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FORM PTO-1595 1-31-92

U.S. DEPARTMENT OF COMMERCE

Patent and Trademark Office

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To The Honorable Commissioner of Patents and Trademarks. Please record the attached documents or copy thereof.

1. Name of conveying party(ies):  
Donna T. Ward, William Gaarde, Brett P. Monia and  
Jacqueline WyattAdditional name(s) of conveying party(ies)  
attached? ( ) YES (X) NO3. Nature of Conveyance:  
(X) Assignment ( ) Merger  
( ) Security Agreement  
( ) Change of Name  
( ) Other:

Execution Date: Sept. 7, 2000

2. Name and address of receiving party(ies):  
Name: Isis Pharmaceuticals Inc.  
Internal Address:Street Address: 2292 Faraday Ave  
City Carlsbad

State California Zip 92008

Additional name(s) & address attached?  
( ) YES (X) NO

09 658688

4. Application number(s) or patent number (s): N/A

If this document is being filed together with a new application, the execution date of the application is: 9/7/00

A. Patent Application No.(s) Not yet assigned

B. Patent No.(s) N/A

Additional numbers attached? ( ) YES (X) NO

5. Name and address of party to whom  
correspondence concerning documents should be  
mailed:Name: Jane Massey Licata  
Address: Law Offices of Jane Massey Licata  
66 East Main Street  
Marlton NJ 080536. Total number of applications and patents  
involved: 17. Total fee (37 CFR 3.41):.....\$40.00  
( ) Enclosed  
(X) Authorized to be charged to deposit account

8. Deposit account number: 500252

(Attach duplicate copy of this page if paying by  
deposit account)

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9. Statement and signature.

To the best of my knowledge and belief, the foregoing information is true and correct and any attached copy is  
a true copy of the original document.

Laurel Spear Bernstein / 37,280

Name of Person Signing/Reg.No.

(Laurel Spear Bernstein)

Signature

Sept 8, 2000

Date

Total number of pages including cover sheet, attachments, and document: 5

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10/06/2000 MTHAI1 00000130 500252 09658688

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PATENT  
REEL: 011131 FRAME: 0955

A S S I G N M E N T

WHEREAS, we Donna T. Ward, residing at 41349 Magnolia Street Murrieta CA 92562, William Gaarde, residing at 3105 Quebrada Circle Carlsbad CA 92009, Brett P. Monia, residing at 7605 Nueva Castilla Way La Costa CA 92009 and Jacqueline Wyatt, residing at 1065 Hymettus Avenue Encinitas CA 92024 hereinafter referred to as the assignors, are the joint inventors of certain inventions or improvements for which we have made application for Letters Patent to the United States, entitled **Antisense Modulation of MEKK3 Expression**; filed concurrently herewith; and

WHEREAS, **Isis Pharmaceuticals Inc.** hereinafter referred to as the assignee, of **2292 Faraday Ave, Carlsbad, California 92008** is desirous of acquiring the entire right, title and interest in and to the said inventions or improvements and in and to the said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in any and all countries:

NOW, THEREFORE, for and in consideration of the sum of One Dollar (\$1.00) to each of us in hand paid by said assignee, and other good and valuable consideration, the receipt of which is hereby acknowledged, we, the said assignors, have sold, assigned, transferred and set over, and by these presents do hereby sell, assign, transfer and set over to said assignee, the entire right, title and interest in and to said inventions or improvements and said application and any and all continuations, divisions and renewals of and substitutes for said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in the United States and any and all other countries, and any reissue or reissues or extension or extensions of said Letters Patent, and assign to and authorize said assignee, to file in our names applications for Letters Patent in all countries, the same to be held and enjoyed by said assignee, its successors, assigns, nominees or legal representatives, to the full end of the term or terms for which said Letters Patent respectively may be granted, reissued or extended, as fully and entirely as the same would have been held and enjoyed by us had this assignment, sale and transfer not been made.

