18-02095-E

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**From:** Mark Edwards <medwards@biosciadvisors.com>
**Sent:** Saturday, January 20, 2018 1:27 AM
**To:** foiapa
**Subject:** FOIA Request

I would like to request access to Exhibits 10.17 and 10.18 to the Form S-1, filed by Aurora Biosciences Corp. on 3/14/1997. Confidential treatment was sought as to certain portions when initially filed with the Commission.

In the event that confidential treatment has not expired or has been extended, I further request that you send me the expiration date(s) from the relevant CT order(s) so I will know when I should resubmit my request.

I authorize up to $61 in search and retrieval fees. Please send the exhibit(s) by PDF if possible.

Sincerely,

Mark

Mark G Edwards
Managing Director
Bioscience Advisors
2855 Mitchell Dr., Suite 103
Walnut Creek, CA 94598
medwards@biosciadvisors.com
925 954-1397

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
STATION PLACE
100 F STREET, NE
WASHINGTON, DC 20549-2465

Office of FOIA Services

February 2, 2018

Mr. Mark G. Edwards
Bioscience Advisors
2855 Mitchell Dr., Suite 103
Walnut Creek, CA 94598

RE: Freedom of Information Act (FOIA), 5 U.S.C. § 552
Request No. 18-02095-E

Dear Mr. Edwards:

This letter is in response to your request, dated January 20, 2018 and received in this office on January 22, 2018, for Exhibits 10.17 and 10.18 to the Form S-1, filed by Aurora Biosciences Corp. on March 14, 1997.

The search for responsive records has resulted in the retrieval of 92 pages of records that may be responsive to your request. They are being provided to you with this letter.

If you have any questions, please contact me at fultonc@sec.gov or 202-551-8186. You may also contact me at foiapa@sec.gov or (202) 551-7900. You also have the right to seek assistance from Lizzette Katilius as a FOIA Public Liaison or contact the Office of Government Information Services (OGIS) for dispute resolution services. OGIS can be reached at 1-877-684-6448 or Archives.gov or via e-mail at ogis@nara.gov.

Sincerely,

Charlotte Fulton
FOIA Research Specialist

Enclosure

CONFIDENTIAL TREATMENT REQUESTED UNDER 17 C.F.R. SECTIONS 200.80(b)(4), 200.83 AND 230.406 * INDICATES OMITTED MATERIAL THAT IS THE SUBJECT OF A CONFIDENTIAL TREATMENT REQUEST THAT IS FILED SEPARATELY WITH THE COMMISSION

10.18

# LICENSE AGREEMENT

This AGREEMENT (the "Agreement") is effective as of the 2nd day of August, 1996 (the "Effective Date"), between California Institute of Technology, 1201 East California Boulevard, Pasadena, California 91125 ("CALTECH") and Aurora Biosciences Corporation, a Delaware corporation, having a principal place of business at 11149 North Torrey Pines Road, La Jolla, California 92037 (hereinafter called "LICENSEE").

WHEREAS, CALTECH has been engaged in basic research in biotechnology conducted for the National Institutes of Health ("NIH") under Grant No. GM 34236 between CALTECH and NIH;

WHEREAS, that research led to that United States provisional patent application described in Paragraph 1.6.2, which is owned by CALTECH;

WHEREAS, LICENSEE is desirous of obtaining, and CALTECH wishes to grant to LICENSEE, an exclusive license to the Licensed Patent Rights (as defined in Paragraph 1.6); and

WHEREAS, on an even date herewith LICENSEE and CALTECH have entered into a Stock Transfer Agreement pursuant to which CALTECH shall receive shares of LICENSEE's common stock.

NOW, THEREFORE, the parties agree as follows:

## ARTICLE I

## DEFINITIONS

1.1 "Confidential Information" means (i) any proprietary or confidential information or material in tangible form disclosed hereunder that is marked as "Confidential" at the time it is delivered to the receiving party, or (ii) proprietary or confidential information disclosed orally hereunder which is identified as confidential or proprietary when disclosed and such disclosure of confidential information is confirmed in writing within thirty (30) days by the disclosing party. To protect the confidentiality of such information, LICENSEE may request the Principal Investigator, who has the right to refuse to accept such information, to sign a confidentiality agreement with LICENSEE in the form of Exhibit B hereto.

1.2 "Dominating Patent" means an unexpired patent that has not been invalidated by a court or governmental agency which is owned by a third party under circumstances such that the LICENSEE or its sublicensee has no commercially reasonable alternative to obtaining a royalty-bearing license under such patent in order to practice the Licensed Methods or make, use, sell or otherwise commercialize Licensed Products.

1.3 "Field" means screening for the identification of drug or agrochemical development candidates.



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1.4 "Licensed Method" means any method, procedure, or process, the use of which is covered by any Valid Claim.

1.5 "Licensed Product" means any product, device, or system which is covered by, or is made by a process covered by, any Valid Claim of any Licensed Patent Rights in the country such product, device, or system is made or sold.

1.6 "Licensed Technology" means Licensed Know-How and Licensed Patent Rights.

1.6.1 "Licensed Know-How" means all information and data, processes, formulas, and materials, including but not limited to those which relate to nucleic acid constructions, genes, DNA or RNA fragments, gene sequences, bacterial or yeast strains, mammalian cell lines, biological material, chemical compounds, proteins, products, substances, experimental plans, formulations, techniques, methods, designs, and drawings which are conceived, reduced to practice, or otherwise developed (i) in the laboratory of Dr. Melvin I. Simon ("Dr. Simon"), a faculty member CALTECH, or by Dr. Simon or another person employed by or affiliated with CALTECH who is working under Dr. Simon's supervision, or (ii) jointly by any of the foregoing and any person employed by or affiliated with LICENSEE, and which are specifically and directly related to experiments or embodiments of inventions covered by or within the scope of a Valid Claim of the Licensed Patent Rights.



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I.6.2 "Licensed Patent Rights" means (i) U.S. provisional patent application 60/001,978, filed July 31, 1995, and entitled "GA15 and GA16 Couple A Wide Variety of Receptors to Phospholipase C"; (ii) any patent application claiming an invention useful in the Field which is conceived, reduced to practice, or otherwise developed on or before the third anniversary of the Effective Date in Dr. Simon's laboratory or by Dr. Simon and/or another person employed by or affiliated with CALTECH who is working under Dr. Simon's supervision; (iii) any patent application claiming an invention useful in the Field which is conceived, reduced to practice, or otherwise developed on or before the third anniversary of the Effective Date in jointly by Dr. Simon and/or another person employed by or affiliated with CALTECH who is working under Dr. Simon's supervision and any person employed by or affiliated with LICENSEE; (iv) any substitution, provisional, regular utility application, division, or continuation (in whole or in part) claiming priority to any patent application in (i), (ii), or (iii); (v) any patent issuing on any of the preceding, including without limitation any reissue, re-examination, or extension; and (vi) any foreign patent application or patent claiming priority to any of the foregoing, including any confirmation, registration, revalidation, or addition.

I.7 "Related Company" means any corporation or other entity which is directly or indirectly controlling, controlled by, or under the common control with LICENSEE. For the purpose of this Agreement, "control" shall mean the direct or indirect ownership of at least fifty percent (50%) of the outstanding shares or other voting rights of the subject entity to elect directors, or if not meeting the preceding, any entity owned or controlled by or owning or controlling at the maximum control or ownership right permitted in the country where such



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entity exists.

