election by the Board of Directors must be made within 60 days following the date on which the event described in Section 11(a)(ii) hereof shall have occurred. Following the occurrence of the event described in Section 11(a)(ii) hereof, a majority of the Board of Directors then in office may suspend the exercisability of the Rights for a period of up to 60 days following the date on which the event described in Section 11(a)(ii) hereof shall have occurred to the extent that such directors have not determined whether to exercise their rights of election under this Section 11(a)(iii). In the event of any such suspension, the Company shall issue a public announcement stating that the exercisability of the Rights has been temporarily suspended.

(b) In case the Company shall fix a record date for the issuance of rights, options or warrants to all holders of Preferred Shares entitling them (for a period expiring within 45 calendar days after such record date) to subscribe for or purchase Preferred Shares (or shares having the same designations and the powers, preferences and rights, and the qualifications, limitations and restrictions as the Preferred Shares ("equivalent preferred shares")) or securities convertible into Preferred Shares or equivalent preferred shares at a price per Preferred Share or equivalent preferred share (or having a conversion price per share, if a security convertible into Preferred Shares or equivalent preferred shares) less than the then current per share market price of the Preferred Shares (as such term is hereinafter defined) on such record date, the Purchase Price to be in effect after such record date shall be determined by multiplying the Purchase Price in effect immediately prior to such record date by a fraction, the numerator of which shall be the number of Preferred Shares outstanding on such record date plus the number of Preferred Shares which the aggregate offering price of the total number of Preferred Shares and/or equivalent preferred shares so to be offered (and/or the aggregate initial conversion price of the convertible securities so to be offered) would purchase at such current market price and the denominator of which shall be the number of Preferred Shares outstanding on such record date plus the number of additional Preferred Shares and/or equivalent preferred shares to be offered for subscription or purchase (or into which the convertible securities so to be offered are initially convertible); PROVIDED, HOWEVER, that in no event shall the consideration to be paid upon the exercise of one

Right be less than the aggregate par value of the shares of capital stock of the Company issuable upon exercise of one Right. In case such subscription price may be paid in a consideration part or all of which shall be in a form other than cash, the value of such consideration shall be as determined in good faith by the Board of Directors, whose determination shall be described in a statement filed with the Rights Agent. Preferred Shares owned by or held for the account of the Company shall not be deemed outstanding for the purpose of any such computation. Such adjustment shall be made successively whenever such a record date is fixed; and in the event that such rights, options or warrants are not so issued, the Purchase Price shall be adjusted to be the Purchase Price which would then be in effect if such record date had not been fixed.

(c) In case the Company shall fix a record date for the making of a distribution to all holders of the Preferred Shares (including any such distribution made in connection with a consolidation or merger in which the Company is the continuing or surviving corporation) of evidences of indebtedness or assets (other than a regular quarterly cash dividend or a dividend payable in Preferred Shares) or subscription rights or warrants (excluding those referred to in Section 11(b) hereof), the Purchase Price to be in effect after such record date shall be determined by multiplying the Purchase Price in effect immediately prior to such record date by a fraction, the numerator of which shall be the then current per share market price (as such term is hereinafter defined) of the Preferred Shares on such record date, less the fair market value (as determined in good faith by the Board of Directors, whose determination shall be described in a statement filed with the Rights Agent) of the portion of the assets or evidences of indebtedness so to be distributed or of such subscription rights or warrants applicable to one Preferred Share and the denominator of which shall be such current per share market price of the Preferred Shares; PROVIDED, HOWEVER, that in no event shall the consideration to be paid upon the exercise of one Right be less than the aggregate par value of the shares of capital stock of the Company to be issued upon exercise of one Right. Such adjustments shall be made successively whenever such a record date is fixed; and in the event that such distribution is not so made, the Purchase Price shall again be adjusted to be the Purchase Price which would then be in effect if such record date had not been fixed.

(d)

(i) For the purpose of any computation hereunder, the "CURRENT PER SHARE MARKET PRICE" of any security (a "Security" for the purpose of this Section 11(d)(i)) on any date shall be deemed to be the average of the daily closing prices per share of such Security for the 30 consecutive Trading Days (as such term is hereinafter defined) immediately prior to such date; PROVIDED, HOWEVER, that in the event that the current per share market price of the Security is determined during a period following the announcement by the issuer of such Security of (A) a dividend or distribution on such Security payable in shares of such Security or securities convertible into such shares, or (B) any subdivision, combination or reclassification of such Security or securities convertible into such shares, or (C) any subdivision, combination or reclassification of such Security, and prior to the expiration of 30 Trading Days after the ex dividend date for such dividend or distribution, or the record date for such subdivision, combination or reclassification, then, and in each such case, the current per share market price shall be appropriately adjusted to reflect the current market price per share equivalent of such Security. The closing price for each day shall be the last sale price, regular way, or, in case no such sale takes place on such day, the average of the closing bid and asked prices, regular way,

in either case as reported in the principal consolidated transaction reporting system with respect to securities listed or admitted to trading on the New York Stock Exchange or, if the Security is not listed or admitted to trading on the New York Stock Exchange, as reported in the principal consolidated transaction reporting system with respect to securities listed on the principal national securities exchange on which the Security is listed or admitted to trading or as reported on the Nasdaq National Market or, if the Security is not listed or admitted to trading on any national securities exchange or reported on the Nasdaq National Market, the last quoted price or, if not so quoted, the average of the high bid and low asked prices in the over-the-counter market, as reported by the National Association of Securities Dealers, Inc. Automated Quotations System ("Nasdaq") or such other system then in use, or, if on any such date the Security is not quoted by any such organization, the average of the closing bid and asked prices as furnished by a professional market maker making a market in the Security selected by the Board of Directors or, if on any such date no professional market maker is making a market in the Security, the price as determined in good faith by the Board of Directors. The term "TRADING DAY" shall mean a day on which the principal national securities exchange on which the Security is listed or admitted to trading is open for the transaction of business or, if the Security is not listed or admitted to trading on any national securities exchange, a Business Day.

(ii) For the purpose of any computation hereunder, the "current per share market price" of the Preferred Shares shall be determined in accordance with the method set forth in Section 11(d)(i) hereof. If the Preferred Shares are not publicly traded, the "current per share market price" of the Preferred Shares shall be conclusively deemed to be the current per share market price of the Common Shares as determined pursuant to Section 11(d)(i) hereof (appropriately adjusted to reflect any stock split, stock dividend or similar transaction occurring after the date hereof) multiplied by one hundred. If neither the Common Shares nor the Preferred Shares are publicly held or so listed or traded, "current per share market price" shall mean the fair value per share as determined in good faith by the Board of Directors, whose determination shall be described in a statement filed with the Rights Agent.

(e) No adjustment in the Purchase Price shall be required unless such adjustment would require an increase or decrease of at least 1% in the Purchase Price; PROVIDED, HOWEVER, that any adjustments which by reason of this Section 11(e) are not required to be made shall be carried forward and taken into account in any subsequent adjustment. All calculations under this Section 11 shall be made to the nearest cent or to the nearest one one-hundredth of a Preferred Share or one ten-thousandth of any other share or security as the case may be. Notwithstanding the first sentence of this Section 11(e), any adjustment required by this Section 11 shall be made no later than the earlier of (i) three years from the date of the transaction which requires such adjustment or (ii) the date of the expiration of the right to exercise any Rights.

(f) If as a result of an adjustment made pursuant to Section 11(a) hereof, the holder of any Right thereafter exercised shall become entitled to receive any shares of capital stock of the Company other than Preferred Shares, thereafter the number of such other shares so receivable upon exercise of any Right shall be subject to adjustment from time to time in a manner and on terms as nearly equivalent as practicable to the provisions with respect to the Preferred Shares contained in Sections 11(a) through 11(c) hereof, inclusive, and the provisions of Sections 7, 9, 10, 13 and 14 hereof with respect to the Preferred Shares shall apply on like terms to any such other shares.

(g) All Rights originally issued by the Company subsequent to any adjustment made to the Purchase Price hereunder shall evidence the right to purchase, at the adjusted Purchase Price, the number of one one-hundredths of a Preferred Share purchasable from time to time hereunder upon exercise of the Rights, all subject to further adjustment as provided herein.

(h) Unless the Company shall have exercised its election as provided in Section 11(i) hereof, upon each adjustment of the Purchase Price as a result of the calculations made in Section 11(b) and Section 11(c) hereof, each Right outstanding immediately prior to the making of such adjustment shall thereafter evidence the right to purchase, at the adjusted Purchase Price, that number of one one-hundredths of a Preferred Share (calculated to the nearest one one-millionth of a Preferred Share) obtained by (i) multiplying (x) the number of one one-hundredths of a Preferred Share covered by a Right immediately prior to this adjustment by (y) the Purchase Price in effect immediately prior to such adjustment of the Purchase Price and (ii) dividing the product so obtained by the Purchase Price in effect immediately after such adjustment of the Purchase Price.

(i) The Company may elect on or after the date of any adjustment of the Purchase Price to adjust the number of Rights, in substitution for any adjustment in the number of one one-hundredths of a Preferred Share purchasable upon the exercise of a Right. Each of the Rights outstanding after such adjustment of the number of Rights shall be exercisable for the number of one one-hundredths of a Preferred Share for which a Right was exercisable immediately prior to such adjustment. Each Right held of record prior to such adjustment of the number of Rights shall become that number of Rights (calculated to the nearest one ten-thousandth) obtained by dividing the Purchase Price in effect immediately prior to adjustment of the Purchase Price by the Purchase Price in effect immediately after adjustment of the Purchase Price. The Company shall make a public announcement of its election to adjust the number of Rights, indicating the record date for the adjustment, and, if known at the time, the amount of the adjustment to be made. This record date may be the date on which the Purchase Price is adjusted or any day thereafter, but, if the Right Certificates have been issued, shall be at least 10 days later than the date of the public announcement. If Right Certificates have been issued, upon each adjustment of the number of Rights pursuant to this Section 11(i), the Company shall, as promptly as practicable, cause to be distributed to holders of record of Right Certificates on such record date Right Certificates evidencing, subject to Section 14 hereof, the additional Rights to which such holders shall be entitled as a result of such adjustment, or, at the option of the Company, shall cause to be distributed to such holders of record in substitution and replacement for the Right Certificates held by such holders prior to the date of adjustment, and upon surrender thereof, if required by the Company, new Right Certificates evidencing all the Rights to which such holders shall be entitled after such adjustment. Right Certificates so to be distributed shall be issued, executed and countersigned in the manner provided for herein and shall be registered in the names of the holders of record of Right Certificates on the record date specified in the public announcement.

(j) Irrespective of any adjustment or change in the Purchase Price or the number of one one-hundredths of a Preferred Share issuable upon the exercise of the Rights, the Right Certificates theretofore and thereafter issued may continue to express the Purchase Price and the number of one one-hundredths of a Preferred Share which were expressed in the initial Right Certificates issued hereunder.

(k) Before taking any action that would cause an adjustment reducing the Purchase Price below one one-hundredth of the then par value, if any, of the Preferred Shares issuable upon exercise of the Rights, the Company shall take any corporate action which may, in the opinion of its counsel, be necessary in order that the Company may validly and legally issue fully paid and nonassessable Preferred Shares at such adjusted Purchase Price.

(l) In any case in which this Section 11 shall require that an adjustment in the Purchase Price be made effective as of a record date for a specified event, the Company may elect to defer until the occurrence of such event the issuing to the holder of any Right exercised after such record date of the Preferred Shares and other capital stock or securities of the Company, if any, issuable upon such exercise on the basis of the Purchase Price in effect prior to such adjustment; PROVIDED, HOWEVER, that the Company shall deliver to such holder a due bill or other appropriate instrument evidencing such holder's right to receive such additional shares upon the occurrence of the event requiring such adjustment.

(m) The Company covenants and agrees that, after the Distribution Date, it will not, except as permitted by Section 23 or Section 27 hereof, take (or permit any Subsidiary to take) any action the purpose of which is to, or if at the time such action is taken it is reasonably foreseeable that the effect of such action is to, materially diminish or eliminate the benefits intended to be afforded by the Rights. Any such action taken by the Company during any period after any Person becomes an Acquiring Person but prior to the Distribution Date shall be null and void unless such action could be taken under this Section 11(m) from and after the Distribution Date.

