

PATENT ASSIGNMENT

Electronic Version v1.1

Stylesheet Version v1.1

| SUBMISSION TYPE:   | NEW ASSIGNMENT             |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
|--|----------------------------|----------------|-----------------|------------|----------------|------------|-------------------|------------|------------------|------------|--------------|------------|--------------------|------------|--|
| NATURE OF CONVEYANCE:  | ASSIGNMENT                 |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| CONVEYING PARTY DATA   |                            |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| <table><thead><tr><th>Name</th><th>Execution Date</th></tr></thead><tbody><tr><td>Balkrishen Bhat</td><td>11/27/2006</td></tr><tr><td>Eric E. Swayze</td><td>11/27/2006</td></tr><tr><td>Thazha P. Prakash</td><td>11/27/2006</td></tr><tr><td>Charles Allerson</td><td>11/27/2006</td></tr><tr><td>Prasad Dande</td><td>11/27/2006</td></tr><tr><td>Richard H. Griffey</td><td>11/16/2006</td></tr></tbody></table> | Name                       | Execution Date | Balkrishen Bhat | 11/27/2006 | Eric E. Swayze | 11/27/2006 | Thazha P. Prakash | 11/27/2006 | Charles Allerson | 11/27/2006 | Prasad Dande | 11/27/2006 | Richard H. Griffey | 11/16/2006 |  |
| Name   | Execution Date             |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| Balkrishen Bhat  | 11/27/2006                 |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| Eric E. Swayze   | 11/27/2006                 |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| Thazha P. Prakash  | 11/27/2006                 |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| Charles Allerson   | 11/27/2006                 |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| Prasad Dande   | 11/27/2006                 |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| Richard H. Griffey   | 11/16/2006                 |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| RECEIVING PARTY DATA   |                            |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| Name:  | Isis Pharmaceuticals, Inc. |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| Street Address:  | 1896 Rutherford Road       |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| City:  | Carlsbad                   |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| State/Country:   | CALIFORNIA                 |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| Postal Code:   | 92008                      |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| PROPERTY NUMBERS Total: 1  |                            |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| <table><thead><tr><th>Property Type</th><th>Number</th></tr></thead><tbody><tr><td>PCT Number:</td><td>US0417485</td></tr></tbody></table>   | Property Type              | Number         | PCT Number:     | US0417485  |                |            |                   |            |                  |            |              |            |                    |            |  |
| Property Type  | Number                     |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| PCT Number:  | US0417485                  |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| CORRESPONDENCE DATA  |                            |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| Fax Number: (760)603-3820<br><i>Correspondence will be sent via US Mail when the fax attempt is unsuccessful.</i>  |                            |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| Phone: 760-603-2553  |                            |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| Email: leames@isisph.com   |                            |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| Correspondent Name: Isis Pharmaceuticals, Inc.   |                            |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| Address Line 1: 1896 Rutherford Road   |                            |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| Address Line 4: Carlsbad, CALIFORNIA 92008   |                            |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| ATTORNEY DOCKET NUMBER:  | CHEM0022WO                 |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |
| NAME OF SUBMITTER:   | Laura Eames                |                |                 |            |                |            |                   |            |                  |            |              |            |                    |            |  |

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PATENT

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**Total Attachments: 8**

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**PATENT**

**REEL: 018566 FRAME: 0422**

DOCKET NO.: **CHEM0022WO**

**A S S I G N M E N T**

WHEREAS, I/we, **Balkrishen Bhat, of Carlsbad, CA, Eric E. Swayze, of Carlsbad, CA , Thazha P. Prakash, of Carlsbad, CA, Charles Allerson, of San Diego, CA, Prasad Dande, of Cambridge, MA, Richard H. Griffey, of Vista, CA,** has/have invented a certain invention entitled **POSITIONALLY MODIFIED SIRNA CONSTRUCTS**, for which I/we have made an application for patents in the United States and foreign jurisdictions through the Patent Cooperation Treaty, said application having been filed **June 3, 2004**, and assigned International Application No. **PCT/US2004/017485**; and

WHEREAS, ISIS Pharmaceuticals, Inc. hereinafter referred to as the assignee, of 1896 Rutherford Road, Carlsbad CA, a corporation of Delaware, desires to acquire 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

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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.