I.8 "Stock Transfer Agreement" means that certain Stock Transfer Agreement entered into by the parties on an even date herewith, a copy of which is appended hereto as Exhibit A.

I.9 "Valid Claim" means a claim of (i) a pending patent application within the Licensed Patent Rights, or (ii) an issued and unexpired patent included within the Licensed Patent Rights.

## ARTICLE II

## PATENT LICENSE GRANT

II.1 CALTECH hereby grants to LICENSEE an exclusive license under the Licensed Technology throughout the world to (i) practice the Licensed Methods and provide services entailing the practice thereof, and (ii) make, have made, use, have used, import, have imported, sell, offer for sale, and have sold and otherwise exploit Licensed Products in the Field. This license is subject to:

II.1.1 the reservation of CALTECH's right, on the part of itself and the Jet Propulsion Laboratory ("JPL"), to make, have made, and use Licensed Methods for noncommercial educational and research purposes, but not for sale, licensure, or other distribution to third parties;



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II.1.2 the rights of the U.S. Government under Title 35, United States Code, Sections 203-204, including but not limited to the grant to the U.S. Government of a nonexclusive, nontransferable, irrevocable, paid-up license to practice or have practiced any invention conceived or first actually reduced to practice in the performance of work under NIH Grant GM 34236 for or on behalf of the U.S. Government throughout the world; and

II.1.3 with respect to any technology developed after the effective date, the right of any third party which sponsors research in Dr. Simon's laboratory at CALTECH. It is understood and agreed that CALTECH will use all reasonable efforts to assist LICENSEE in obtaining an exclusive license or other transfer of such third party rights in and to the results and related intellectual property which arise from or in connection with the research sponsored by such third party.

II.2 This license is not transferable by LICENSEE except as provided in Paragraph 13.2, but LICENSEE shall have the right to grant and authorize nonexclusive and/or exclusive sublicenses hereunder, provided that LICENSEE shall furnish CALTECH within thirty (30) days of the execution thereof a true and complete copy of each sublicense and any changes or additions thereto. Any such sublicense (including, without limitation, any non-exclusive sublicense) shall remain in effect in the event of any termination of this Agreement.

II.3 The license granted herein, and the term of this Agreement, shall commence on the Effective Date and continue, unless terminated in accordance with the provisions of this Agreement, until the last of the patents within the Licensed Patent Rights expires.

II.4 LICENSEE shall have a paid-up option to acquire, upon mutually agreeable terms, a royalty bearing, exclusive or non-exclusive, world-wide license, including the right to sublicense, to make, have made, use, lease, and sell products and services embodying or produced through the use of any inventions, discoveries, or improvements in the Field conceived, reduced to practice or otherwise developed in Dr. Simon's laboratory at CALTECH in the period from the third anniversary of the Effective Date until the sixth anniversary of the Effective Date, subject to the rights of any third party which sponsors research in Dr. Simon's laboratory at CALTECH. Said option must be exercised by written notice to CALTECH within six (6) months after receiving from CALTECH written notice of the filing of a patent application with respect thereto. If LICENSEE elects to exercise its option to acquire a license on mutually agreeable terms within the prescribed time period, both parties agree to negotiate license terms in good faith. All such negotiations, including the execution of a license agreement, shall be completed within six (6) months of written notice to CALTECH of LICENSEE's exercise of said option. If LICENSEE fails to agree to terms and conditions within the six (6) month time period, LICENSEE shall be deemed to have waived said option, and CALTECH shall be free to license a third party; provided, however, that for a period of three (3) years after written notice of LICENSEE's exercise of its option to any such invention, discovery, or improvement, CALTECH shall not agree to license a third party on more favorable terms than were last offered to LICENSEE without first offering



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LICENSEE a license on those more favorable terms and providing LICENSEE with ninety (90) days in which to accept such offer. If LICENSEE fails to notify CALTECH within the ninety (90) days that it has accepted such terms, LICENSEE shall be deemed to have rejected the offer, and CALTECH shall, thereafter, be free to license its rights in such invention, discovery, or improvement to other parties. If LICENSEE notifies CALTECH within the ninety (90) days that it accepts such an offer, CALTECH shall be deemed to have entered into a binding license agreement with LICENSEE with respect to such terms.

## ARTICLE III

## USE OF NAME

III.1 LICENSEE agrees that it shall not use the name of CALTECH, the California Institute of Technology, the Jet Propulsion Laboratory, or JPL in any advertising or publicity material, or make any form of representation or statement which would constitute an express or implied endorsement by CALTECH of any Licensed Product, and that it shall not authorize others to do so, without first having obtained written approval from CALTECH. LICENSEE may make further disclosures containing information previously approved for release by CALTECH without any need for further approvals by CALTECH.

III.2 Notwithstanding Paragraph 3.1, LICENSEE may make such disclosures as may be required by law or court order, and disclose to its professional advisors and actual and prospective investors that it has entered into this Agreement with CALTECH.

ARTICLE IV

DUE DILIGENCE

IV.1 LICENSEE shall have discretion over the commercialization of Licensed Methods and Licensed Products. LICENSEE shall be deemed to have satisfied its obligations under this Paragraph if LICENSEE has an ongoing and active research program or marketing program, as appropriate, directed toward the use of Licensed Methods in the Field. Any efforts of LICENSEE's sublicensees shall be considered efforts of LICENSEE for the purpose of determining LICENSEE's compliance with its obligation under this Paragraph.

IV.2 After the first year from the Effective Date, CALTECH shall have the right, exercisable no more often than twice each year, to require LICENSEE to report to CALTECH in writing on its progress in using Licensed Methods in the United States.

ARTICLE V

INFRINGEMENT BY THIRD PARTY

V.1 CALTECH shall, at its expense, have the initial right, but not the obligation, to protect Licensed Technology solely owned by CALTECH from infringement or misappropriation and prosecute infringers or others when, in its sole judgment, such action may be reasonably necessary, proper, and justified. Notwithstanding the foregoing, LICENSEE shall have the right to



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sublicense any alleged infringer pursuant to Paragraph 2.2. LICENSEE shall, at its expense, have the initial right, but not the obligation, to protect Licensed Technology jointly owned by CALTECH and LICENSEE from infringement or misappropriation and prosecute infringers or others when, in its sole judgment, such action may be reasonably necessary, proper, and justified.

V.2 If LICENSEE shall have supplied CALTECH with evidence of infringement or misappropriation by a third party of Licensed Technology solely owned by CALTECH, LICENSEE may by notice request CALTECH to take steps to enforce such Licensed Technology. If LICENSEE does so, and CALTECH does not, within three (3) months of the receipt of such notice, either (i) cause the infringement or misappropriation to terminate or (ii) initiate a legal action against the infringer or misappropriating third party, LICENSEE may, upon notice to CALTECH, initiate an action against the infringer or misappropriating third party at LICENSEE's expense, either in LICENSEE's name or in CALTECH's name if so required by law. If LICENSEE does so for infringement or misappropriation within the Field, LICENSEE shall have sole control of the action.

V.3 If a declaratory judgment action alleging invalidity, unenforceability, or noninfringement of any of the Licensed Patent Rights is brought against LICENSEE and/or CALTECH, LICENSEE shall have sole control of the action if LICENSEE agrees to bear all the costs of the action.