(n) Anything in this Section 11 to the contrary notwithstanding, the Company shall be entitled to make such reductions in the Purchase Price, in addition to those adjustments expressly required by this Section 11, as and to the extent that it in its sole discretion shall determine to be advisable in order that any consolidation or subdivision of the Preferred Shares, issuance wholly for cash of any Preferred Shares at less than the current market price, issuance wholly for cash of Preferred Shares or securities which by their terms are convertible into or exchangeable for Preferred Shares, dividends on Preferred Shares payable in Preferred Shares or issuance of rights, options or warrants referred to hereinabove in Section 11(b), hereafter made by the Company to holders of its Preferred Shares shall not be taxable to such stockholders.

(o) In the event that at any time after the date of this Agreement and prior to the Distribution Date, the Company shall (i) declare or pay any dividend on the Common Shares payable in Common Shares or (ii) effect a subdivision, combination or consolidation of the Common Shares (by reclassification or otherwise than by payment of dividends in Common Shares) into a greater or lesser number of Common Shares, then in any such case (A) the number of one one-hundredths of a Preferred Share purchasable after such event upon proper exercise of each Right shall be determined by multiplying the number of one one-hundredths of a Preferred Share so purchasable immediately prior to such event by a fraction, the numerator of which is the number of Common Shares outstanding immediately before such event and the denominator of which is the number of Common Shares outstanding immediately after such event, and (B) each Common Share outstanding immediately after such event shall have issued with respect to it that number of Rights which each Common Share outstanding immediately prior to such event had issued with respect to it. The adjustments provided for in this Section 11(o) shall be made

successively whenever such a dividend is declared or paid or such a subdivision, combination or consolidation is effected.

(p) The exercise of Rights under Section 11(a)(ii) hereof shall only result in the loss of rights under Section 11(a)(ii) hereof to the extent so exercised and shall not otherwise affect the rights represented by the Rights under this Agreement, including the rights represented by Section 13 hereof.

SECTION 12. CERTIFICATE OF ADJUSTED PURCHASE PRICE OR NUMBER OF SHARES. Whenever an adjustment is made as provided in Sections 11 and 13 hereof, the Company shall promptly (a) prepare a certificate setting forth such adjustment, and a brief statement of the facts accounting for such adjustment, (b) file with the Rights Agent and with each transfer agent for the Common Shares or the Preferred Shares a copy of such certificate and (c) mail a brief summary thereof to each holder of a Right Certificate in accordance with Section 25 hereof. The Rights Agent shall be fully protected in relying on any such certificate and on any adjustment therein contained and shall not be deemed to have knowledge of any adjustment unless and until it shall have received such certificate.

SECTION 13. CONSOLIDATION, MERGER OR SALE OR TRANSFER OF ASSETS OR EARNING POWER.

(a) In the event that, following the Distribution Date, directly or indirectly (x) the Company shall consolidate with, or merge with and into, any Interested Stockholder, or if in such merger or consolidation all holders of Common Stock are not treated alike, any other Person, (y) any Interested Stockholder, or if in such merger or consolidation all holders of Common Stock are not treated alike, any other Person shall consolidate with the Company, or merge with and into the Company, and the Company shall be the continuing or surviving corporation of such merger (other than, in the case of either transaction described in (x) or (y), a merger or consolidation which would result in all of the voting power represented by the securities of the Company outstanding immediately prior thereto continuing to represent (either by remaining outstanding or by being converted into securities of the surviving entity) all of the voting power represented by the securities of the Company or such surviving entity outstanding immediately after such merger or consolidation and the holders of such securities not having changed as a result of such merger or consolidation), or (z) the Company shall sell, mortgage or otherwise transfer (or one or more of its subsidiaries shall sell, mortgage or otherwise transfer), in one or more transactions, assets or earning power aggregating more than 50% of the assets or earning power of the Company and its subsidiaries (taken as a whole) to any Interested Stockholder or Stockholders, or if in such transaction all holders of Common Stock are not treated alike, any other Person, (other than the Company or any Subsidiary of the Company in one or more transactions each of which individually and the aggregate does not violate Section 13(d) hereof) then, and in each such case, proper provision shall be made so that (i) each holder of a Right, subject to Section 11(a)(ii) hereof, shall have the right to receive, upon the exercise thereof at a price equal to the then current Purchase Price multiplied by the number of one one-hundredths of a Preferred Share for which a Right is then exercisable in accordance with the terms of this Agreement and in lieu of Preferred Shares, such number of freely tradeable Common Shares of the Principal Party (as such term is hereinafter defined), free and clear of liens, rights of call or first refusal, encumbrances or other adverse claims, as shall be equal to the result obtained by (A)

multiplying the then current Purchase Price by the number of one one-hundredths of a Preferred Share for which a Right is then exercisable (without taking into account any adjustment previously made pursuant to Section 11(a)(ii) hereof) and dividing that product by (B) 50% of the then current per share market price of the Common Shares of such Principal Party (determined pursuant to Section 11(d) hereof) on the date of consummation of such consolidation, merger, sale or transfer; (ii) such Principal Party shall thereafter be liable for, and shall assume, by virtue of such consolidation, merger, sale or transfer, all the obligations and duties of the Company pursuant to this Agreement; (iii) the term "Company" shall thereafter be deemed to refer to such Principal Party, it being specifically intended that the provisions of Section 11 hereof shall apply to such Principal Party; and (iv) such Principal Party shall take such steps (including, but not limited to, the reservation of a sufficient number of shares of its Common Shares in accordance with Section 9 hereof) in connection with such consummation as may be necessary to assure that the provisions hereof shall thereafter be applicable, as nearly as reasonably may be, in relation to its Common Shares thereafter deliverable upon the exercise of the Rights.

(b) "PRINCIPAL PARTY" shall mean:

(i) in the case of any transaction described in clause (x) or (y) of the first sentence of Section 13(a) hereof, the Person that is the issuer of any securities into which Common Shares are converted in such merger or consolidation, and if no securities are so issued, the Person that is the other party to the merger or consolidation (or, if applicable, the Company, if it is the surviving corporation); and

(ii) in the case of any transaction described in (z) of the first sentence of Section 13(a) hereof, the Person that is the party receiving the greatest portion of the assets or earning power transferred pursuant to such transaction or transactions;

PROVIDED, HOWEVER, that in any case, (1) if the Common Shares of such Person are not at such time and have not been continuously over the preceding 12-month period registered under Section 12 of the Exchange Act, and such Person is a direct or indirect Subsidiary or Affiliate of another Person the Common Shares of which are and have been so registered, "Principal Party" shall refer to such other Person; (2) if such Person is a Subsidiary, directly or indirectly, or Affiliate of more than one Person, the Common Shares of two or more of which are and have been so registered, "Principal Party" shall refer to whichever of such Persons is the issuer of the Common Shares having the greatest aggregate market value; and (3) if such Person is owned, directly or indirectly, by a joint venture formed by two or more Persons that are not owned, directly or indirectly, by the same Person, the rules set forth in (1) and (2) above shall apply to each of the chains of ownership having an interest in such joint venture as if such party were a "Subsidiary" of both or all of such joint venturers and the Principal Parties in each such chain shall bear the obligations set forth in this Section 13 in the same ratio as their direct or indirect interests in such Person bear to the total of such interests.

(c) The Company shall not consummate any such consolidation, merger, sale or transfer unless the Principal Party shall have a sufficient number of authorized Common Shares that have not been issued or reserved for issuance to permit the exercise in full of the Rights in accordance with this Section 13 and unless prior thereto the Company and each Principal Party

and each other Person who may become a Principal Party as a result of such consolidation, merger, sale or transfer shall have (i) executed and delivered to the Rights Agent a supplemental agreement providing for the terms set forth in paragraphs (a) and (b) of this Section 13 and (ii) prepared, filed and had declared and remain effective a registration statement under the Act on the appropriate form with respect to the Rights and the securities exercisable upon exercise of the Rights and further providing that, as soon as practicable after the date of any consolidation, merger, sale or transfer of assets mentioned in paragraph (a) of this Section 13, the Principal Party at its own expense will:

(i) cause the registration statement under the Act with respect to the Rights and the securities purchasable upon exercise of the Rights on an appropriate form to remain effective (with a prospectus at all times meeting the requirements of the Act) until the Final Expiration Date;

(ii) use its best efforts to qualify or register the Rights and the securities purchasable upon exercise of the Rights under the blue sky laws of such jurisdictions as may be necessary or appropriate;

(iii) list the Rights and the securities purchasable upon exercise of the Rights on each national securities exchange on which the Common Shares were listed prior to the consummation of such consolidation, merger, sale or transfer of assets or on the Nasdaq National Market if the Common Shares were listed on the Nasdaq National Market or, if the Common Shares were not listed on a national securities exchange or the Nasdaq National Market prior to the consummation of such consolidation, merger, sale or transfer of assets, on a national securities exchange or the Nasdaq National Market; and

(iv) deliver to holders of the Rights historical financial statements for the Principal Party and each of its Affiliates which comply in all material respects with the requirements for registration on Form 10 under the Exchange Act.

The provisions of this Section 13 shall similarly apply to successive mergers or consolidations or sales or other transfers.

(d) After the Distribution Date, the Company covenants and agrees that it shall not (i) consolidate with, (ii) merge with or into, or (iii) sell or transfer to, in one or more transactions, assets or earning power aggregating more than 50% of the assets or earning power of the Company and its subsidiaries taken as a whole, any other Person (other than a Subsidiary of the Company in a transaction which does not violate Section 11(m) hereof), if (x) at the time of or after such consolidation, merger or sale there are any charter or bylaw provisions or any rights, warrants or other instruments or securities outstanding, agreements in effect or any other action taken which would diminish or otherwise eliminate the benefits intended to be afforded by the Rights or (y) prior to, simultaneously with or immediately after such consolidation, merger or sale, the stockholders of the Person who constitutes, or would constitute, the "Principal Party" for purposes of Section 13(a) hereof shall have received a distribution of Rights previously owned by such Person or any of its Affiliates and Associates. The Company shall not consummate any such consolidation, merger, sale or transfer unless prior thereto the Company

and such other Person shall have executed and delivered to the Rights Agent a supplemental agreement evidencing compliance with this Section 13(d).

SECTION 14. FRACTIONAL RIGHTS AND FRACTIONAL SHARES.

(a) The Company shall not be required to issue fractions of Rights or to distribute Right Certificates which evidence fractional Rights. In lieu of such fractional Rights, there shall be paid to the registered holders of the Right Certificates with regard to which such fractional Rights would otherwise be issuable, an amount in cash equal to the same fraction of the current market value of a whole Right. For the purposes of this Section 14(a), the current market value of a whole Right shall be the closing price of the Rights for the Trading Day immediately prior to the date on which such fractional Rights would have been otherwise issuable. The closing price for any day shall be the last sale price, regular way, or, in case no such sale takes place on such day, the average of the closing bid and asked prices, regular way, in either case as reported in the principal consolidated transaction reporting system with respect to securities listed or admitted to trading on the New York Stock Exchange or, if the Rights are not listed or admitted to trading on the New York Stock Exchange, as reported in the principal consolidated transaction reporting system with respect to securities listed on the principal national securities exchange on which the Rights are listed or admitted to trading or as reported on the Nasdaq National Market or, if the Rights are not listed or admitted to trading on any national securities exchange or reported on the Nasdaq National Market, the last quoted price or, if not so quoted, the average of the high bid and low asked prices in the over-the-counter market, as reported by Nasdaq or such other system then in use or, if on any such date the Rights are not quoted by any such organization, the average of the closing bid and asked prices as furnished by a professional market maker making a market in the Rights selected by the Board of Directors. If on any such date no such market maker is making a market in the Rights, the fair value of the Rights on such date as determined in good faith by the Board of Directors shall be used.

(b) The Company shall not be required to issue fractions of Preferred Shares (other than fractions which are integral multiples of one one-hundredth of a Preferred Share) upon exercise of the Rights or to distribute certificates which evidence fractional Preferred Shares (other than fractions which are integral multiples of one one-hundredth of a Preferred Share). Fractions of Preferred Shares in integral multiples of one one-hundredth of a Preferred Share may, at the election of the Company, be evidenced by depositary receipts; PROVIDED, HOWEVER, that holders of such depositary receipts shall have all of the designations and the powers, preferences and rights, and the qualifications, limitations and restrictions to which they are entitled as beneficial owners of the Preferred Shares represented by such depositary receipts. In lieu of fractional Preferred Shares that are not integral multiples of one one-hundredth of a Preferred Share, the Company shall pay to the registered holders of Right Certificates at the time such Rights are exercised as herein provided an amount in cash equal to the same fraction of the current market value of one Preferred Share. For the purposes of this Section 14(b), the current market value of a Preferred Share shall be the current per share market price of the Preferred Shares (as determined pursuant to the second sentence of Section 11(d)(i) hereof) for the Trading Day immediately prior to the date of such exercise (or, if not publicly traded, in accordance with Section 11(d)(ii) hereof).