AND we hereby covenant that we have full right to convey the entire interest herein assigned, and that we have not executed and will not execute any agreement in conflict herewith, and we further covenant and agree that we will each time request is made and without undue delay, execute and deliver all such papers as may be necessary or desirable to perfect the title to said inventions or improvements, said application and said Letters Patent to said assignee, its successors, assigns, nominees, or legal representatives, and each of us agrees to communicate to said assignee or to its nominee all known facts respecting said inventions or improvements, said application and said Letters Patent, to testify in any legal proceedings, to sign all lawful papers, to execute all disclaimers and divisional, continuing, reissue and foreign applications, to make all rightful oaths, and generally to do everything possible to aid said assignee, its successors, assigns, nominees and legal representatives to obtain and enforce for its or

their own benefit proper patent protection for said inventions or improvements in any and all countries.

AND we hereby authorize and request the Commissioner of Patents and Trademarks of the United States and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue to said assignee, as assignee of the entire right, title and interest, any and all Letters Patent for said inventions or improvements, including any and all Letters Patent of the United States which may be issued and granted on or as a result of the application aforesaid, in accordance with the terms of this assignment.

We further authorize and direct our attorneys to insert below\* the serial number and filing date of said application as soon as the same shall have been made known to them by the United States Patent Office.

IN WITNESS WHEREOF, we have hereunto set our hands and seals.

Dated: 9-5-00

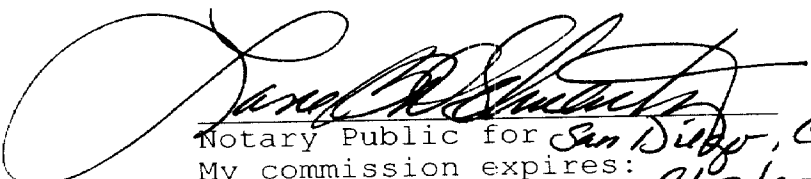
  
Donna T. Ward

STATE OF California )  
COUNTY OF San Diego )

ss.

This 5th day of September, 2000, before me personally came the above-named Donna T. Ward, who executed the foregoing Assignment in my presence, and who acknowledged to me that he/she executed the same of his/her own free will for the purposes set forth therein.



  
Notary Public for San Diego, CA  
My commission expires: 9/13/02

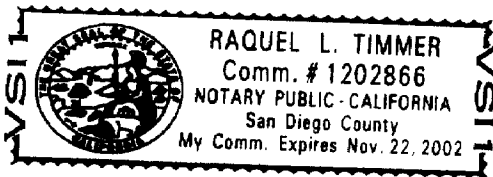
[SEAL]

Dated: 9/7/00

William A. Gaarde  
William Gaarde

STATE OF California )  
COUNTY OF San Diego ) ss.

This 7<sup>th</sup> day of September 2000, before me personally came the above-named William Gaarde, who executed the foregoing Assignment in my presence, and who acknowledged to me that he/~~she~~ executed the same of his/~~her~~ own free will for the purposes set forth therein.



Raquel L. Timmer  
Notary Public for  
My commission expires:

[SEAL]

Dated: 9/6/00

Brett P. Monia  
Brett P. Monia

STATE OF California )  
COUNTY OF San Diego ) ss.

This 6<sup>th</sup> day of September, 2000, before me personally came the above-named Brett P. Monia, who executed the foregoing Assignment in my presence, and who acknowledged to me that he/~~she~~ executed the same of his/~~her~~ own free will for the purposes set forth therein.



Lane B.D. Schwartz  
Notary Public for San Diego, CA  
My commission expires: 9-13-02

[SEAL]

Dated: 8/31/00

Jacqueline R Wyatt  
Jacqueline Wyatt

STATE OF CALIFORNIA )  
 )  
COUNTY OF SAN DIEGO ) ss.

This 31<sup>st</sup> day of AUGUST, 2000, before me personally came the above-named Jacqueline Wyatt, who executed the foregoing Assignment in my presence, and who acknowledged to me that he/she executed the same of his/her own free will for the purposes set forth therein.



[SEAL]

Carol A. Collins  
Notary Public for CALIFORNIA  
My commission expires: 7/8/02