V.4 In the event one party shall carry on a legal action pursuant to Paragraph 5.2 or 5.3, the other party shall fully cooperate with and supply all assistance reasonably requested by the

party carrying on such action, including by using its best efforts to have its employees testify when requested and to make available relevant records, papers, information, samples, specimens, and the like. A party controlling an action pursuant to Paragraph 5.2 or 5.3 shall bear the reasonable expenses incurred by said other party in providing such assistance and cooperation as is requested pursuant to this Paragraph. A party controlling such an action shall keep the other party informed of the progress of such action, and said other party shall be entitled to be represented by counsel in connection with such action at its own expense.

V.5 The party controlling any action referred to in this Article V shall have the right to settle any claim, but only upon terms and conditions that are reasonably acceptable to the other party. Should either party elect to abandon such an action other than pursuant to a settlement with the alleged infringer that is reasonably acceptable to the other party, the party controlling the action shall give timely notice to the other party who, if it so desires, may continue the action; provided, however, that the sharing of expenses and any recovery in such suit shall be as agreed upon between the parties.

V.6 Any amounts paid to a party hereto by a third party as the result of such an action (such as in satisfaction of a judgment or pursuant to a settlement) shall first be applied to reimbursement of the unreimbursed expenses (including, without limitation, attorneys' and expert fees) incurred by either party. Any remainder shall be divided between the parties as follows:

V.6.1 To the extent the amount recovered reflects lost profits or a reasonable royalty, LICENSEE shall retain the remainder, and

V.6.2 To the extent the amount recovered constitutes damages for wilful infringement, sixty percent (60%) shall be paid to the party initiating the action and forty percent (40%) to the other party.

ARTICLE VI

ALLEGATION OF INFRINGEMENT AGAINST LICENSEE

VI.1 If the practice by LICENSEE of the license granted herein results in any allegation or claim of infringement of an intellectual property right of third party against LICENSEE, LICENSEE shall have the exclusive right to defend any such claim, suit, or proceeding, at its own expense, by counsel of its own choice, and shall have the sole right and authority to settle any such suit; provided, however, that CALTECH shall cooperate with LICENSEE, at LICENSEE's reasonable request, in connection with the defense of such claim.

ARTICLE VII

PAYMENT OF PATENT COSTS

VII.1 Starting from the Effective Date, LICENSEE shall, in connection with the preparation, filing, prosecution, issuance, and maintenance of the Licensed Patent Rights both in the United States and foreign jurisdictions:



CONFIDENTIAL TREATMENT REQUESTED

VII.1.1 pay all reasonable attorneys fees for services performed to obtain the issuance of the Licensed Patent Rights, and all patent and government fees for services performed after the issuance of Licensed Patent Rights, and

VII.1.2 pay all domestic and foreign patent office maintenance fees.

VII.2 Payment shall be made to CALTECH within thirty (30) days following receipt by LICENSEE from CALTECH of (i) an invoice covering such fees and (ii) evidence reasonably satisfactory to LICENSEE that such fees were paid. To the extent that LICENSEE terminates this Agreement pursuant to Paragraph 9.1, LICENSEE shall have no further liability under Paragraph 7.1 for fees relating to applications or patents affected by the termination.

VII.3 CALTECH shall apply for, prosecute, and maintain during the term of this Agreement the Licensed Patent Rights; provided, however, that LICENSEE shall have reasonable opportunity to advise and consult with CALTECH on such matters and may instruct CALTECH to take such action as LICENSEE reasonably believes necessary to protect the Licensed Patent Rights. The preparation, filing, prosecution, maintenance, and payment of all fees and expenses, including legal fees, relating to such Licensed Patent Rights shall be the responsibility of CALTECH, provided that LICENSEE shall reimburse CALTECH for all reasonable fees and expenses, including reasonable legal fees, incurred by CALTECH in such application preparation filing, prosecution, and maintenance preparation, as provided in Paragraph 7.1. Patent attorneys

chosen by CALTECH and acceptable to LICENSEE shall handle all patent preparation, filing, prosecution, and maintenance on behalf of CALTECH; provided, however, that LICENSEE shall be entitled to review and comment upon and approve all actions undertaken in the prosecution of all patents and applications. Patent counsel shall concurrently provide CALTECH and LICENSEE with copies of all material correspondence related to the prosecution and maintenance of the patent applications and patents within the Licensed Patent Rights. In the event CALTECH declines to apply for, prosecute, or maintain any Licensed Patent Rights as requested by LICENSEE, LICENSEE shall have the right to pursue the same in CALTECH's name and at LICENSEE's expense, and CALTECH shall give sufficient and timely notice to LICENSEE so as to permit LICENSEE to apply for, prosecute, and/or maintain such Licensed Patent Rights.

## ARTICLE VIII

## CONFIDENTIALITY

VIII.1 Dr. Simon shall provide to LICENSEE copies of any proposed publication or abstract relating to Licensed Technology prior to the submission of such documents. Proposed publications and abstracts shall be supplied at least thirty (30) days in advance of submission to a journal, editor, or third party. In addition, if Dr. Simon submits a copy of the proposed publication to LICENSEE less than thirty (30) days prior to submission for publication, then LICENSEE can request CALTECH to file, at CALTECH's expense, a provisisonal patent application enabling the technology disclosed in the proposed publication at the United States Patent and Trademark Office, and shall provide LICENSEE with evidence of the filing of such provisional patent

application. All such documents are to be forwarded to the address given in Paragraph 13.8. LICENSEE may request reasonable changes and/or deletions be made in any proposed publication. The Principal Investigator will consider such changes but retains the sole right to determine whether such changes or deletions will be made. Dr. Simon agrees that he will honor LICENSEE's reasonable requests to remove Confidential Information of LICENSEE included in any such public disclosure. If LICENSEE believes that the subject matter to be published warrants patent protection, it will identify the subject matter requiring protection and notify CALTECH. CALTECH agrees to use its best efforts to file a U.S. patent application prior to any date that would result in preventing the obtaining of valid patent rights throughout the world when LICENSEE so identifies subject matter requiring patent protection from a review of the planned publication. Notwithstanding any other provision of this Paragraph 8.1, if CALTECH is unable to file a U.S. patent application in accordance with the preceding sentence, CALTECH shall file a U.S. provisional patent application prior to the date that would result in preventing the obtaining of valid patent rights throughout the world when LICENSEE so identifies subject matter requiring patent protection from a review of a planned publication.

VIII.2 Except as expressly provided herein, each party agrees not to disclose any terms of this Agreement to any third party without the consent of the other party; provided, however, that disclosures may be made as required by securities or other applicable laws, or to actual or prospective investors or corporate partners, or to a party's accountants, attorneys, and other professional advisors.

## ARTICLE IX

## TERMINATION

IX.1 If either party materially breaches this Agreement, the other party may elect to give the breaching party written notice describing the alleged breach. If the breaching party has not cured such breach within sixty (60) days after receipt of such notice, the notifying party will be entitled, in addition to any other rights it may have under this Agreement, to terminate this Agreement effective immediately; provided, however, that if either party receives notification from the other of a material breach and if the party alleged to be in default notifies the other party in writing within thirty (30) days of receipt of such default notice that it disputes the asserted default, the matter will be submitted to arbitration as provided in Article XI of this Agreement. In such event, the nonbreaching party shall not have the right to terminate this Agreement until it has been determined in such arbitration proceeding that the other party materially breached this Agreement, and the breaching party fails to cure such breach within ninety (90) days after the conclusion of such arbitration proceeding.