DOCKET NO.: **CHEM0022WO**

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

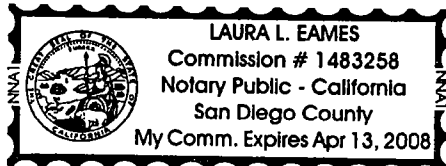
Dated: 11-27 2006

Balkrishen Bhat

**Balkrishen Bhat**

State of California )  
County of San Diego ) ss.

On this 27<sup>th</sup> day of November, 2006, before me, the undersigned, a Notary Public for the state, personally appeared **Balkrishen Bhat**, 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.

Laura Eames  
Signature of Notary

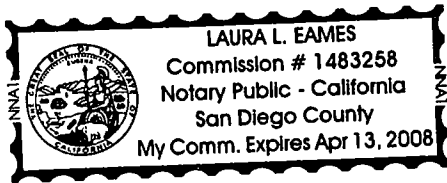
DOCKET NO.: CHEM0022WO

Dated: 11/27 2006

Eric E. Swayze  
Eric E. Swayze

State of California )  
County of San Diego ) ss.

On this 27<sup>th</sup> day of November, 2006, before me, the undersigned, a Notary Public for the state, personally appeared **Eric E. Swayze**, 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.

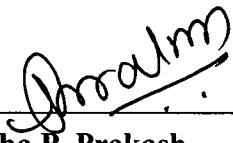


WITNESS my hand and official seal.

Laura Eames  
Signature of Notary

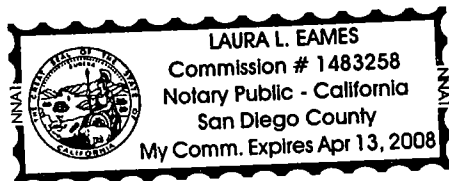
DOCKET NO.: CHEM0022WO

Dated: 11 | 27 | 2006


  
\_\_\_\_\_  
**Thazha P. Prakash**

State of California )  
County of San Diego ) SS.

On this 27<sup>th</sup> day of November, 2006, before me, the undersigned, a Notary Public for the state, personally appeared **Thazha P. Prakash**, 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.

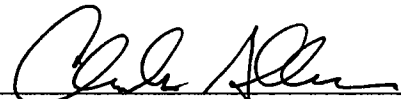


WITNESS my hand and official seal.

  
\_\_\_\_\_  
Signature of Notary

DOCKET NO.: CHEM0022WO

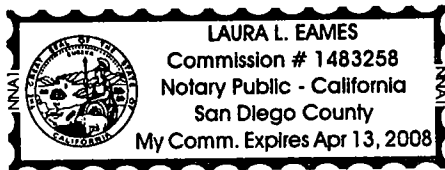
Dated: 11/27 20 06

  
Charles Allerson


State of California )  
County of San Diego )

ss.

On this 27<sup>th</sup> day of November, 20 06, before me, the undersigned, a Notary Public for the state, personally appeared **Charles Allerson**, 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.



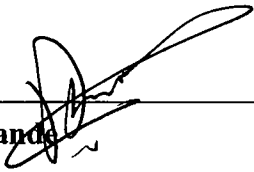
WITNESS my hand and official seal.

  
Signature of Notary



DOCKET NO.: CHEM0022WO

Dated: 11/27/ 2006

  
\_\_\_\_\_  
Prasad Dande

STATEMENT OF WITNESSES

I was personally present and did see **Prasad Dande** execute the above assignment, and he is personally known to me to be the person described in this document.

(1) Dennis Burt

Date: 11/27/06

(2) D. M. Shah

Date: 11/27/06

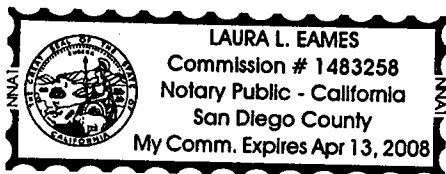
DOCKET NO.: CHEM0022WO

Dated: 11/16 2006

Richard H. Griffey  
Richard H. Griffey

State of California )  
County of San Diego ) ss.

On this 16<sup>th</sup> day of November, 2006, before me, the undersigned, a Notary Public for the state, personally appeared **Richard H. Griffey**, 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.

Laura Eames  
Signature of Notary