

12-01-1999

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To The Honorable Commissioner of Patent
thereof.

101211405

attached original documents or copy

1. Name of conveying party(ies):

Phillip Dan Cook and Muthiah Manoharan

Additional name(s) of conveying party(ies)
attached? () YES (X) NO

3. Nature of Conveyance:

(X) Assignment () Merger

() Security Agreement

() Change of Name

() Other:

Execution Date(s): August 5, 1999

2. Name and address of receiving party(ies):

Name: ISIS Pharmaceuticals, Inc.

Street Address: 2292 Faraday Avenue

City: Carlsbad

State California

ZIP 92008

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

4. Application number(s) or patent number(s):

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

A. Patent Application No.(s)

09/352,058 filed 07/14/99

B. Patent No.(s)

Additional numbers attached? () YES (X) NO

5. Name and address of party to whom correspondence
concerning documents should be mailed:

Name: Michael P. Straher

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One Liberty Place - 46th Floor

1650 Market Street

Philadelphia, Pennsylvania 19103-7301

6. Total number of applications and patents involved:

One (1)

7. Total fee (37 CFR 3.41):.....\$40.00

(X) Enclosed

() Authorized to be charged to Deposit Account
Number 23-30508. Please charge any deficiency or credit any
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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.*

Michael P. Straher/38,325

Name of Person Signing/Reg. No.

Signature

November 16, 1999

Date

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

Mail documents to be recorded with required cover sheet information to:

11/30/1999 DMGUYEN 00000176 09352058

FC:581

40.00 00

Commissioner of Patents and Trademarks

Box Assignments

Washington, D.C. 20231

A S S I G N M E N T

WHEREAS, We, **Phillip Dan Cook, of Fallbrook, State of California and Muthiah Manoharan, of Carlsbad, State of California**, have invented a certain invention entitled **OLIGONUCLEOTIDES HAVING SITE SPECIFIC CHIRAL PHOSPHOROTHIOATE INTERNUCLEOSIDE LINKAGES**, for which we have made application for Letters Patent of the United States, said application having been **filed July 14, 1999 and assigned Application No. 09/352,058**; and

WHEREAS, ISIS Pharmaceuticals, Inc. hereinafter referred to as the assignee, of 2292 Faraday Avenue, Carlsbad CA, a corporation of Delaware, 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.

ASSIGNMENT - PAGE 1 OF 4

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.

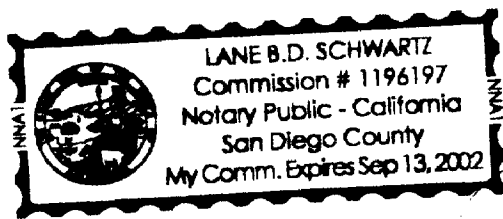
AND we hereby authorize and request the Commissioner of Patents and Trademarks of the United States and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue to said assignee, as assignee of the entire right, title 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.

ASSIGNMENT - PAGE 2 OF 4

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

Dated: 8/05/99, 1999Phillip Dan Cook
PHILLIP DAN COOKState of California)
) ss.
County of San Diego)

On this 5th day of August, 1999, before me, the undersigned, a Notary Public for the state, personally appeared **PHILLIP DAN COOK** personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that ~~he~~ she executed the same in ~~his~~ her authorized capacity, and that by ~~his~~ her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



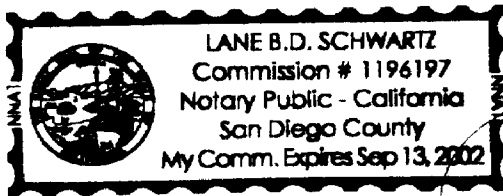
WITNESS my hand and official seal.

Lane B.D. Schwartz
Signature of Notary


ASSIGNMENT - PAGE 3 OF 4

Dated: August 5, 1999
MUTHIAH MANOHARANState of California)
)
County of San Diego) ss.

On this 5th day of August, 1999, before me, the undersigned, a Notary Public for the state, personally appeared **MUTHIAH MANOHARAN** personally known to me/~~proved to me on the basis of satisfactory evidence to be~~ the person who subscribed the foregoing Assignment and acknowledged to me that ~~he~~/she executed the same in ~~his~~/her authorized capacity, and that by ~~his~~/her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.


Signature of Notary

ASSIGNMENT - PAGE 4 OF 4