IX.2 LICENSEE shall have the right to terminate this Agreement either in its entirety or as to any jurisdiction or any part of the Licensed Technology upon sixty (60) days written notice.

IX.3 Termination of this Agreement for any reason shall not release any party hereto from any liability which, at the time of such termination, has already accrued to the other party or

which is attributable to a period prior to such termination, nor preclude either party from pursuing any rights and remedies it may have hereunder or at law or in equity which accrued or are based upon any event occurring prior to such termination.

IX.4 In the event of any termination of this Agreement, it is understood that LICENSEE shall retain its ownership interest in any jointly owned intellectual property within the Licensed Technology and shall have the right to exploit the same for any purpose without having to account to CALTECH therefor.

IX.5 The last sentence of Paragraph 2.2, Paragraphs 9.3, 9.4, and 9.5, and Articles III, VIII, XI, XII, and XIII of this Agreement shall survive termination of this Agreement for any reason.

## ARTICLE X

## WARRANTIES AND NEGATION OF WARRANTIES, IMPLIED LICENSES AND AGENCY

X.1 CALTECH represents and warrants that: (i) it owns all right, title, and interest in and to the Licensed Technology, subject to the license and march-in rights of the United States Government under Title 35, United States Code, Sections 203-204, and ARPA Grant No. MDA972-93-1-0009, except as for such right, title, and interest as may be owned by LICENSEE; (ii) it has complied with all of its obligations under NIH Grant No. GM 34236, such as those described in Title 35, United States Code, Section 202, with respect to all of the Licensed

Patent Rights; (iii) it has not granted and during the term of this Agreement will not grant any right or interest in any of the Licensed Technology that is inconsistent with the rights granted to LICENSEE herein; (iv) the execution, delivery, and performance of this Agreement have been duly authorized by all necessary corporate action on the part of CALTECH; (v) it is the sole and exclusive owner of all right, title, and interest in the Licensed Technology, except for such right, title, and interest therein as may be owned by LICENSEE; (vi) it has the right to grant the rights and licenses granted herein, and the Licensed Technology is free and clear of any lien, encumbrance, security interest, or restriction on license; and (vii) there are no threatened or pending actions, suits, investigations, claims, or proceedings in any way relating to the Licensed Technology.

X.2 Nothing in this Agreement shall be construed as:

X.2.1 a representation or warranty of CALTECH as to the validity or scope of Licensed Patent Rights or any claim thereof; or

X.2.2 a representation or warranty that any Licensed Product is or will be free from infringement of rights of third parties; or

X.2.3 an obligation to bring or prosecute actions or suits against third parties for infringement; or

X.2.4 conferring by implication, estoppel, or otherwise any license or rights under any patents of CALTECH other than Licensed Patent Rights, regardless of whether such other patents are dominant or subordinate to the Licensed Patent Rights.

X.3 CALTECH MAKES NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, AND ASSUMES NO RESPONSIBILITIES WHATEVER WITH RESPECT TO THE USE, SALE, OR OTHER DISPOSITION BY LICENSEE OF LICENSED PRODUCT(S).

## ARTICLE XI

## ARBITRATION

XI.1 CALTECH and LICENSEE agree that any dispute or controversy arising out of, in relation to, or in connection with this Agreement, or the validity, enforceability, construction, performance or breach hereof, shall be settled by binding arbitration in Los Angeles, California, United States of America, under the then-current Commercial Arbitration Agreement Rules of the American Arbitration Association by one (1) arbitrator appointed in accordance with such Rules. The arbitrators shall determine what discovery will be permitted, based on the principle of limiting the cost and time which the parties must expend on discovery; provided, however, that the arbitrator shall permit such discovery as he/she deems necessary to achieve an equitable resolution of the dispute. The decision and/or award rendered by the arbitrator shall be written, final, and

non-appealable and may be entered in any court of competent jurisdiction. The parties agree that, any provision of applicable law notwithstanding, they will not request, and the arbitrator shall have no authority to award, punitive or exemplary damages against any party. The costs of any arbitration, including administrative fees and fees of the arbitrator, shall be shared equally by the parties. Each party shall bear the cost of its own attorneys' fees and expert fees.

## ARTICLE XII

## PRODUCT LIABILITY

XII.1 LICENSEE agrees that CALTECH shall have no liability to LICENSEE or to any purchasers or users of Licensed Products made or sold by LICENSEE or its sublicensees for any claims, demands, losses, costs, or damages suffered by LICENSEE, or purchasers or users of Licensed Products, or any other party, which may result from personal injury, death, or property damage related to the manufacture, use, or sale of such Licensed Products ("Claims"). LICENSEE agrees to defend, indemnify, and hold harmless CALTECH, its trustees, officers, agents, and employees from any such Claims, provided that (i) LICENSEE is notified promptly of any Claims, (ii) LICENSEE has the sole right to control and defend or settle any litigation within the scope of this indemnity, and (iii) all indemnified parties cooperate fully in the defense of any Claims. No indemnified party shall voluntarily make any payment or incur any expense with respect to any claims without the prior written consent of LICENSEE.

XII.2 At such time as LICENSEE begins to sell or distribute or sublicense Licensed Products (other than for the purpose of obtaining regulatory approvals) based upon use of Licensed Methods, LICENSEE shall, at its sole expense, procure and maintain policies of comprehensive general liability insurance in amounts not less than $2,000,000 per incident and $2,000,000 in annual aggregate and naming those indemnified under Paragraph 12.1 as additional insureds. Such comprehensive general liability insurance shall provide (i) product liability coverage and (ii) broad form contractual liability coverage for LICENSEE's indemnification under Paragraph 12.1. In the event the aforesaid product liability coverage does not provide for occurrence liability, LICENSEE shall maintain such comprehensive general liability insurance for a reasonable period of not more than seven (7) years after it has ceased commercial distribution or use of any Licensed Product or Licensed Method.

XII.3 LICENSEE shall provide CALTECH with written evidence of such insurance upon request of CALTECH. LICENSEE shall provide CALTECH with notice at least fifteen (15) days prior to any cancellation, non-renewal, or material change in such insurance, to the extent LICENSEE receives advance notice of such matters from its insurer. If LICENSEE does not obtain replacement insurance providing comparable coverage within sixty (60) days following the date of such cancellation, non-renewal, or material change, CALTECH shall have the right to terminate this Agreement effective at the end of such sixty (60) day period without any additional waiting period; provided, however, that if LICENSEE uses reasonable efforts but is unable to obtain the required insurance at commercially reasonable rates, CALTECH shall not have the right to terminate this Agreement, and CALTECH instead shall cooperate with LICENSEE to either

grant a waiver of LICENSEE's obligations under this Article XII, assist LICENSEE in identifying a carrier to provide such insurance, or in developing a program for self-insurance or other alternative measures.

## ARTICLE XIII

## MISCELLANEOUS

XIII.1 This Agreement sets forth the complete agreement of the parties concerning the subject matter hereof. No claimed oral agreement in respect thereto shall be considered as any part hereof. No waiver of or change in any of the terms hereof subsequent to the execution hereof claimed to have been made by any representative of either party shall have any force or effect unless in writing, signed by duly authorized representatives of the parties.