(c) Following the occurrence of one of the transactions or events specified in Section 11 hereof giving rise to the right to receive Common Shares, capital stock equivalents (other than Preferred Shares) or other securities upon the exercise of a Right, the Company shall not be required to issue fractions of Common Shares or units of such Common Shares, capital stock equivalents or other securities upon exercise of the Rights or to distribute certificates which evidence fractional Common Shares, capital stock equivalents or other securities. In lieu of fractional Common Shares, capital stock equivalents or other securities, the Company shall pay to the registered holders of Right Certificates at the time such Rights are exercised as herein provided an amount in cash equal to the same fraction of the current market value of one Common Share or unit of such Common Shares, capital stock equivalents or other securities. For purposes of this Section 14(c), the current market value shall be the current per share market price (as determined pursuant to Section 11(d)(i) hereof) for the Trading Day immediately prior to the date of such exercise and, if such capital stock equivalent is not traded, each such capital stock equivalent shall have the value of one one-hundredth of a Preferred Share.

(d) The holder of a Right by the acceptance of the Right expressly waives his right to receive any fractional Rights or any fractional shares upon exercise of a Right (except as provided above).

SECTION 15. RIGHTS OF ACTION. All rights of action in respect of this Agreement, excepting the rights of action given to the Rights Agent under Sections 18 and 20 hereof, are vested in the respective registered holders of the Right Certificates (and, prior to the Distribution Date, the registered holders of the Common Shares) and any registered holder of any Right Certificate (or, prior to the Distribution Date, of the Common Shares), without the consent of the Rights Agent or of the holder of any other Right Certificate (or, prior to the Distribution Date, of the Common Shares), may, in his own behalf and for his own benefit, enforce, and may institute and maintain any suit, action or proceeding against the Company to enforce, or otherwise act in respect of, his right to exercise the Rights evidenced by such Right Certificate in the manner provided in such Right Certificate and in this Agreement. Without limiting the foregoing or any remedies available to the holders of Rights, it is specifically acknowledged that the holders of Rights would not have an adequate remedy at law for any breach of this Agreement and will be entitled to specific performance of the obligations under, and injunctive relief against actual or threatened violations of the obligations of any Person subject to, this Agreement. Holders of Rights shall be entitled to recover the reasonable costs and expenses, including attorneys fees, incurred by them in any action to enforce the provisions of this Agreement.

SECTION 16. AGREEMENT OF RIGHT HOLDERS. Every holder of a Right, by accepting the same, consents and agrees with the Company and the Rights Agent and with every other holder of a Right that:

(a) prior to the Distribution Date, the Rights will be transferable only in connection with the transfer of the Common Shares;

(b) after the Distribution Date, the Right Certificates are transferable (subject to the provisions of this Agreement) only on the registry books of the Rights Agent if surrendered at the principal office of the Rights Agent, duly endorsed or accompanied by a proper instrument of transfer; and

(c) the Company and the Rights Agent may deem and treat the person in whose name the Right Certificate (or, prior to the Distribution Date, the associated Common Shares certificate) is registered as the absolute owner thereof and of the Rights evidenced thereby (notwithstanding any notations of ownership or writing on the Right Certificates or the associated Common Shares certificate made by anyone other than the Company or the Rights Agent) for all purposes whatsoever, and neither the Company nor the Rights Agent shall be affected by any notice to the contrary.

SECTION 17. RIGHT CERTIFICATE HOLDER NOT DEEMED A STOCKHOLDER. No holder, as such, of any Right Certificate shall be entitled to vote, receive dividends or be deemed for any purpose the holder of the Preferred Shares or any other securities of the Company which may at any time be issuable on the exercise of the Rights represented thereby, nor shall anything contained herein or in any Right Certificate be construed to confer upon the holder of any Right Certificate, as such, any of the rights of a stockholder of the Company or any right to vote for the election of directors or upon any matter submitted to stockholders at any meeting thereof, or to give or withhold consent to any corporate action, or to receive notice of meetings or other actions affecting stockholders (except as provided in Section 25 hereof), or to receive dividends or subscription rights, or otherwise, until the Right or Rights evidenced by such Right Certificate shall have been exercised in accordance with the provisions hereof.

SECTION 18. CONCERNING THE RIGHTS AGENT. The Company agrees to pay to the Rights Agent reasonable compensation for all services rendered by it hereunder and, from time to time, on demand of the Rights Agent, its reasonable expenses and counsel fees and other disbursements incurred in the administration and execution of this Agreement and the exercise and performance of its duties hereunder. The Company also agrees to indemnify the Rights Agent for, and to hold it harmless against, any loss, liability, or expense, incurred without negligence, bad faith or willful misconduct on the part of the Rights Agent, for anything done or omitted by the Rights Agent in connection with the acceptance and administration of this Agreement, including the costs and expenses of defending against any claim of liability in the premises. The indemnity provided herein shall survive the expiration of the Rights and the termination of this Agreement.

The Rights Agent shall be protected and shall incur no liability for, or in respect of any action taken, suffered or omitted by it in connection with, its administration of this Agreement in reliance upon any Right Certificate or certificate for the Preferred Shares or Common Shares or for other securities of the Company, instrument of assignment or transfer, power of attorney, endorsement, affidavit, letter, notice, direction, consent, certificate, statement, or other paper or document believed by it to be genuine and to be signed, executed and, where necessary, verified or acknowledged, by the proper person or persons, or otherwise upon the advice of counsel as set forth in Section 20 hereof. In no case will the Rights Agent be liable for special, indirect, incidental or consequential loss or damage of any kind whatsoever (including but not limited to lost profits), even if the Rights Agent has been advised of such loss or damage.

SECTION 19. MERGER OR CONSOLIDATION OR CHANGE OF NAME OF RIGHTS AGENT. Any corporation into which the Rights Agent or any successor Rights Agent may be merged or with which it may be consolidated, or any corporation resulting from any merger or consolidation to which the Rights Agent or any successor Rights Agent shall be a party, or any corporation

succeeding to the shareholder services or corporate trust business of the Rights Agent or any successor Rights Agent, shall be the successor to the Rights Agent under this Agreement without the execution or filing of any paper or any further act on the part of any of the parties hereto, provided that such corporation would be eligible for appointment as a successor Rights Agent under the provisions of Section 21 hereof. In case at the time such successor Rights Agent shall succeed to the agency created by this Agreement any of the Right Certificates shall have been countersigned but not delivered, any such successor Rights Agent may adopt the countersignature of the predecessor Rights Agent and deliver such Right Certificates so countersigned; and in case at that time any of the Right Certificates shall not have been countersigned, any successor Rights Agent may countersign such Right Certificates either in the name of the predecessor Rights Agent or in the name of the successor Rights Agent; and in all such cases such Right Certificates shall have the full force provided in the Right Certificates and in this Agreement.

In case at any time the name of the Rights Agent shall be changed and at such time any of the Right Certificates shall have been countersigned but not delivered, the Rights Agent may adopt the countersignature under its prior name and deliver Right Certificates so countersigned; and in case at that time any of the Right Certificates shall not have been countersigned, the Rights Agent may countersign such Right Certificates either in its prior name or in its changed name; and in all such cases such Right Certificates shall have the full force provided in the Right Certificates and in this Agreement.

SECTION 20. DUTIES OF RIGHTS AGENT. The Rights Agent undertakes the duties and obligations imposed by this Agreement upon the following terms and conditions, by all of which the Company and the holders of Right Certificates, by their acceptance thereof, shall be bound:

(a) The Rights Agent may consult with legal counsel of its choice (who may be legal counsel for the Company), and the opinion of such counsel shall be full and complete authorization and protection to the Rights Agent as to any action taken or omitted by it in good faith and in accordance with such opinion.

(b) Whenever in the performance of its duties under this Agreement the Rights Agent shall deem it necessary or desirable that any fact or matter be proved or established by the Company prior to taking or suffering any action hereunder, such fact or matter (unless other evidence in respect thereof be herein specifically prescribed) may be deemed to be conclusively proved and established by a certificate signed by any one of the Chairman of the Board, the Chief Executive Officer, the President, the Chief Financial Officer, any Vice President, the Treasurer or the Secretary of the Company and delivered to the Rights Agent; and such certificate shall be full authorization to the Rights Agent for any action taken or suffered in good faith by it under the provisions of this Agreement in reliance upon such certificate.

(c) The Rights Agent shall be liable hereunder to the Company and any other Person only for its own negligence, bad faith or willful misconduct.

(d) The Rights Agent shall not be liable for or by reason of any of the statements of fact or recitals contained in this Agreement or in the Right Certificates (except its

countersignature thereof) or be required to verify the same, but all such statements and recitals are and shall be deemed to have been made by the Company only.

(e) The Rights Agent shall not be under any responsibility in respect of the validity of this Agreement or the execution and delivery hereof (except the due execution hereof by the Rights Agent) or in respect of the validity or execution of any Right Certificate (except its countersignature thereof); nor shall it be responsible for any breach by the Company of any covenant or condition contained in this Agreement or in any Right Certificate; nor shall it be responsible for any change in the exercisability of the Rights (including the Rights becoming void pursuant to Section 11(a)(ii) hereof) or any adjustment in the terms of the Rights (including the manner, method or amount thereof) provided for in Sections 3, 11, 13, 23 or 24 hereof, or the ascertaining of the existence of facts that would require any such change or adjustment (except with respect to the exercise of Rights evidenced by Right Certificates after receipt of a certificate pursuant to Section 12 hereof describing such change or adjustment); nor shall it by any act hereunder be deemed to make any representation or warranty as to the authorization or reservation of any Preferred Shares to be issued pursuant to this Agreement or any Right Certificate or as to whether any Preferred Shares will, when issued, be validly authorized and issued, fully paid and nonassessable.

(f) The Company agrees that it will perform, execute, acknowledge and deliver or cause to be performed, executed, acknowledged and delivered all such further and other acts, instruments and assurances as may reasonably be required by the Rights Agent for the carrying out or performing by the Rights Agent of the provisions of this Agreement.

(g) The Rights Agent is hereby authorized and directed to accept instructions with respect to the performance of its duties hereunder from any one of the Chairman of the Board, the Chief Executive Officer, the President, the Chief Financial Officer, any Vice President, the Secretary or the Treasurer of the Company, and to apply to such officers for advice or instructions in connection with its duties, and it shall not be liable for any action taken or suffered by it in good faith in accordance with instructions of any such officer or for any delay in acting while waiting for those instructions. Any application by the Rights Agent for written instructions from the Company may, at the option of the Rights Agent, set forth in writing any action proposed to be taken or omitted by the Rights Agent with respect to its duties or obligations under this Agreement and the date on and/or after which such action shall be taken or omitted and the Rights Agent shall not be liable for any action taken or omitted in accordance with a proposal included in any such application on or after the date specified therein (which date shall not be less than three Business Days after the date indicated in such application unless any such officer shall have consented in writing to an earlier date) unless, prior to taking or omitting any such action, the Rights Agent has received written instructions in response to such application specifying the action to be taken or omitted.

(h) The Rights Agent and any stockholder, director, officer or employee of the Rights Agent may buy, sell or deal in any of the Rights or other securities of the Company or become pecuniarily interested in any transaction in which the Company may be interested, or contract with or lend money to the Company or otherwise act as fully and freely as though it were not Rights Agent under this Agreement. Nothing herein shall preclude the Rights Agent from acting in any other capacity for the Company or for any other legal entity.

(i) The Rights Agent may execute and exercise any of the rights or powers hereby vested in it or perform any duty hereunder either itself or by or through its attorneys or agents, and the Rights Agent shall not be answerable or accountable for any act, default, neglect or misconduct of any such attorneys or agents or for any loss to the Company resulting from any such act, default, neglect or misconduct, provided reasonable care was exercised in the selection and continued employment thereof.

(j) No provision of this Agreement shall require the Rights Agent to expend or risk its own funds or otherwise incur any financial liability in the performance of any of its duties hereunder or in the exercise of its rights if there shall be reasonable grounds for believing that repayment of such funds or adequate indemnification against such risk or liability is not reasonably assured to it.

(k) If, with respect to any Right Certificate surrendered to the Rights Agent for exercise or transfer, the certificate attached to the form of assignment or form of election to purchase, as the case may be, has not been executed, the Rights Agent shall not take any further action with respect to such requested exercise of transfer without first consulting with the Company.

