Total number of pages including cover sheet, assignment document and additional pages attached thereto:

Commissioner of Patents and Trademarks Box Assignments Washington, D.C. 20231

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00000153 09965551 40.00 DP

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

PATENT

REEL: 012226 FRAME: 0991

DOCKET NO.: ISIS-3863 PATENT

ASSIGNMENT

WHEREAS, I, Muthiah Manoharan, of Carlsbad, State of California, have invented a

certain invention entitled CARBOHYDRATE OR 2'-MODIFIED OLIGONUCLEOTIDES

HAVING ALTERNATING INTERNUCLEOSIDE LINKAGES, for which I have made

application for Letters Patent of the United States, said application having been filed July 7, 1999

and assigned Application No. 09/349,007; 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, I, the said assignor, 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 my name 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 me had this assignment, sale and transfer not been made.

ASSIGNMENT - PAGE 1 OF 3

PATENT

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AND I hereby covenant that we have full right to convey the entire interest herein assigned, and that I have not executed and will not execute any agreement in conflict herewith, and I further covenant and agree that I 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 I agree 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 I 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 3

PATENT REEL: 012226 FRAME: 0993

IN WITNESS WI	<b>IEREO</b>	F, I have h	ereunto set my hand and sea	al.
Dated: kugur		, 1999	•	Meshen
		MUTHIAH MANOHARAN		
State of California	)			
County of San Diego	)	SS.		

On this \_\_\_\_\_ day of \_\_\_\_\_\_\_, 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.

LANE B.D. SCHWARTZ
Commission # 1196197
Notary Public - California
San Diega County
My Comm. Expires Sep 13, 2002

WITNESS my hand and official seal.

ASSIGNMENT - PAGE 3 OF 3

PATENT REEL: 012226 FRAME: 0994

**RECORDED: 09/27/2001**