XIII.2 This Agreement shall be binding upon and inure to the benefit of any successor or assignee of CALTECH. This Agreement is not assignable by LICENSEE without the prior written consent of CALTECH, except that LICENSEE may assign this Agreement without the prior written consent of CALTECH to (i) any Related Company, or (ii) any successor or purchaser of a substantial part of the assets of the business to which this Agreement pertains. Any permitted assignee shall succeed to all of the rights and obligations of LICENSEE under this Agreement.

XIII.3 CALTECH and LICENSEE are independent parties in this Agreement. Accordingly, there is no agency relationship between CALTECH and LICENSEE under this

Agreement with respect to any products made or sold, or any methods used, by LICENSEE under this Agreement.

XIII.4 Nothing in this Agreement will impair LICENSEE's right to independently acquire, license, develop for itself, or have others develop for it, intellectual property and technology performing similar functions as the Licensed Technology or to market and distribute products other than Licensed Products based on such other intellectual property and technology.

XIII.5 NEITHER PARTY SHALL BE LIABLE TO THE OTHER FOR ANY SPECIAL, CONSEQUENTIAL, INCIDENTAL, OR INDIRECT DAMAGES ARISING OUT OF THIS AGREEMENT, HOWEVER CAUSED, UNDER ANY THEORY OF LIABILITY.

XIII.6 This Agreement is subject in all respects to the laws and regulations of the United States of America, including the Export Administration Act of 1979, as amended, and any regulations thereunder.

XIII.7 This Agreement shall be deemed to have been entered into in California and shall be construed and enforced in accordance with California law.

XIII.8 Any notice or communication required or permitted to be given or made under this Agreement shall be addressed as follows:

CALTECH: Office of Technology Transfer

California Institute of Technology
1201 East California Boulevard (MC 315-6)
Pasadena, California 91125
FAX No.: (818) 577-2528

LICENSEE: Aurora Biosciences Corporation
11149 Torrey Pines Road
La Jolla, CA 92037
Phone No.: (619) 452-5000
FAX No.: (619) 452-5723

Either party may notify the other in writing of a change of address or FAX number, in which event any subsequent communication relative to this Agreement shall be sent to the last said notified address or number. All notices and communications relating to this Agreement shall be deemed to have been given when received.

XIII.9 Neither party shall lose any rights hereunder or be liable to the other party for damages or losses (except for payment obligations) on account of failure of performance by the defaulting party if the failure is occasioned by war, strike, fire, Act of God, earthquake, flood, lockout, embargo, governmental acts or orders or restrictions, failure of suppliers, or any other reason where failure to perform is beyond the reasonable control and not caused by the negligence or intentional conduct or misconduct of the nonperforming party, and such party has exerted all reasonable efforts to avoid or remedy such force majeure; provided, however, that in no event shall a party be required to settle any labor dispute or disturbance.

XIII.10 In the event that any provisions of this Agreement are determined to be invalid or unenforceable by a court of competent jurisdiction, the remainder of the Agreement shall remain in full force and effect without said provision. The parties shall in good faith

negotiate a substitute clause for any provision declared invalid or unenforceable, which shall most nearly approximate the intent of the parties in entering this Agreement.

XIII.11 This Agreement may not be altered, amended, or modified in any way except by a writing signed by both parties. The failure of a party to enforce any provision of the Agreement shall not be construed to be a waiver of the right of such party to thereafter enforce that provision or any other provision or right.

IN WITNESS WHEREOF, the parties have caused this Agreement to be executed:

CALIFORNIA INSTITUTE OF TECHNOLOGY
(CALTECH)

Date: 8/29/96

By: Lawrence Gilbert
Name: Lawrence Gilbert
Title: Director, Office of Technology Transfer

AURORA BIOSCIENCES CORPORATION

Date: 8/7/96

By: Tim Rink
Name: Tim Rink
Title: President and CEO

CONFIDENTIAL TREATMENT REQUESTED UNDER 17 C.F.R. SECTIONS 200.80(b)(4), 200.83 AND 230.406 * INDICATES OMITTED MATERIAL THAT IS THE SUBJECT OF A CONFIDENTIAL TREATMENT REQUEST THAT IS FILED SEPARATELY WITH THE COMMISSION

10.17

# Exclusive License Agreement

between

The Regents of the University of California

and

Aurora Biosciences, Corp.

for

Fluorescent Assay Technologies

U.C. Case Nos. 93-289, 95-110, 95-219, 96-044, 96-160, 96-161, 96-162, 96-191

U. C. AGREEMENT CONTROL NUMBER 96-04-0769

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# Exclusive License Agreement
# for
# Fluorescent Assay Technologies

This license agreement ("Agreement") is effective this 17th day of June, 1996, (the Effective Date") by and between The Regents of the University of California ("The Regents"), a California corporation, having its statewide administrative offices at 300 Lakeside Drive, 22nd Floor, Oakland, California 94612-3550 and Aurora Biosciences Corporation ("Licensee"), a Delaware corporation, having a principal place of business at 11149 North Torrey Pines Road, La Jolla, CA 92037.

## Recitals

Whereas, certain inventions, generally characterized as fluorescent assay technologies, including DNA encoding a green fluorescent protein and fluorogenic substrates for Beta-lactamase ("Inventions"), useful for cell screening, were made at the University of California, San Diego ("UCSD") by Dr. Roger Tsien, et al., and are claimed in Patent Rights or within the Property Rights as defined below;

Whereas, Licensee entered into secrecy agreements ("Secrecy Agreements") with The Regents covering UC Case Nos. 93-289 on August 10, 1994; 95-110 on January 1, 1995; 96-160, 96-161, 96-162 on December 8 1995; and 96-191 on February 22, 1996 for the purpose of evaluating the Invention;



* CONFIDENTIAL TREATMENT REQUESTED

U. C. AGREEMENT
CONTROL NUMBER
96-04-0769

Whereas, Licensee entered into an option agreement ("Option Agreement") with The Regents on June 1, 1995 and ending on December 1, 1995 in order to evaluate its commercial interest in the Invention;

Whereas, Licensee entered into a letter agreement with The Regents on March 6, 1996 covering certain negotiated provisions that are contained in this Agreement and a letter agreement with The Regents on April 26, 1996, with respect to the Biological Materials ("Letter Agreements");

Whereas, the Invention was made under research funding provided in part by the Department of Health and Human Services (DHHS) and in part by the Howard Hughes Medical Institute (HHMI), and as a consequence, this Agreement is subject to overriding obligations to the federal government and to HHMI;

Whereas, under 35 USC §200-212, The Regents may elect to retain title to any invention (including the Invention) made by it under U.S. Government funding;

Whereas, if The Regents elects to retain title to the Invention, then the law requires that The Regents grant to the U.S. Government a nontransferable, paid-up, nonexclusive, irrevocable license to use the Invention by or on behalf of the U.S. Government throughout the world;

Whereas, The Regents elected to retain title to the Invention covered by UC Case Nos. [93-289] on November 19, 1993; [95-110] on February 5, 1996; [95-219] on October 25, 1995; and [96-161] and [96-191] on January 8, 1996, and granted the required licenses to the U.S. Government;

Whereas, The Regents has acquired the right to grant this license from the Howard Hughes Medical Institute (HHMI) under the terms of the interinstitutional agreement ("Interinstitutional Agreement"), having UC Control No. 86-18-0017;



* CONFIDENTIAL TREATMENT REQUESTED

Whereas, The Regents is required under the terms of Interinstitutional Agreement to grant to the HHMI a paid-up, non-exclusive, irrevocable license to use the Invention for its non-commercial purposes, but with no right to sublicense;

Whereas, the Licensee is a "small entity" as defined in 37 CFR §1.9 and a "small-business concern" defined in 15 U.S.C. §632;

Whereas, it is the intent of the parties to this Agreement to create a bailment (as provided for in Sections 2.2, 2.3 and 2.4 herein), among other things, for the Biological Materials as defined below subject to Licensee's rights as set forth herein;

Whereas, both parties recognize that royalties due under this Agreement will be paid on pending patent applications and issued patents;

Whereas, Licensee requested certain rights from The Regents to commercialize the Invention; and

Whereas, The Regents responded to the request of Licensee by granting the following rights to Licensee so that the products and other benefits derived from the Invention can be enjoyed by the general public.