SECTION 21. CHANGE OF RIGHTS AGENT. The Rights Agent or any successor Rights Agent may resign and be discharged from its duties under this Agreement upon 30 days' notice in writing mailed to the Company and to each transfer agent for the Common Shares or Preferred Shares by registered or certified mail, and to the holders of the Right Certificates by first-class mail. The Company may remove the Rights Agent or any successor Rights Agent upon 30 days' notice in writing, mailed to the Rights Agent or successor Rights Agent, as the case may be, and to each transfer agent for the Common Shares or Preferred Shares by registered or certified mail, and to the holders of the Right Certificates by first-class mail. If the Rights Agent shall resign or be removed or shall otherwise become incapable of acting, the Company shall appoint a successor to the Rights Agent. If the Company shall fail to make such appointment within a period of 30 days after giving notice of such removal or after it has been notified in writing of such resignation or incapacity by the resigning or incapacitated Rights Agent or by the holder of a Right Certificate (who shall, with such notice, submit his Right Certificate for inspection by the Company), then the registered holder of any Right Certificate may apply to any court of competent jurisdiction for the appointment of a new Rights Agent. Any successor Rights Agent, whether appointed by the Company or by such a court, shall be either (a) a corporation, business trust or limited liability company organized and doing business under the laws of the United States or of any other state of the United States which is authorized under such laws to exercise corporate trust or stock transfer powers and is subject to supervision or examination by federal or state authority and which has at the time of its appointment as Rights Agent a combined capital and surplus of at least \$50 million or (b) a direct or indirect wholly owned Subsidiary of such an entity or its wholly-owning parent. After appointment, the successor Rights Agent shall be vested with the same powers, rights, duties and responsibilities as if it had been originally named as Rights Agent without further act or deed; but the predecessor Rights Agent shall deliver and transfer to the successor Rights Agent any property at the time held by it hereunder, and execute and deliver any further assurance, conveyance, act or deed necessary for the purpose. Not later than the effective date of any such appointment the Company shall file notice thereof in writing with the predecessor Rights Agent and each transfer agent for the Common Shares or Preferred

Shares, and mail a notice thereof in writing to the registered holders of the Right Certificates. Failure to give any notice provided for in this Section 21, HOWEVER, or any defect therein, shall not affect the legality or validity of the resignation or removal of the Rights Agent or the appointment of the successor Rights Agent, as the case may be.

SECTION 22. ISSUANCE OF NEW RIGHT CERTIFICATES. Notwithstanding any of the provisions of this Agreement or of the Rights to the contrary, the Company may, at its option, issue new Right Certificates evidencing Rights in such form as may be approved by its Board of Directors to reflect any adjustment or change in the Purchase Price and the number or kind or class of shares or other securities or property purchasable under the Right Certificates made in accordance with the provisions of this Agreement. In addition, in connection with the issuance or sale of Common Shares following the Distribution Date and prior to the earlier of the Redemption Date and the Final Expiration Date, the Company (a) shall with respect to Common Shares so issued or sold pursuant to the exercise of stock options or under any employee plan or arrangement in existence prior to the Distribution Date, or upon the exercise, conversion or exchange of securities, notes or debentures issued by the Company and in existence prior to the Distribution Date, and (b) may, in any other case, if deemed necessary or appropriate by the Board of Directors, issue Right Certificates representing the appropriate number of Rights in connection with such issuance or sale; PROVIDED, HOWEVER, that (i) the Company shall not be obligated to issue any such Right Certificates if, and to the extent that, the Company shall be advised by counsel that such issuance would create a significant risk of material adverse tax consequences to the Company or the Person to whom such Right Certificate would be issued, and (ii) no Right Certificate shall be issued if, and to the extent that, appropriate adjustment shall otherwise have been made in lieu of the issuance thereof.

SECTION 23. REDEMPTION.

(a) The Rights may be redeemed by action of the Board of Directors pursuant to Section 23(b) hereof and shall not be redeemed in any other manner.

(b)

(i) The Board of Directors may, at its option, at any time prior to the earlier of (A) such time as any Person becomes an Acquiring Person or (B) the Final Expiration Date, redeem all but not less than all of the then outstanding Rights at a redemption price of \$0.001 per Right, appropriately adjusted to reflect any stock split, stock dividend or similar transaction occurring after the date hereof (such redemption price being hereinafter referred to as the "Redemption Price"), and the Company may, at its option, pay the Redemption Price in Common Shares (based on the "current per-share market price," as such term is defined in Section 11(d) hereof, of the Common Shares at the time of redemption), cash or any other form of consideration deemed appropriate by the Board of Directors. The redemption of the Rights by the Board of Directors may be made effective at such time, on such basis and subject to such conditions as the Board of Directors in its sole discretion may establish. Notwithstanding anything contained in this Agreement to the contrary, the Rights shall not be exercisable pursuant to Section 11(a)(ii) hereof prior to the expiration or termination of the Company's right of redemption under this Section 23(b)(i).

(ii) In addition, the Board of Directors may, at its option, at any time after the time a Person becomes an Acquiring Person and after the expiration of any period during which the holder of Rights may exercise the rights under Section 11(a)(ii) hereof but prior to any event described in clause (x), (y) or (z) of the first sentence of Section 13 hereof, redeem all but not less than all of the then outstanding Rights at the Redemption Price (x) in connection with any merger, consolidation or sale or other transfer (in one transaction or in a series of related transactions) of assets or earning power aggregating 50% or more of the assets or earning power of the Company and its subsidiaries (taken as a whole) in which all holders of Common Shares are treated alike and not involving (other than as a holder of Common Shares being treated like all other such holders) an Interested Stockholder or a Transaction Person or (y)(A) if and for so long as the Acquiring Person is not thereafter the Beneficial Owner of 20% or more of the then outstanding Common Shares, and (B) at the time of redemption no other Persons are Acquiring Persons.

(c) Immediately upon the action of the Board of Directors ordering the redemption of the Rights pursuant to Section 23(b) hereof, and without any further action and without any notice, the right to exercise the Rights will terminate and the only right thereafter of the holders of Rights shall be to receive the Redemption Price. The Company shall promptly give public notice of any such redemption; PROVIDED, HOWEVER, that the failure to give, or any defect in, any such notice shall not affect the validity of such redemption. Within 10 days after such action of the Board of Directors ordering the redemption of the Rights pursuant to Section 23(b) hereof, the Company shall mail a notice of redemption to all the holders of the then outstanding Rights at their last addresses as they appear upon the registry books of the Rights Agent or, prior to the Distribution Date, on the registry books of the transfer agent for the Common Shares, PROVIDED, HOWEVER, that failure to give, or any defect in, any such notice shall not affect the validity of such redemption. Any notice which is mailed in the manner herein provided shall be deemed given, whether or not the holder receives the notice. Each such notice of redemption will state the method by which the payment of the Redemption Price will be made. Neither the Company nor any of its Affiliates or Associates may redeem, acquire or purchase for value any Rights at any time in any manner other than that specifically set forth in this Section 23 or in Section 24 hereof, and other than in connection with the purchase of Common Shares prior to the Distribution Date.

(d) The Company may, at its option, discharge all of its obligations with respect to any redemption of the Rights by (i) issuing a press release announcing the manner of redemption of the Rights and (ii) mailing payment of the Redemption Price to the registered holders of the Rights at their last addresses as they appear on the registry books of the Rights Agent or, prior to the Distribution Date, on the registry books of the transfer agent for the Common Shares, and upon such action, all outstanding Right Certificates shall be null and void without any further action by the Company.

SECTION 24. EXCHANGE.

(a) The Board of Directors may, at its option, at any time after any Person becomes an Acquiring Person, exchange all or part of the then outstanding and exercisable Rights (which shall not include Rights that have become void pursuant to the provisions of Section 11(a)(ii) hereof) for Common Shares at an exchange ratio of one Common Share per Right, appropriately

adjusted to reflect any stock split, stock dividend or similar transaction occurring after the date hereof (such exchange ratio being hereinafter referred to as the "Exchange Ratio"). Notwithstanding the foregoing, the Board of Directors shall not be empowered to effect such exchange at any time after any Person (other than the Company, any Subsidiary of the Company, any employee benefit plan of the Company or any such Subsidiary, or any entity holding Common Shares for or pursuant to the terms of any such plan), together with all Affiliates and Associates of such Person, becomes the Beneficial Owner of 50% or more of the Common Shares then outstanding.

(b) Immediately upon the action of the Board of Directors ordering the exchange of any Rights pursuant to Section 24(a) hereof and without any further action and without any notice, the right to exercise such Rights shall terminate and the only right thereafter of a holder of such Rights shall be to receive that number of Common Shares equal to the number of such Rights held by such holder multiplied by the Exchange Ratio. The Company shall promptly give public notice of any such exchange; PROVIDED, HOWEVER, that the failure to give, or any defect in, such notice shall not affect the validity of such exchange. The Company promptly shall mail a notice of any such exchange to all of the holders of such Rights at their last addresses as they appear upon the registry books of the Rights Agent; PROVIDED, HOWEVER, that the failure to give, or any defect in, such notice shall not affect the validity of such exchange. Any notice which is mailed in the manner herein provided shall be deemed given, whether or not the holder receives the notice. Each such notice of exchange will state the method by which the exchange of the Common Shares for Rights will be effected and, in the event of any partial exchange, the number of Rights which will be exchanged. Any partial exchange shall be effected pro rata based on the number of Rights (other than Rights which have become void pursuant to the provisions of Section 11(a)(ii) hereof) held by each holder of Rights.

(c) In lieu of issuing Common Shares in accordance with Section 24(a) hereof, the Company may, if a majority of the Board of Directors then in office determines that such action is necessary or appropriate and not contrary to the interests of the holders of Rights, elect to (and, in the event that there are not sufficient treasury shares and authorized but unissued Common Shares to permit any exchange of the Rights in accordance with Section 24(a) hereof, the Company shall) take all such action as may be necessary to authorize, issue or pay, upon the exchange of the Rights, cash (including by way of a reduction of the Purchase Price), property, Common Shares, other securities or any combination thereof having an aggregate value equal to the value of the Common Shares which otherwise would have been issuable pursuant to Section 24(a) hereof, which aggregate value shall be determined by a nationally recognized investment banking firm selected by a majority of the Board of Directors then in office. For purposes of the preceding sentence, the value of the Common Shares shall be determined pursuant to Section 11(d) hereof. Any election pursuant to this Section 24(c) by the Board of Directors must be made by resolution within 60 days following the date on which the event described in Section 11(a)(ii) hereof shall have occurred. Following the occurrence of the event described in Section 11(a)(ii) hereof, a majority of the Board of Directors then in office may suspend the exercisability of the Rights for a period of up to 60 days following the date on which the event described in Section 11(a)(ii) hereof shall have occurred to the extent that such directors have not determined whether to exercise their right of election under this Section 24(c). In the event of any such suspension, the Company shall issue a public announcement stating that the exercisability of the Rights has been temporarily suspended.

(d) The Company shall not be required to issue fractions of Common Shares or to distribute certificates which evidence fractional Common Shares. In lieu of such fractional Common Shares, the Company shall pay to the registered holders of the Right Certificates with regard to which such fractional Common Shares would otherwise be issuable an amount in cash equal to the same fraction of the current market value of a whole Common Share. For the purposes of this Section 24(d), the current market value of a whole Common Share shall be the closing price of a Common Share (as determined pursuant to the second sentence of Section 11(d)(i) hereof) for the Trading Day immediately after the date of the first public announcement by the Company that an exchange is to be effected pursuant to this Section 24.

(e) The Company shall not be required to issue fractions of Preferred Shares (other than fractions which are integral multiples of one one-hundredth of a Preferred Share) upon exchange of the Rights or to distribute certificates which evidence fractional Preferred Shares (other than fractions which are integral multiples of one one-hundredth of a Preferred Share). Fractions of Preferred Shares in integral multiples of one one-hundredth of a Preferred Share may, at the election of the Company, be evidenced by depositary receipts; PROVIDED, HOWEVER, that holders of such depositary receipts shall have all of the designations and the powers, preferences and rights, and the qualifications, limitations and restrictions to which they are entitled as beneficial owners of the Preferred Shares represented by such depositary receipts. In lieu of fractional Preferred Shares that are not integral multiples of one one-hundredth of a Preferred Share, the Company shall pay to the registered holders of Right Certificates at the time such Rights are exercised as herein provided an amount in cash equal to the same fraction of the current market value of one Preferred Share. For the purposes of this Section 24(e), the current market value of a Preferred Share shall be one hundred (100) times the closing price of a Common Share (as determined pursuant to the second sentence of Section 11(d)(i) hereof) for the Trading Day immediately after the date of the first public announcement by the Company that an exchange is to be effected pursuant to this Section 24.

SECTION 25. NOTICE OF CERTAIN EVENTS.