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The parties agree as follows:

## 1. Definitions

As used in this Agreement, the following terms will have the meaning set forth below:

1.1. "Patent Rights" means all U.S. patents and patent applications and foreign patents and patent applications assigned to The Regents, and in the case of foreign patents and patent applications, those requested under Section 16.4 herein, including any reissues, extensions, substitutions, continuations, divisions, and continuation-in-part applications (only to the extent, however, 1) that such continuation-in-part applications are covered in Section 1.1.9 below; or 2) that claims in the continuation-in-part applications are entitled to the priority filing date of one or more of the following patent applications listed in Sections 1.1.1 through 1.1.8 below) based on and including any subject matter claimed in or covered by the following:

X 1.1.1. Pending U.S. Patent Application Serial No. 08/337,915, entitled "Modified Green Fluorescent Proteins," filed November 10, 1994, by Dr. Roger Tsien, et al. and assigned to The Regents (UC Case No. 93-289-1);

X 1.1.2. Pending U.S. Patent Application Serial No. 08/407,544 entitled "Fluorogenic Substrates for Beta-Lactamase and Their Use in Assaying Reporter Gene Expression, Protein Localization, and Bacterial Resistance," filed March 20, 1995, by Dr. Roger Tsien, et al. and assigned to The Regents (UC Case No. 95-110-1);

X 1.1.3. Pending U.S. Patent Application Serial No. 08/481,977 entitled "Voltage Sensing by Resonance Energy Transfer," filed June 7, 1995, by Dr. Roger Tsien, et al. and assigned to The Regents (UC Case No. 95-219-1);

X 1.1.4. Pending PCT Application Serial No. PCT/US95/14692 entitled "Modified Green Fluorescent Proteins," filed November 10, 1995, by Dr. Roger Tsien, et al. and assigned to The Regents (UC Case No. 96-044-1);

X 1.1.5. Pending U.S. Patent Application Serial No. 08/481,977 entitled "Tandem Fluorescent Protein Constructs," filed January 31, 1996, by Dr. Roger Tsien, et al. and assigned to The Regents (UC Case No. 96-160-1);

X 1.1.6. Any U.S. Patent Application based on subject matter described in UC Case Number 96-161-1, entitled "Beta-Lactamase Substrates for

Assay of Bacterial Resistance and Gene Expression," disclosed by Dr. Roger Tsien, et al. and assigned to The Regents; and

1.1.7. Any U.S. Patent Application based on subject matter described in UC Case Number 96-162-1, entitled "Fluorescent Protein Substrates for Protein Kinases," disclosed by Dr. Roger Tsien, et al. and assigned to The Regents; and

1.1.8. Any U.S. Patent Application based on subject matter described in UC Case Number 96-191-1, entitled "Indicators That Memorize Analytes," disclosed by Dr. Roger Tsien, et al. and assigned to The Regents.

1.1.9. any continuation-in-part applications that are filed by June 30, 1996, where such continuation-in-part applications disclosed Inventions at UCSD and name Roger Tsien or an employee of The Regents in Roger Tsien's laboratory at UCSD as an inventor, and are based on one or more of the patent applications described in Sections 1.1.1 through 1.1.8 immediately above.

1.2. "Biological Materials" means (i) the chemical reagents and biological materials owned by The Regents and listed in Appendix D attached hereto and provided to Licensee by The Regents pursuant to the April 26, 1996 Letter Agreement, and (ii) any other chemical reagents or biological materials elected for inclusion under this Agreement by Licensee pursuant to Section 2.11 below.

1.3. "Biological Product" means any product containing: (a) a plasmid, a protein structure, a cDNA clone, a promoter, a gene or a chimeric gene, antibodies, or fragments thereof and their sequences derived from or containing the Biological Materials; (b) any protein structure produced or encoded by the Biological Materials; or (c) a compound (substantially similar or identical to a compound in (a) or (b) above), produced by chemical synthesis or by any other method which could not have been produced but for the use of the Biological Materials. Biological Products may either be Patent Products or Proprietary Products.

1.4. "Identified Product" means any product, compound, biological agent, or other material not claimed by the Patent Rights and not comprising a Biological

Product, but identified by Licensee or a sublicensee using the Biological Materials or Biological Products.

1.5. "Patent Products" means:

1.5.1. any kit, composition of matter, material, product, or Biological Product;

1.5.2. any kit, composition of matter, material, product, or Biological Product to be used in a manner requiring the performance of the Patent Method; or

1.5.3. any kit, composition of matter, material, product, or Biological Product produced by the Patent Method;

the extent that the manufacture, use, or sale of such kit, composition of matter, material, product, or Biological Product, in a particular country, would be covered by or infringe, but for the license granted to Licensee pursuant to this Agreement, an unexpired claim of a patent or pending claim of a patent application were it issued as a claim in a patent under Patent Rights in that country in which such patent has issued or application is pending.

1.6. "Patent Method" means any process or method covered by the claims of a patent application or patent within Patent Rights or the use or practice of which would constitute in a particular country, but for the license granted to Licensee pursuant to this Agreement, an infringement of an unexpired claim of a patent or pending claim of a patent application were it issued as a claim in a patent within Patent Rights in that country in which the Patent Method is used or practiced.

1.7. "Proprietary Products" means any kit, composition of matter, material, or product containing a Biological Product, the manufacture, use, or sale of which in a particular country is not within an unexpired, valid claim of a patent or a pending claim of a patent application under Patent Rights in such country.

1.8. "Products" means Patent Products, Identified Product, Proprietary Products, and Services.

1.9. "Property Rights" means all personal proprietary rights of The Regents covering the tangible personal property in the Biological Materials. In no case, however, will Property Rights include Patent Rights.

1.10. "Research Reagent" means the Biological Materials listed in Appendix E hereto, and such further Biological Materials as Licensee may elect to sell, in each case, as reagents for research applications, labeled for experimental use only and not for use in humans. A Research Reagent may be a Patent Product or a Proprietary Product.

1.11. "Net Sales" means the gross invoice prices from the sale of Products, subject to Sections 4.1.1b through 4.1.1d, by Licensee, an Affiliate, a Joint Venture, or a sublicensee to independent third parties for cash or other forms of consideration in accordance with generally accepted accounting principles limited to the following deductions (if not already deducted from the gross invoice price and at rates customary within the industry): (a) allowances (actually paid and limited to rejections, returns, and prompt payment and volume discounts granted to customers of Products, whether in cash or Products in lieu of cash); (b) freight, transport packing, insurance charges associated with transportation; and (c) taxes, tariff, or import/export duties based on sales when included in gross sales, but not value-added taxes or taxes assessed on income derived from such sales. Where Licensee distributes Products to an Affiliate, a Joint Venture, or a sublicensee for end use by such Affiliate, Joint Venture, or sublicensee, then such distribution will be considered a sale at list price normally charged to independent third parties, and The Regents will be entitled to collect a royalty on such sale in accordance with Article 4. (Royalties).