(a) In case the Company shall propose (i) to pay any dividend payable in stock of any class to the holders of its Preferred Shares or to make any other distribution to the holders of its Preferred Shares (other than a regular quarterly cash dividend), (ii) to offer to the holders of its Preferred Shares rights or warrants to subscribe for or to purchase any additional Preferred Shares or shares of stock of any class or any other securities, rights or options, (iii) to effect any reclassification of its Preferred Shares (other than a reclassification involving only the subdivision of outstanding Preferred Shares), (iv) to effect any consolidation or merger into or with, or to effect any sale or other transfer (or to permit one or more of its Subsidiaries to effect any sale or other transfer), in one or more transactions, of 50% or more of the assets or earning power of the Company and its Subsidiaries (taken as a whole), to any other Person, (v) to effect the liquidation, dissolution or winding up of the Company, or (vi) to declare or pay any dividend on the Common Shares payable in Common Shares or to effect a subdivision, combination or consolidation of the Common Shares (by reclassification or otherwise than by payment of dividends in Common Shares), then, in each such case, the Company shall give to each holder of a Right Certificate, in accordance with Section 26 hereof, a notice of such proposed action, which shall specify the record date for the purpose of such stock dividend, or distribution of rights or warrants, or the date on which such reclassification, consolidation, merger, sale,

transfer, liquidation, dissolution, or winding up is to take place and the date of participation therein by the holders of the Common Shares and/or the Preferred Shares, if any such date is to be fixed, and such notice shall be so given in the case of any action covered by clause (i) or (ii) above at least 10 days prior to the record date for determining holders of the Preferred Shares for purposes of such action, and in the case of any such other action, at least 10 days prior to the date of the taking of such proposed action or the date of participation therein by the holders of the Common Shares and/or the Preferred Shares, whichever shall be the earlier.

(b) In case the event set forth in Section 11(a)(ii) hereof shall occur, then the Company shall as soon as practicable thereafter give to each holder of a Right Certificate, in accordance with Section 26 hereof, a notice of the occurrence of such event, which notice shall describe the event and the consequences of the event to holders of Rights under Section 11(a)(ii) hereof.

SECTION 26. NOTICES. Notices or demands authorized by this Agreement to be given or made by the Rights Agent or by the holder of any Right Certificate to or on the Company shall be sufficiently given or made if sent by first-class mail, postage prepaid, addressed (until another address is filed in writing with the Rights Agent) as follows:

Isis Pharmaceuticals, Inc.
2292 Faraday Avenue
Carlsbad, CA 92008
Attn: Corporate Secretary

Subject to the provisions of Section 21 hereof, any notice or demand authorized by this Agreement to be given or made by the Company or by the holder of any Right Certificate to or on the Rights Agent shall be sufficiently given or made if sent by first-class mail, postage prepaid, addressed (until another address is filed in writing with the Company) as follows:

American Stock Transfer & Trust Company
59 Maiden Lane
New York, NY 10038

Notices or demands authorized by this Agreement to be given or made by the Company or the Rights Agent to the holder of any Right Certificate shall be sufficiently given or made if sent by first-class mail, postage prepaid, addressed to such holder at the address of such holder as shown on the registry books of the Company.

SECTION 27. SUPPLEMENTS AND AMENDMENTS. Prior to the Distribution Date, the Company and the Rights Agent shall, if the Company so directs, supplement or amend any provision of this Agreement without the approval of any holders of the Rights. From and after the Distribution Date, the Company and the Rights Agent shall, if the Company so directs, from time to time supplement or amend any provision of this Agreement without the approval of any holders of Right Certificates in order to (i) cure any ambiguity, (ii) correct or supplement any provision contained herein which may be defective or inconsistent with any other provisions herein, or (iii) change any other provisions with respect to the Rights which the Company may deem necessary or desirable; PROVIDED, HOWEVER, that no such supplement or amendment shall be made which

would adversely affect the interests of the holders of Rights (other than the interests of an Acquiring Person or its Affiliates or Associates). Any supplement or amendment adopted during any period after any Person has become an Acquiring Person but prior to the Distribution Date shall become null and void unless such supplement or amendment could have been adopted by the Company from and after the Distribution Date. Any such supplement or amendment shall be evidenced by a writing signed by the Company and the Rights Agent. Upon delivery of a certificate from an appropriate officer of the Company which states that the proposed supplement or amendment is in compliance with the terms of this Section 27, the Rights Agent shall execute such supplement or amendment unless the Rights Agent shall have determined in good faith that such supplement or amendment would adversely affect its interest under this Agreement. Prior to the Distribution Date, the interests of the holders of Rights shall be deemed coincident with the interests of the holders of Common Shares.

SECTION 28. DETERMINATION AND ACTIONS BY THE BOARD OF DIRECTORS, ETC. For all purposes of this Agreement, any calculation of the number of Common Shares outstanding at any particular time, including for purposes of determining the particular percentage of such outstanding Common Shares or any other securities of which any Person is the Beneficial Owner, shall be made in accordance with the last sentence of Rule 13d-3(d)(1)(i) of the General Rules and Regulations under the Exchange Act as in effect on the date of this Agreement. The Board of Directors shall have the exclusive power and authority to administer this Agreement and to exercise all rights and powers specifically granted to the Board, or the Company, or as may be necessary or advisable in the administration of this Agreement, including without limitation, the right and power to (i) interpret the provisions of this Agreement, and (ii) make all determinations deemed necessary or advisable for the administration of this Agreement (including a determination to redeem or not redeem the Rights or to amend this Agreement). All such actions, calculations, interpretations and determinations (including, for purposes of clause (y) below, all omissions with respect to the foregoing) which are done or made by the Board in good faith, shall (x) be final, conclusive and binding on the Rights Agent and the holders of the Rights, and (y) not subject the Board to any liability to the holders of the Rights.

SECTION 29. SUCCESSORS. All the covenants and provisions of this Agreement by or for the benefit of the Company or the Rights Agent shall bind and inure to the benefit of their respective successors and assigns hereunder.

SECTION 30. BENEFITS OF THIS AGREEMENT. Nothing in this Agreement shall be construed to give to any person or corporation other than the Company, the Rights Agent and the registered holders of the Right Certificates (and, prior to the Distribution Date, the Common Shares) any legal or equitable right, remedy or claim under this Agreement; but this Agreement shall be for the sole and exclusive benefit of the Company, the Rights Agent and the registered holders of the Right Certificates (and, prior to the Distribution Date, the Common Shares).

SECTION 31. SEVERABILITY If any term, provision, covenant or restriction of this Agreement is held by a court of competent jurisdiction or other authority to be invalid, void or unenforceable, the remainder of the terms, provisions, covenants and restrictions of this Agreement shall remain in full force and effect and shall in no way be affected, impaired or invalidated.

SECTION 32. GOVERNING LAW. This Agreement and each Right Certificate issued hereunder shall be deemed to be a contract made under the laws of the State of Delaware and for all purposes shall be governed by and construed in accordance with the laws of such State applicable to contracts to be made and performed entirely within such State.

SECTION 33. COUNTERPARTS. This Agreement may be executed in any number of counterparts and each of such counterparts shall for all purposes be deemed to be an original, and all such counterparts shall together constitute but one and the same instrument.

SECTION 34. DESCRIPTIVE HEADINGS. Descriptive headings of the several Sections of this Agreement are inserted for convenience only and shall not control or affect the meaning or construction of any of the provisions hereof.

IN WITNESS WHEREOF, parties whereto have caused this Agreement to be duly executed, all as of the day and year first above written.

ATTEST: ISIS PHARMACEUTICALS, INC.

By: /s/ B. LYNNE PARSHALL

By: /s/ STANLEY T. CROOKE

Print Name: B. LYNNE PARSHALL

Print Name: STANLEY T. CROOKE

Secretary

Title: Chairman of the Board and Chief
Executive Officer

ATTEST: AMERICAN STOCK TRANSFER & TRUST COMPANY

By: /s/ GERALDINE ZARBO

By: /s/ CAROLYN B. O'NEILL

Print Name: GERALDINE ZARBO

Print Name: CAROLYN B. O'NEILL

Title: Vice President

Title: Vice President

FORM OF
CERTIFICATE OF DESIGNATION

OF

SERIES C JUNIOR PARTICIPATING PREFERRED STOCK

(EXHIBIT A TO RIGHTS AGREEMENT)

(PURSUANT TO SECTION 151 OF THE
DELAWARE GENERAL CORPORATION LAW)

ISIS PHARMACEUTICALS, INC., a corporation organized and existing under the General Corporation Law of the State of Delaware (hereinafter called the "Company"), hereby certifies that the following resolution was adopted by the Board of Directors of the Corporation as required by Section 151 of the General Corporation Law at a meeting duly called and held on December 8, 2000:

RESOLVED, that pursuant to the authority granted to and vested in the Board of Directors of the Company in accordance with the provisions of its Restated Certificate of Incorporation, the Board of Directors hereby creates a series of Preferred Stock, par value \$.001 per share, of the Company and hereby states the designation and number of shares, and fixes the relative designations and the powers, preferences and rights, and the qualifications, limitations and restrictions thereof (in addition to the provisions set forth in the Restated Certificate of Incorporation of the Company, which are applicable to the Preferred Stock of all classes and series), as follows:

Series C Junior Participating Preferred Stock:

SECTION 1. DESIGNATION AND AMOUNT. One million (1,000,000) shares of Preferred Stock, \$.001 par value, are designated "Series C Junior Participating Preferred Stock" with the designations and the powers, preferences and rights, and the qualifications, limitations and restrictions specified herein (the "Junior Preferred Stock"). Such number of shares may be increased or decreased by resolution of the Board of Directors; PROVIDED, that no decrease shall reduce the number of shares of Junior Preferred Stock to a number less than the number of shares then outstanding plus the number of shares reserved for issuance upon the exercise of outstanding options, rights or warrants or upon the conversion of any outstanding securities issued by the Company convertible into Junior Preferred Stock.

SECTION 2. DIVIDENDS AND DISTRIBUTIONS.

(A) Subject to the rights of the holders of any shares of any series of Preferred Stock (or any similar stock) ranking prior and superior to the Junior Preferred Stock with respect

to dividends, the holders of shares of Junior Preferred Stock, in preference to the holders of Common Stock, par value \$.001 per share (the "Common Stock"), of the Company, and of any other junior stock, shall be entitled to receive, when, as and if declared by the Board of Directors out of funds legally available for the purpose, quarterly dividends payable in cash on the first day of April, July, October and January in each year (each such date being referred to herein as a "Quarterly Dividend Payment Date"), commencing on the first Quarterly Dividend Payment Date after the first issuance of a share or fraction of a share of Junior Preferred Stock, in an amount per share (rounded to the nearest cent) equal to the greater of (a) \$1.00 or (b) subject to the provision for adjustment hereinafter set forth, 100 times the aggregate per share amount of all cash dividends, and 100 times the aggregate per share amount (payable in kind) of all non-cash dividends or other distributions, other than a dividend payable in shares of Common Stock or a subdivision of the outstanding shares of Common Stock (by reclassification or otherwise), declared on the Common Stock since the immediately preceding Quarterly Dividend Payment Date or, with respect to the first Quarterly Dividend Payment Date, since the first issuance of any share or fraction of a share of Junior Preferred Stock. In the event the Company shall at any time declare or pay any dividend on the Common Stock payable in shares of Common Stock, or effect a subdivision or combination or consolidation of the outstanding shares of Common Stock (by reclassification or otherwise than by payment of a dividend in shares of Common Stock) into a greater or lesser number of shares of Common Stock, then in each such case the amount to which holders of shares of Junior Preferred Stock were entitled immediately prior to such event under clause (b) of the preceding sentence shall be adjusted by multiplying such amount by a fraction, the numerator of which is the number of shares of Common Stock outstanding immediately after such event and the denominator of which is the number of shares of Common Stock that were outstanding immediately prior to such event.

(B) The Company shall declare a dividend or distribution on the Junior Preferred Stock as provided in paragraph (A) of this Section immediately after it declares a dividend or distribution on the Common Stock (other than a dividend payable in shares of Common Stock); PROVIDED, that in the event no dividend or distribution shall have been declared on the Common Stock during the period between any Quarterly Dividend Payment Date and the next subsequent Quarterly Dividend Payment Date, a dividend of \$1.00 per share on the Junior Preferred Stock shall nevertheless be payable on such subsequent Quarterly Dividend Payment Date.

(C) Dividends shall begin to accrue and be cumulative on outstanding shares of Junior Preferred Stock from the Quarterly Dividend Payment Date next preceding the date of issue of such shares, unless the date of issue of such shares is prior to the record date for the first Quarterly Dividend Payment Date, in which case dividends on such shares shall begin to accrue from the date of issue of such shares, or unless the date of issue is a Quarterly Dividend Payment Date or is a date after the record date for the determination of holders of shares of Junior Preferred Stock entitled to receive a quarterly dividend and before such Quarterly Dividend Payment Date, in either of which events such dividends shall begin to accrue and be cumulative from such Quarterly Dividend Payment Date. Accrued but unpaid dividends shall not bear interest. Dividends paid on the shares of Junior Preferred Stock in an amount less than the total amount of such dividends at the time accrued and payable on such shares shall be allocated pro rata on a share-by-share basis among all such shares at the time outstanding. The Board of Directors may fix a record date for the determination of holders of shares of Junior Preferred

Stock entitled to receive payment of a dividend or distribution declared thereon, which record date shall be not more than 60 days prior to the date fixed for the payment thereof.

SECTION 3. VOTING RIGHTS. The holders of shares of Junior Preferred Stock shall have the following voting rights:

(A) Subject to the provision for adjustment hereinafter set forth, each share of Junior Preferred Stock shall entitle the holder thereof to 100 votes on all matters submitted to a vote of the stockholders of the Company. In the event the Company shall at any time declare or pay any dividend on the Common Stock payable in shares of Common Stock, or effect a subdivision or combination or consolidation of the outstanding shares of Common Stock (by reclassification or otherwise than by payment of a dividend in shares of Common Stock) into a greater or lesser number of shares of Common Stock, then in each such case the number of votes per share to which holders of shares of Junior Preferred Stock were entitled immediately prior to such event shall be adjusted by multiplying such number by a fraction, the numerator of which is the number of shares of Common Stock outstanding immediately after such event and the denominator of which is the number of shares of Common Stock that were outstanding immediately prior to such event.

(B) Except as otherwise provided herein, in any other Certificate of Designation creating a series of Preferred Stock or any similar stock, or by law, the holders of shares of Junior Preferred Stock and the holders of shares of Common Stock and any other capital stock of the Company having general voting rights shall vote together as one class on all matters submitted to a vote of stockholders of the Company.

(C) Except as set forth herein, or as otherwise provided by law, holders of Junior Preferred Stock shall have no special voting rights and their consent shall not be required (except to the extent they are entitled to vote with holders of Common Stock as set forth herein) for taking any corporate action.

SECTION 4. CERTAIN RESTRICTIONS.

(A) Whenever quarterly dividends or other dividends or distributions payable on the Junior Preferred Stock as provided in Section 2 are in arrears, thereafter and until all accrued and unpaid dividends and distributions, whether or not declared, on shares of Junior Preferred Stock outstanding shall have been paid in full, the Company shall not:

(i) declare or pay dividends, or make any other distributions, on any shares of stock ranking junior (either as to dividends or upon liquidation, dissolution or winding up) to the Junior Preferred Stock;

(ii) declare or pay dividends, or make any other distributions, on any shares of stock ranking on a parity (either as to dividends or upon liquidation, dissolution or winding up) with the Junior Preferred Stock, except dividends paid ratably on the Junior Preferred Stock and all such parity stock on which dividends are payable or in arrears in proportion to the total amounts to which the holders of all such shares are then entitled;

(iii) redeem or purchase or otherwise acquire for consideration shares of any stock ranking junior (either as to dividends or upon liquidation, dissolution or winding up) to the Junior Preferred Stock, provided that the Company may at any time redeem, purchase or otherwise acquire shares of any such junior stock in exchange for shares of any stock of the Company ranking junior (either as to dividends or upon dissolution, liquidation or winding up) to the Junior Preferred Stock; or

(iv) redeem or purchase or otherwise acquire for consideration any shares of Junior Preferred Stock, or any shares of stock ranking on a parity (either as to dividends or upon liquidation, dissolution or winding up) with the Junior Preferred Stock, except in accordance with a purchase offer made in writing or by publication (as determined by the Board of Directors) to all holders of such shares upon such terms as the Board of Directors, after consideration of the respective annual dividend rates and other relative rights and preferences of the respective series and classes, shall determine in good faith will result in fair and equitable treatment among the respective series or classes.

(B) The Company shall not permit any subsidiary of the Company to purchase or otherwise acquire for consideration any shares of stock of the Company unless the Company could, under paragraph (A) of this Section 4, purchase or otherwise acquire such shares at such time and in such manner.

SECTION 5. REACQUIRED SHARES. Any shares of Junior Preferred Stock purchased or otherwise acquired by the Company in any manner whatsoever shall be retired and cancelled promptly after the acquisition thereof. All such shares shall upon their cancellation become authorized but unissued shares of Preferred Stock and may be reissued as part of a new series of Preferred Stock subject to the conditions and restrictions on issuance set forth herein, in the Restated Certificate of Incorporation, or in any other Certificate of Designation creating a series of Preferred Stock or any similar stock or as otherwise required by law.

SECTION 6. LIQUIDATION, DISSOLUTION OR WINDING UP. Upon any liquidation, dissolution or winding up of the Company, no distribution shall be made (1) to the holders of shares of stock ranking junior (either as to dividends or upon liquidation, dissolution or winding up) to the Junior Preferred Stock unless, prior thereto, the holders of shares of Junior Preferred Stock shall have received \$100 per share, plus an amount equal to accrued and unpaid dividends and distributions thereon, whether or not declared, to the date of such payment, or if greater, the holders of shares of Junior Preferred Stock shall be entitled to receive an aggregate amount per share, subject to the provision for adjustment hereinafter set forth, equal to 100 times the aggregate amount to be distributed per share to holders of shares of Common Stock; or (2) to the holders of shares of stock ranking on a parity (either as to dividends or upon liquidation, dissolution or winding up) with the Junior Preferred Stock, except distributions made ratably on the Junior Preferred Stock and all such parity stock in proportion to the total amounts to which the holders of all such shares are entitled upon such liquidation, dissolution or winding up. In the event the Company shall at any time declare or pay any dividend on the Common Stock payable in shares of Common Stock, or effect a subdivision or combination or consolidation of the outstanding shares of Common Stock (by reclassification or otherwise than by payment of a dividend in shares of Common Stock) into a greater or lesser number of shares of Common Stock, then in each such case the aggregate amount to which holders of shares of Junior

Preferred Stock were entitled immediately prior to such event under the proviso in clause (1) of the preceding sentence shall be adjusted by multiplying such amount by a fraction the numerator of which is the number of shares of Common Stock outstanding immediately after such event and the denominator of which is the number of shares of Common Stock that were outstanding immediately prior to such event.

SECTION 7. CONSOLIDATION, MERGER, ETC. In case the Company shall enter into any consolidation, merger, combination or other transaction in which the shares of Common Stock are exchanged for or changed into other stock or securities, cash and/or any other property, then in any such case each share of Junior Preferred Stock shall at the same time be similarly exchanged or changed into an amount per share, subject to the provision for adjustment hereinafter set forth, equal to 100 times the aggregate amount of stock, securities, cash and/or any other property (payable in kind), as the case may be, into which or for which each share of Common Stock is changed or exchanged. In the event the Company shall at any time declare or pay any dividend on the Common Stock payable in shares of Common Stock, or effect a subdivision or combination or consolidation of the outstanding shares of Common Stock (by reclassification or otherwise than by payment of a dividend in shares of Common Stock) into a greater or lesser number of shares of Common Stock, then in each such case the amount set forth in the preceding sentence with respect to the exchange or change of shares of Junior Preferred Stock shall be adjusted by multiplying such amount by a fraction, the numerator of which is the number of shares of Common Stock outstanding immediately after such event and the denominator of which is the number of shares of Common Stock that were outstanding immediately prior to such event.

SECTION 8. NO REDEMPTION. The shares of Junior Preferred Stock shall not be redeemable.

SECTION 9. RANK. The Junior Preferred Stock shall rank, with respect to the payment of dividends and the distribution of assets, junior to all series of any other class of the Company's Preferred Stock.

SECTION 10. AMENDMENT. The Restated Certificate of Incorporation of the Company shall not be amended in any manner which would materially alter or change the powers, preferences or special rights of the Junior Preferred Stock so as to affect them adversely without the affirmative vote of the holders of at least two-thirds of the outstanding shares of Junior Preferred Stock, voting together as a single class.

IN WITNESS WHEREOF, the undersigned have executed this certificate as
of December __, 2000.

By: _____

Print Name: B. Lynne Parshall
Secretary

FORM OF RIGHT CERTIFICATE
(EXHIBIT B TO RIGHTS AGREEMENT)

CERTIFICATE NO. R-

_____ RIGHTS

NOT EXERCISABLE AFTER DECEMBER 7, 2010 OR EARLIER IF REDEMPTION OR EXCHANGE OCCURS. THE RIGHTS ARE SUBJECT TO REDEMPTION AT \$.001 PER RIGHT AND TO EXCHANGE ON THE TERMS SET FORTH IN THE RIGHTS AGREEMENT.

RIGHT CERTIFICATE
ISIS PHARMACEUTICALS, INC.

This certifies that _____ or registered assigns, is the registered owner of the number of Rights set forth above, each of which entitles the owner thereof, subject to the terms, provisions and conditions of the Rights Agreement, dated as of December 8, 2000 (the "Rights Agreement"), between Isis Pharmaceuticals, Inc., a Delaware corporation (the "Company"), and American Stock Transfer & Trust Company (the "Rights Agent"), to purchase from the Company at any time after the Distribution Date (as such term is defined in the Rights Agreement) and prior to 5:00 p.m., Pacific Time, on December 7, 2010 at the office of the Rights Agent designated for such purpose, or at the office of its successor as Rights Agent, one one-hundredth of a fully paid non-assessable share of Series C Junior Participating Preferred Stock, par value \$.001 per share (the "Preferred Shares"), of the Company, at a purchase price of \$85 per one one-hundredth of a Preferred Share (the "Purchase Price"), upon presentation and surrender of this Right Certificate with the Form of Election to Purchase duly executed. The number of Rights evidenced by this Right Certificate (and the number of one one-hundredths of a Preferred Share which may be purchased upon exercise hereof) set forth above, and the Purchase Price set forth above, are the number and Purchase Price as of December 8, 2000, based on the Preferred Shares as constituted at such date.

From and after the time any Person becomes an Acquiring Person (as such terms are defined in the Rights Agreement), if the Rights evidenced by this Right Certificate are beneficially owned by (i) an Acquiring Person or an Affiliate or Associate of any such Acquiring Person (as such terms are defined in the Rights Agreement), (ii) a transferee of any such Acquiring Person, Associate or Affiliate who becomes a transferee after the Acquiring Person becomes such, or (iii) under certain circumstances specified in the Rights Agreement, a transferee of any such Acquiring Person, Associate or Affiliate who becomes a transferee prior to or concurrently with the Acquiring Person becoming such, such Rights shall become null and void without any further action and no holder hereof shall have any right with respect to such Rights from and after the time any Person becomes an Acquiring Person.

As provided in the Rights Agreement, the Purchase Price and the number of one one-hundredths of a Preferred Share which may be purchased upon the exercise of the Rights

evidenced by this Right Certificate are subject to modification and adjustment upon the happening of certain events.

This Right Certificate is subject to all of the terms, provisions and conditions of the Rights Agreement, as amended from time to time, which terms, provisions and conditions are hereby incorporated herein by reference and made a part hereof and to which Rights Agreement reference is hereby made for a full description of the rights, limitations of rights, obligations, duties and immunities hereunder of the Rights Agent, the Company and the holders of the Right Certificates. Copies of the Rights Agreement are on file at the principal executive offices of the Company and the offices of the above-mentioned Rights Agent.

This Right Certificate, with or without other Right Certificates, upon surrender at the office of the Rights Agent designated for such purpose, may be exchanged for another Right Certificate or Right Certificates of like tenor and date evidencing Rights entitling the holder to purchase a like aggregate number of Preferred Shares as the Rights evidenced by the Right Certificate or Right Certificates surrendered shall have entitled such holder to purchase. If this Right Certificate shall be exercised in part, the holder shall be entitled to receive upon surrender hereof another Right Certificate or Right Certificates for the number of whole Rights not exercised.

Subject to the provisions of the Rights Agreement, the Rights evidenced by this Certificate (i) may be redeemed by the Company at a redemption price of \$.001 per Right or (ii) may be exchanged in whole or in part for shares of the Company's Common Stock, par value \$.001 per share, or, upon circumstances set forth in the Rights Agreement, cash, property or other securities of the Company, including fractions of a share of Preferred Stock.