1.12. "Services" means services provided by Licensee or its sublicensees to its customers when such services require the use of the Patent Rights or Property Rights.

1.13. "Service Revenues" means revenues paid to Licensee or its sublicensees for Services.



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1.14. "Affiliate(s)" of Licensee means any entity which, directly or indirectly, controls Licensee, is controlled by Licensee, or is under common control with Licensee ("control" for these purposes being defined as the actual, present capacity to elect a majority of the directors of such affiliate, or if not, the capacity to elect the members that control forty percent of the outstanding stock or other voting rights entitled to elect directors) provided, however, that in any country where the local law will not permit foreign equity participation of a majority, then an "Affiliate" will include any company in which Licensee will own or control, directly or indirectly, the maximum percentage of such outstanding stock or voting rights permitted by local law. Each reference to Licensee herein will be meant to include its Affiliates.

1.15. "Joint Venture" means any separate entity established pursuant to an agreement between a third party and Licensee to constitute a vehicle for a joint venture, in which the separate entity manufactures, uses, purchases, sells, or acquires Products from Licensee. Each reference to Licensee herein will be meant to include its Joint Venture(s).

## 2. Grant

2.1. Subject to the limitations set forth in this Agreement and subject to the license granted to the U.S. Government and to HHMI as set forth in the Recitals above, where Patent Rights exists, The Regents hereby grants to the Licensee an exclusive license under Patent Rights to (i) make, have made, and use the Biological Materials and Biological Products; (ii) to make, have made, use, import, offer for sale, and sell Patent Products; (iii) to practice the Patent Methods; and (iv) to provide Services to others.

2.2. Subject to the limitations set forth in this Agreement and subject to the licenses granted to the U.S. Government and to HHMI as set forth in the Recitals above, where The Regents may lawfully grant such a license, The Regents hereby



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grants to Licensee an exclusive license under the Property Rights to (i) make, have made, and use the Biological Materials and Biological Products, (ii) to make, have made, use, import, offer for sale, and sell Proprietary Products; and (iii) to provide Services to others.

2.3. Licensee acknowledges that title to the tangible material comprising the Biological Materials is owned by The Regents and is not transferred to Licensee under this Agreement, except that Licensee may transfer title of such Biological Materials as are sold as Biological Products or Research Reagents under the terms of this Agreement.

2.4. The licenses granted under Property Rights set forth in Section 2.2 above expressly limit the rights granted to Licensee to those licenses expressly stated in this Agreement and for no other purpose.

2.5. The licenses granted hereunder will be subject to the overriding obligations to the U.S. Government including those set forth in 35 U.S.C. §200-212 and applicable governmental implementing regulations.

2.6. The manufacture of Products and the practice of the Patent Method will be subject to applicable government importation laws and regulations.

2.7. The Regents also grants to Licensee the right to issue sublicenses under the rights granted in Sections 2.1 and 2.2 above to third parties, provided Licensee retains current exclusive rights thereto under this Agreement. To the extent applicable, such sublicenses will include all of the rights of and obligations due to The Regents (and, if applicable, the United States Government) that are contained in this Agreement including payment of fees and royalties at the rates provided for in Section 3.2 and Article 4. (Royalties).

2.8. Licensee will notify The Regents of each sublicense granted hereunder and provide The Regents with a copy of each sublicense, which shall be treated as

Proprietary Information of Licensee as defined in Article 29. (Confidentiality). Licensee will collect and pay all such fees and royalties due The Regents from sublicensees as set forth in Sections 3.2 and 4.1 below (and guarantee all such payments due from sublicensees). Licensee will require sublicensees to provide it with progress and royalty reports in accordance with the provisions herein, and Licensee will collect and deliver to The Regents all such reports due from sublicensees.

2.9. Upon termination of this Agreement for any reason, all sublicenses granted by Licensee in accordance with this Agreement will remain subject to the terms of such sublicenses in effect, and shall be assigned to and assumed by The Regents except that sublicenses which: (i) are in a state of breach as yet uncured by the sublicensee; or (ii) sublicenses which conflict with state, or federal law, or the previously established written policy of The Regents, shall not be assigned to and assumed by The Regents. The Regents will not be bound by any duties and obligations contained in the sublicenses that extend beyond the duties and obligations assumed by The Regents in this Agreement and shall have no right to receive any payment from such sublicensees except the amounts due under this Agreement for the activities of such sublicensees.

2.10. The Regents may, at its own discretion, disclose to Licensee certain chemical and biological materials relating to the Patent Rights and Property Rights that are developed in Dr. Roger Tsien's laboratory at UCSD. The Regents hereby grants to Licensee the right to elect to include under this Agreement any or all of such chemicals and biological materials.

2.11. In accordance with Section 2.10, Licensee will notify The Regents in writing within 60 days of the disclosure by The Regents of any such further chemicals and/or biological materials which Licensee elects to be included under this Agreement, and such chemicals and biological materials shall be Biological Materials for all purposes of this Agreement.

2.12. Because this Agreement grants the exclusive right to use or sell the Products in the United States, Licensee acknowledges that any component of a Product which embodies a patented Invention or is produced through the use thereof for sale in the United States will be manufactured substantially in the United States to the extent required by 35 U.S.C. §204.

2.13. Nothing in this Agreement will be deemed to limit the right of The Regents to publish any and all technical data resulting from any research performed by The Regents relating to the Invention, Biological Materials, Biological Products, and Patent Methods and to make and use the Invention, Biological Materials, Biological Products, and Patent Methods, and associated technology owned by The Regents solely for educational and research purposes.

## 3. License Issue Fee

3.1. As partial consideration for all the rights and licenses granted to Licensee, Licensee will pay to The Regents a license issue fee of Nine Hundred Thousand Dollars ($900,000), payable according to the following schedule:

3.1.1. One Hundred Thousand Dollars ($100,000) will be sent by Licensee to The Regents together with two copies of this Agreement executed by Licensee;

3.1.2. Eighty Thousand Dollars ($80,000) will be sent by Licensee to The Regents on or before the first anniversary of the Effective Date;

3.1.3. One Hundred and Five Thousand Dollars ($105,000) will be sent by Licensee to The Regents on or before the second anniversary of the Effective Date;

3.1.4. One Hundred and Five Thousand Dollars ($105,000) will be sent by Licensee to The Regents on or before the third anniversary of the Effective Date;

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CONFIDENTIAL TREATMENT REQUESTED

3.1.5. One Hundred and Five Thousand Dollars ($105,000) will be sent by Licensee to The Regents on or before the fourth anniversary of the Effective Date;

3.1.6. One Hundred and Five Thousand Dollars ($105,000) will be sent by Licensee to The Regents on or before the fifth anniversary of the Effective Date;

3.1.7. One Hundred Fifty Thousand Dollars ($150,000) will be sent by Licensee to The Regents on or before the sixth anniversary of the Effective Date; and

3.1.8. One Hundred Fifty Thousand Dollars ($150,000) will be sent by Licensee to The Regents on or before the seventh anniversary of the Effective Date.