No fractional Preferred Shares will be issued upon the exercise of any Right or Rights evidenced hereby (other than fractions which are integral multiples of one one-hundredth of a Preferred Share, which may, at the election of the Company, be evidenced by depositary receipts) but in lieu thereof a cash payment will be made, as provided in the Rights Agreement.

No holder of this Right Certificate shall be entitled to vote or receive dividends or be deemed for any purpose the holder of the Preferred Shares or of any other securities of the Company which may at any time be issuable on the exercise hereof, nor shall anything contained in the Rights Agreement or herein be construed to confer upon the holder hereof, as such, any of the rights of a stockholder of the Company or any right to vote for the election of directors or upon any matter submitted to stockholders at any meeting thereof, or to give or withhold consent to any corporate action, or to receive notice of meetings or other actions affecting stockholders (except as provided in the Rights Agreement), or to receive dividends or subscription rights, or otherwise, until the Right or Rights evidenced by this Right Certificate shall have been exercised as provided in the Rights Agreement.

This Right Certificate shall not be valid or obligatory for any purpose until it shall have been countersigned by the Rights Agent.

WITNESS the facsimile signature of the proper officers of the Company and its corporate seal. Dated as of _____.

ATTEST:

ISIS PHARMACEUTICALS, INC.

By: _____
Print Name: _____
Secretary

By: _____
Print Name: _____
Title: _____

COUNTERSIGNED:

as Rights Agent

By: _____
Print Name: _____
Title: _____

FORM OF REVERSE SIDE OF RIGHT CERTIFICATE

FORM OF ASSIGNMENT

(TO BE EXECUTED BY THE REGISTERED HOLDER IF SUCH
HOLDER DESIRES TO TRANSFER THE RIGHT CERTIFICATE.)

FOR VALUE RECEIVED _____ hereby sells,
assigns and transfers unto

(Please print name and address of transferee)

_____ this Right
Certificate, together with all right, title and interest therein, and does
hereby irrevocably constitute and appoint _____ Attorney, to
transfer the within Right Certificate on the books of the within-named Company,
with full power of substitution.

Dated: _____

Signature

SIGNATURE GUARANTEED:

Signatures must be guaranteed by an "eligible guarantor institution" as defined in Rule 17Ad-15 promulgated under the Securities Exchange Act of 1934, as amended.

The undersigned hereby certifies that (1) the Rights evidenced by this Right Certificate are not being sold, assigned or transferred by or on behalf of a Person who is or was an Acquiring Person, an Interested Stockholder or an Affiliate or Associate thereof (as such terms are defined in the Rights Agreement); and (2) after due inquiry and to the best of the knowledge of the undersigned, the undersigned did not acquire the Rights evidenced by this Right Certificate from any Person who is or was an Acquiring Person, an Interested Stockholder, or an Affiliate or Associate thereof.

Signature

FORM OF REVERSE SIDE OF RIGHT CERTIFICATE

FORM OF ELECTION TO PURCHASE

(TO BE EXECUTED IF HOLDER DESIRES TO EXERCISE RIGHTS REPRESENTED BY THE RIGHT CERTIFICATE.)

To American Stock Transfer & Trust Company:

The undersigned hereby irrevocably elects to exercise _____ Rights represented by this Right Certificate to purchase the Preferred Shares issuable upon the exercise of such Rights and requests that certificates for such Preferred Shares be issued in the name of:

Please insert social security or other identifying number: _____

(Please print name and address)

If such number of Rights shall not be all the Rights evidenced by this Right Certificate, a new Right Certificate for the balance remaining of such Rights shall be registered in the name of and delivered to:

Please insert social security or other identifying number: _____

(Please print name and address)

Dated: _____

Signature

SIGNATURE GUARANTEED:

Signatures must be guaranteed by an "eligible guarantor institution" as defined in Rule 17Ad-15 promulgated under the Securities Exchange Act of 1934, as amended.

The undersigned hereby certifies that (1) the Rights evidenced by this Right Certificate are not beneficially owned by nor are they being exercised on behalf of an Acquiring Person, an Interested Stockholder or an Affiliate or Associate thereof (as such terms are defined in the Rights Agreement); and (2) after due inquiry and to the best of the knowledge of the undersigned, the undersigned did not acquire the Rights evidenced by this Right Certificate from any Person who is or was an Acquiring Person, an Interested Stockholder, or an Affiliate or Associate thereof.

Signature

NOTICE

The signature in the Form of Assignment or Form of Election to Purchase, as the case may be, must conform to the name as written upon the face of this Right Certificate in every particular, without alteration or enlargement or any change whatsoever.

In the event the certification set forth above in the Form of Assignment or the Form of Election to Purchase, as the case may be, is not completed, the Company and the Rights Agent will deem the beneficial owner of the Rights evidenced by this Right Certificate to be an Acquiring Person or an Affiliate or Associate thereof (as defined in the Rights Agreement) and such Assignment or Election to Purchase will not be honored.

ISIS PHARMACEUTICALS, INC.

SUMMARY OF RIGHTS TO PURCHASE
PREFERRED SHARES

(EXHIBIT C TO RIGHTS PLAN)

On December 8, 2000, the Board of Directors of ISIS PHARMACEUTICALS, INC. (the "Company") declared a dividend of one preferred share purchase right (a "Right") for each outstanding share of common stock, par value \$.001 per share (the "Common Shares"), of the Company. The dividend is effective as of January 10, 2001 (the "Record Date") with respect to the stockholders of record on that date. The Rights will also attach to new Common Shares issued after the Record Date. Each Right entitles the registered holder to purchase from the Company one one-hundredth of a share of Series C Junior Participating Preferred Stock, par value \$.001 per share (the "Preferred Shares"), of the Company at a price of \$85 per one one-hundredth of a Preferred Share (the "Purchase Price"), subject to adjustment. Each Preferred Share is designed to be the economic equivalent of 100 Common Shares. The description and terms of the Rights are set forth in a Rights Agreement dated as of December 8, 2000 (the "Rights Agreement"), between the Company and American Stock Transfer & Trust Company (the "Rights Agent").

DETACHMENT AND TRANSFER OF RIGHTS

Initially, the Rights will be evidenced by the stock certificates representing Common Shares then outstanding, and no separate Right Certificates will be distributed. Until the earlier to occur of (i) a public announcement that a person or group of affiliated or associated persons, has become an "Acquiring Person" (as such term is defined in the Rights Agreement) or (ii) 10 business days (or such later date as the Board may determine) following the commencement of, or announcement of an intention to make, a tender offer or exchange offer which would result in the beneficial ownership by an Acquiring Person of 20% or more of the outstanding Common Shares (the earlier of such dates being called the "Distribution Date"), the Rights will be evidenced, with respect to any of the Common Share certificates outstanding as of the Record Date, by such Common Share certificate. In general, an "Acquiring Person" is a person, the affiliates or associates of such person, or a group, which has acquired beneficial ownership of 20% or more of the outstanding Common Shares after the date of the adoption of the Rights Agreement, subject to certain exceptions set forth in the Rights Agreement.

The Rights Agreement provides that, until the Distribution Date (or earlier redemption or expiration of the Rights), the Rights will be transferable with and only with the Common Shares. Until the Distribution Date (or earlier redemption or expiration of the Rights), new Common Share certificates issued after the Record Date upon transfer or new issuance of Common Shares will contain a notation incorporating the Rights Agreement by reference. Until the Distribution Date (or earlier redemption or expiration of the Rights) the surrender or transfer of any certificates for Common Shares outstanding as of the Record Date, even without such notation or

a copy of this Summary of Rights being attached thereto, will also constitute the transfer of the Rights associated with the Common Shares represented by such certificate. As soon as practicable following the Distribution Date, separate certificates evidencing the Rights ("Right Certificates") will be mailed to holders of record of the Common Shares as of the close of business on the Distribution Date and such separate Right Certificates alone will evidence the Rights.

EXERCISABILITY OF RIGHTS

The Rights are not exercisable until the Distribution Date. The Rights will expire on December 7, 2010 (the "Final Expiration Date"), unless the Final Expiration Date is extended or unless the Rights are earlier redeemed or exchanged by the Company, in each case as described below. Until a Right is exercised, the holder thereof, as such, will have no rights as a stockholder of the Company, including, without limitation, the right to vote or to receive dividends.

The Purchase Price payable, and the number of Preferred Shares or other securities or property issuable or payable, upon exercise of the Rights are subject to adjustment from time to time to prevent dilution. The number of outstanding Rights and the number of one one-hundredths of a Preferred Share issuable upon exercise of each Right are also subject to adjustment in the event of a stock split of the Common Shares or a stock dividend on the Common Shares payable in Common Shares, or subdivisions, consolidations or combinations of the Common Shares occurring, in any such case, prior to the Distribution Date. With certain exceptions, no adjustment in the Purchase Price will be required until cumulative adjustments require an adjustment of at least 1% in such Purchase Price. No fractional Preferred Shares will be issued (other than fractions which are integral multiples of one one-hundredth of a Preferred Share, which may, at the election of the Company, be evidenced by depositary receipts) and in lieu thereof, an adjustment in cash will be made based on the market price of the Preferred Shares on the last trading day prior to the date of exercise.

TERMS OF PREFERRED SHARES

Preferred Shares purchasable upon exercise of the Rights will not be redeemable. Each Preferred Share will be entitled to a minimum preferential quarterly dividend payment of \$1 per share but will be entitled to an aggregate dividend of 100 times the dividend declared per Common Share. In the event of liquidation, the holders of the Preferred Shares will be entitled to a minimum preferential liquidation payment of \$100 per share but will be entitled to an aggregate payment of 100 times the payment made per Common Share. Each Preferred Share will have 100 votes, voting together with the Common Shares. Finally, in the event of any merger, consolidation or other transaction in which Common Shares are exchanged, each Preferred Share will be entitled to receive 100 times the amount received per Common Share. These rights are protected by customary anti-dilution provisions. Because of the nature of the Preferred Shares' dividend, liquidation and voting rights, the value of the one one-hundredth interest in a Preferred Share purchasable upon exercise of each Right should approximate the value of one Common Share. The Preferred Shares would rank junior to any other series of the Company's preferred stock.

TRIGGER OF FLIP-IN AND FLIP-OVER RIGHTS

In the event that any person or group of affiliated or associated persons becomes an Acquiring Person, proper provision shall be made so that each holder of a Right, other than Rights beneficially owned by the Acquiring Person or any affiliate or associate thereof (which will thereafter be void), will thereafter have the right to receive upon exercise that number of Common Shares having a market value of two times the exercise price of the Right. This right will commence on the date of public announcement that a person has become an Acquiring Person (or the effective date of a registration statement relating to distribution of the rights, if later) and terminate 60 days later (subject to adjustment in the event exercise of the rights is enjoined).

In the event that the Company is acquired in a merger or other business combination transaction or 50% or more of its consolidated assets or earning power are sold to an Acquiring Person, its affiliates or associates or certain other persons in which such persons have an interest, proper provision will be made so that each such holder of a Right will thereafter have the right to receive, upon the exercise thereof at the then current exercise price of the Right, that number of shares of common stock of the acquiring company which at the time of such transaction will have a market value of two times the exercise price of the Right.

REDEMPTION AND EXCHANGE OF RIGHTS

At any time prior to the earliest of (i) the close of business on the day of the first public announcement that a person has become an Acquiring Person, or (ii) the Final Expiration Date, the Board of Directors of the Company may redeem the Rights in whole, but not in part, at a price of \$.001 per Right (the "Redemption Price"). In general, the redemption of the Rights may be made effective at such time on such basis with such conditions as the Board of Directors in its sole discretion may establish Immediately upon any redemption of the Rights, the right to exercise the Rights will terminate and the only right of the holders of Rights will be to receive the Redemption Price.

At any time after any Person becomes an Acquiring Person and prior to the acquisition by such person or group of 50% or more of the outstanding Common Shares, the Board of Directors of the Company may exchange the Rights (other than Rights owned by such person or group which will have become void), in whole or in part, at an exchange ratio of one Common Share, or, under circumstances set forth in the Rights Agreement, cash, property or other securities of the Company, including fractions of a Preferred Share (or of a share of a class or series of the Company's preferred stock having equivalent designations and the powers, preferences and rights, and the qualifications, limitations and restrictions), per Right (with value equal to such Common Shares).

AMENDMENT OF RIGHTS

The terms of the Rights generally may be amended by the Board of Directors of the Company without the consent of the holders of the Rights, except that from and after such time as the Rights are distributed no such amendment may adversely affect the interests of the holders of the Rights (excluding the interest of any Acquiring Person).

ADDITIONAL INFORMATION

A copy of the Rights Agreement has been filed with the Securities and Exchange Commission as an Exhibit to a Current Report on Form 8-K dated December 13, 2000. A copy of the Rights Agreement is available from the Company by writing to: Isis Pharmaceuticals, Inc., 2292 Faraday Avenue, Carlsbad, CA 92008, Attention: Corporate Secretary. This summary description of the Rights is not intended to be complete and is qualified in its entirety by reference to the Rights Agreement, which is hereby incorporated herein by reference.

TABLE OF CONTENTS

SECTION 1. CERTAIN DEFINITIONS.....2

SECTION 2. APPOINTMENT OF RIGHTS AGENT.....5

SECTION 3. ISSUE OF RIGHT CERTIFICATES.....5

SECTION 4. FORM OF RIGHT CERTIFICATES.....7

SECTION 5. COUNTERSIGNATURE AND REGISTRATION.....8

SECTION 6. TRANSFER, SPLIT UP, COMBINATION AND EXCHANGE OF RIGHT CERTIFICATES;
MUTILATED, DESTROYED, LOST OR STOLEN RIGHT CERTIFICATES.....8

SECTION 7. EXERCISE OF RIGHTS; PURCHASE PRICE; EXPIRATION DATE OF RIGHTS.....9

SECTION 8. CANCELLATION AND DESTRUCTION OF RIGHT CERTIFICATES.....11

SECTION 9. AVAILABILITY OF PREFERRED SHARES.....11

SECTION 10. PREFERRED SHARES RECORD DATE.....12

SECTION 11. ADJUSTMENT OF PURCHASE PRICE, NUMBER OF SHARES OR NUMBER OF RIGHTS.....12

SECTION 12. CERTIFICATE OF ADJUSTED PURCHASE PRICE OR NUMBER OF SHARES.....19

SECTION 13. CONSOLIDATION, MERGER OR SALE OR TRANSFER OF ASSETS OR EARNING POWER.....19

SECTION 14. FRACTIONAL RIGHTS AND FRACTIONAL SHARES.....22

SECTION 15. RIGHTS OF ACTION.....23

SECTION 16. AGREEMENT OF RIGHT HOLDERS.....23

SECTION 17. RIGHT CERTIFICATE HOLDER NOT DEEMED A STOCKHOLDER.....24

SECTION 18. CONCERNING THE RIGHTS AGENT.....24

SECTION 19. MERGER OR CONSOLIDATION OR CHANGE OF NAME OF RIGHTS AGENT.....24

SECTION 20. DUTIES OF RIGHTS AGENT.....25

SECTION 21. CHANGE OF RIGHTS AGENT.....27

SECTION 22. ISSUANCE OF NEW RIGHT CERTIFICATES.....28

SECTION 23. REDEMPTION.....28

SECTION 24. EXCHANGE.....29

SECTION 25. NOTICE OF CERTAIN EVENTS.....31

SECTION 26. NOTICES.....32

SECTION 27. SUPPLEMENTS AND AMENDMENTS.....32

SECTION 28. DETERMINATION AND ACTIONS BY THE BOARD OF DIRECTORS, ETC.....33

SECTION 29. SUCCESSORS.....	33
SECTION 30. BENEFITS OF THIS AGREEMENT.....	33
SECTION 31. SEVERABILITY.....	33
SECTION 32. GOVERNING LAW.....	34
SECTION 33. COUNTERPARTS.....	34
SECTION 34. DESCRIPTIVE HEADINGS.....	34

EXHIBITS

FORM OF CERTIFICATE OF DESIGNATION OF SERIES C JUNIOR PARTICIPATING PREFERRED STOCK.....	EXHIBIT A
FORM OF RIGHT CERTIFICATE.....	EXHIBIT B
SUMMARY OF RIGHTS TO PURCHASE PREFERRED SHARES.....	EXHIBIT C

FORM OF RIGHT CERTIFICATE
(EXHIBIT B TO RIGHTS AGREEMENT)

CERTIFICATE NO. R-

_____ RIGHTS

NOT EXERCISABLE AFTER DECEMBER 7, 2010 OR EARLIER IF REDEMPTION OR EXCHANGE OCCURS. THE RIGHTS ARE SUBJECT TO REDEMPTION AT \$.001 PER RIGHT AND TO EXCHANGE ON THE TERMS SET FORTH IN THE RIGHTS AGREEMENT.

RIGHT CERTIFICATE
ISIS PHARMACEUTICALS, INC.

This certifies that _____ or registered assigns, is the registered owner of the number of Rights set forth above, each of which entitles the owner thereof, subject to the terms, provisions and conditions of the Rights Agreement, dated as of December 8, 2000 (the "Rights Agreement"), between Isis Pharmaceuticals, Inc., a Delaware corporation (the "Company"), and American Stock Transfer & Trust Company (the "Rights Agent"), to purchase from the Company at any time after the Distribution Date (as such term is defined in the Rights Agreement) and prior to 5:00 p.m., Pacific Time, on December 7, 2010 at the office of the Rights Agent designated for such purpose, or at the office of its successor as Rights Agent, one one-hundredth of a fully paid non-assessable share of Series C Junior Participating Preferred Stock, par value \$.001 per share (the "Preferred Shares"), of the Company, at a purchase price of \$85 per one one-hundredth of a Preferred Share (the "Purchase Price"), upon presentation and surrender of this Right Certificate with the Form of Election to Purchase duly executed. The number of Rights evidenced by this Right Certificate (and the number of one one-hundredths of a Preferred Share which may be purchased upon exercise hereof) set forth above, and the Purchase Price set forth above, are the number and Purchase Price as of December 8, 2000, based on the Preferred Shares as constituted at such date.

From and after the time any Person becomes an Acquiring Person (as such terms are defined in the Rights Agreement), if the Rights evidenced by this Right Certificate are beneficially owned by (i) an Acquiring Person or an Affiliate or Associate of any such Acquiring Person (as such terms are defined in the Rights Agreement), (ii) a transferee of any such Acquiring Person, Associate or Affiliate who becomes a transferee after the Acquiring Person becomes such, or (iii) under certain circumstances specified in the Rights Agreement, a transferee of any such Acquiring Person, Associate or Affiliate who becomes a transferee prior to or concurrently with the Acquiring Person becoming such, such Rights shall become null and void without any further action and no holder hereof shall have any right with respect to such Rights from and after the time any Person becomes an Acquiring Person.

As provided in the Rights Agreement, the Purchase Price and the number of one one-hundredths of a Preferred Share which may be purchased upon the exercise of the Rights

evidenced by this Right Certificate are subject to modification and adjustment upon the happening of certain events.

This Right Certificate is subject to all of the terms, provisions and conditions of the Rights Agreement, as amended from time to time, which terms, provisions and conditions are hereby incorporated herein by reference and made a part hereof and to which Rights Agreement reference is hereby made for a full description of the rights, limitations of rights, obligations, duties and immunities hereunder of the Rights Agent, the Company and the holders of the Right Certificates. Copies of the Rights Agreement are on file at the principal executive offices of the Company and the offices of the above-mentioned Rights Agent.

This Right Certificate, with or without other Right Certificates, upon surrender at the office of the Rights Agent designated for such purpose, may be exchanged for another Right Certificate or Right Certificates of like tenor and date evidencing Rights entitling the holder to purchase a like aggregate number of Preferred Shares as the Rights evidenced by the Right Certificate or Right Certificates surrendered shall have entitled such holder to purchase. If this Right Certificate shall be exercised in part, the holder shall be entitled to receive upon surrender hereof another Right Certificate or Right Certificates for the number of whole Rights not exercised.

Subject to the provisions of the Rights Agreement, the Rights evidenced by this Certificate (i) may be redeemed by the Company at a redemption price of \$.001 per Right or (ii) may be exchanged in whole or in part for shares of the Company's Common Stock, par value \$.001 per share, or, upon circumstances set forth in the Rights Agreement, cash, property or other securities of the Company, including fractions of a share of Preferred Stock.

No fractional Preferred Shares will be issued upon the exercise of any Right or Rights evidenced hereby (other than fractions which are integral multiples of one one-hundredth of a Preferred Share, which may, at the election of the Company, be evidenced by depositary receipts) but in lieu thereof a cash payment will be made, as provided in the Rights Agreement.

No holder of this Right Certificate shall be entitled to vote or receive dividends or be deemed for any purpose the holder of the Preferred Shares or of any other securities of the Company which may at any time be issuable on the exercise hereof, nor shall anything contained in the Rights Agreement or herein be construed to confer upon the holder hereof, as such, any of the rights of a stockholder of the Company or any right to vote for the election of directors or upon any matter submitted to stockholders at any meeting thereof, or to give or withhold consent to any corporate action, or to receive notice of meetings or other actions affecting stockholders (except as provided in the Rights Agreement), or to receive dividends or subscription rights, or otherwise, until the Right or Rights evidenced by this Right Certificate shall have been exercised as provided in the Rights Agreement.

This Right Certificate shall not be valid or obligatory for any purpose until it shall have been countersigned by the Rights Agent.

WITNESS the facsimile signature of the proper officers of the Company and its corporate seal. Dated as of _____.

ATTEST:

ISIS PHARMACEUTICALS, INC.

By: _____

By: _____

Print Name: _____

Print Name: _____

Secretary

Title: _____

COUNTERSIGNED:

as Rights Agent

By: _____

Print Name: _____

Title: _____

FORM OF REVERSE SIDE OF RIGHT CERTIFICATE

FORM OF ASSIGNMENT

(TO BE EXECUTED BY THE REGISTERED HOLDER IF SUCH
HOLDER DESIRES TO TRANSFER THE RIGHT CERTIFICATE.)

FOR VALUE RECEIVED _____ hereby sells,
assigns and transfers unto

(Please print name and address of transferee)

_____ this Right
Certificate, together with all right, title and interest therein, and does
hereby irrevocably constitute and appoint _____ Attorney, to
transfer the within Right Certificate on the books of the within-named Company,
with full power of substitution.

Dated:

Signature

SIGNATURE GUARANTEED:

Signatures must be guaranteed by an "eligible guarantor institution" as defined in Rule 17Ad-15 promulgated under the Securities Exchange Act of 1934, as amended.

The undersigned hereby certifies that (1) the Rights evidenced by this Right Certificate are not being sold, assigned or transferred by or on behalf of a Person who is or was an Acquiring Person, an Interested Stockholder or an Affiliate or Associate thereof (as such terms are defined in the Rights Agreement); and (2) after due inquiry and to the best of the knowledge of the undersigned, the undersigned did not acquire the Rights evidenced by this Right Certificate from any Person who is or was an Acquiring Person, an Interested Stockholder, or an Affiliate or Associate thereof.

Signature

FORM OF REVERSE SIDE OF RIGHT CERTIFICATE

FORM OF ELECTION TO PURCHASE

(TO BE EXECUTED IF HOLDER DESIRES TO EXERCISE RIGHTS REPRESENTED BY THE RIGHT CERTIFICATE.)

To American Stock Transfer & Trust Company:

The undersigned hereby irrevocably elects to exercise _____ Rights represented by this Right Certificate to purchase the Preferred Shares issuable upon the exercise of such Rights and requests that certificates for such Preferred Shares be issued in the name of:

Please insert social security or other identifying number: _____

(Please print name and address)

If such number of Rights shall not be all the Rights evidenced by this Right Certificate, a new Right Certificate for the balance remaining of such Rights shall be registered in the name of and delivered to:

Please insert social security or other identifying number: _____

(Please print name and address)

Dated: _____

Signature

SIGNATURE GUARANTEED:

Signatures must be guaranteed by an "eligible guarantor institution" as defined in Rule 17Ad-15 promulgated under the Securities Exchange Act of 1934, as amended.

The undersigned hereby certifies that (1) the Rights evidenced by this Right Certificate are not beneficially owned by nor are they being exercised on behalf of an Acquiring Person, an Interested Stockholder or an Affiliate or Associate thereof (as such terms are defined in the Rights Agreement); and (2) after due inquiry and to the best of the knowledge of the undersigned, the undersigned did not acquire the Rights evidenced by this Right Certificate from any Person who is or was an Acquiring Person, an Interested Stockholder, or an Affiliate or Associate thereof.

Signature

NOTICE

The signature in the Form of Assignment or Form of Election to Purchase, as the case may be, must conform to the name as written upon the face of this Right Certificate in every particular, without alteration or enlargement or any change whatsoever.

In the event the certification set forth above in the Form of Assignment or the Form of Election to Purchase, as the case may be, is not completed, the Company and the Rights Agent will deem the beneficial owner of the Rights evidenced by this Right Certificate to be an Acquiring Person or an Affiliate or Associate thereof (as defined in the Rights Agreement) and such Assignment or Election to Purchase will not be honored.