3.2. Licensee will also pay to The Regents fees equal to Two Percent (2%) of the first One Million Dollars ($1M) of Service Revenues and One Percent (1%) of the Service Revenues in excess of One Million Dollars ($1M) received by Licensee from each third party with which it enters into a corporate alliance for screening services using Patent Rights and Property Rights. Notwithstanding the above, Licensee shall have no obligation to pay to The Regents any amounts it receives from a third party for the purchase of equity, research funding, debt financing, reimbursement of patent filing, prosecution, and/or maintenance expenses or other expenses.

3.3. The fees set forth in Sections 3.1 and 3.2 above are nonrefundable, noncreditable, and not an advance against royalties.

## 4. Royalties

4.1. As further consideration for all the rights and licenses granted to Licensee, Licensee will also pay to The Regents an earned royalty based on Net Sales according to the following:

4.1.1. (a) A royalty rate of One Percent (1%) of the Net Sales paid to Licensee and its sublicensees with respect to each Identified Product up to an accumulated amount of Twenty Million Dollars

($20M) in Net Sales for each Identified Product, and a royalty rate of One-Half of One Percent (0.5%) of the Net Sales paid to Licensee and its sublicensees of each Identified Product in an accumulated amount in excess of Twenty Million Dollars ($20M) in Net Sales for each such Identified Product.

(b) Notwithstanding Section 4.1.1(a) above, if Licensee and a particular sublicensee are unable to agree on a royalty of at least Two Percent (2.0%) of the Net Sales of Identified Products by such sublicensee for the first Twenty Million Dollars ($20M) in Net Sales and a royalty rate of at least One Percent (1%) of the Net Sales of Identified Products for Net Sales in excess of Twenty Million Dollars ($20M), then the royalty due to The Regents on such Net Sales will be equal to one-half (1/2) of the royalty rate, if any, agreed to between Licensee and such sublicensee with respect to the Net Sales of such Identified Product by such sublicensee.

(c) In the event Licensee is unable to negotiate with a particular sublicensee any royalty on the Net Sales of Identified Products, then in such case Licensee will not be entitled to take, in lieu of royalties on Net Sales by such sublicensee of Identified Products, consideration in any form for: (i) equity in Licensee above fair market value; (ii) research funding for screening to identify Identified Products in excess of fully burdened direct and indirect costs therefore; or (iii) reimbursement of patent filing, prosecution, and maintenance expenses; and

(d) For the avoidance of doubt, it is understood and agreed that, except as provided in Section 4.1.1(a) and (b) above, The Regents shall not be entitled to any royalty on Net Sales of Identified Products, and if Section 4.1.1(c) applies to a particular sublicense, the consideration received by Licensee from such sublicensee will be in the form of Service Revenues, and the only amounts due The Regents under this Agreement with respect thereto shall be the amounts set forth in Section 3.2, and not a royalty based on the Net Sales of Identified Products.

4.1.2. (a) A royalty rate of eight percent (8%) of the Net Sales by Licensee and its sublicensees of Research Reagents and any other Product that is not an Identified Product or Services. Licensee will be entitled to reduce the royalty due The Regents



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on the Net Sales of such Research Reagents and other Products if Licensee must pay a royalty to The Regents on Patent Rights and Property Rights and a third party with respect to intellectual property rights in which The Regents has no ownership interest. In such event, if the combined royalties due The Regents and the third party(s) exceeds Twelve Percent (12%), Licensee may reduce the royalty due The Regents by one-half the royalty rate due to the third party(s), provided, however, that in no event will the royalty rate due The Regents on the Research Reagent or such Product be less than four percent (4%).

(b) For the avoidance of doubt, it is understood and agreed that Licensee shall have no obligation to sell or have sold any Research Reagents except those listed on Appendix E hereto.

4.2. Licensee will not be entitled to apply the royalty reduction specified in Section 4.1.2(a) of this section to royalties due The Regents under Section 4.1.1 of this Article 4. (Royalties) or any other provisions of this Agreement except the provisions set forth in Section 4.1.2(a).

4.3. Sections 1.1, 1.5, and 1.6 define Patent Rights, Patent Products, and Patent Methods so that royalties will be payable on Patent Products and Patent Methods covered by both pending patent applications and issued patents. Earned royalties will accrue on Patent Products on a Product-by-Product basis in each country for the duration of Patent Rights in that country and will be payable to The Regents when Patent Products are invoiced, or if not invoiced, when delivered to a third party or to itself, an Affiliate, Joint Venture, or sublicensee in the case where such delivery of the Patent Products to Licensee, an Affiliate, Joint Venture, or sublicensee is intended for end use. If no Patent Rights exist in a country, earned royalties will accrue on a Proprietary Product, on a Product-by-Product basis, until the tenth anniversary of the first commercial sale of a particular Proprietary Product in such country. Earned royalties will accrue on Identified Products, on a Product-by-Product basis, until the

tenth anniversary of the first commercial sale of a particular Identified Product in such country.

4.4. Royalties accruing to The Regents will be paid to The Regents quarterly on or before the following dates of each calendar year:

- February 28 for the calendar quarter ending December 31
- May 31 for the calendar quarter ending March 31
- August 31 for the calendar quarter ending June 30
- November 30 for the calendar quarter ending September 30

Each such payment will be for royalties which accrued up to the most recently completed calendar quarter of Licensee.

4.5. Beginning in the year 2004, and in each succeeding calendar year after the year 2004, Licensee will pay a minimum annual royalty of One Hundred Seventy Five Thousand Dollars ($175,000) and thereafter for the life of this Agreement. This minimum annual royalty will be paid to The Regents by February 28 of each year and will be credited against the earned royalty due and owing for the calendar year in which the minimum payment was made.

4.6. All monies due The Regents will be payable in United States funds collectible at par in San Francisco, California. When Products are sold for monies other than United States dollars, the earned royalties will first be determined in the foreign currency of the country in which such Products were sold and then converted into equivalent United States funds. The exchange rate will be that rate quoted in the Wall Street Journal on the last business day of the reporting period.

4.7. Earned royalties on sales of Products occurring in any country outside the United States will not be reduced by any taxes, fees, or other charges imposed by the government of such country except those taxes, fees, and charges allowed under the provisions of Section 1.11 (Net Sales). Notwithstanding the foregoing, if The Regents



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is required to pay taxes on its royalties under the laws of any country, then Licensee will pay such amounts to the proper authorities, withhold such amounts from royalties paid to The Regents, and provide The Regents with all documents and assistance reasonably necessary to enable The Regents to recover all or part of such amounts pursuant to any double taxation treaty or otherwise. Licensee will also be responsible for all bank transfer charges.

4.8. Notwithstanding the provisions of Article 28. (Force Majeure), if at any time legal restrictions prevent prompt remittance of part or all royalties owed to The Regents by Licensee with respect to any country where a Product is sold or distributed, Licensee will convert the amount owed to The Regents into United States funds and will pay The Regents directly from another source of funds for the amount impounded.

4.9. In the event that any patent or any claim thereof included within the Patent Rights is held invalid or unenforceable in a final decision by a court of competent jurisdiction and last resort and from which no appeal has or can be taken, all obligation to pay royalties based on such patent or claim or any claim patentably indistinct therefrom will cease as of the date of such final decision. Licensee will not, however, be relieved from paying any royalties that accrued before such decision or that are based on another patent or claim that has not expired or that is not involved in such decision or that are based on Property Rights.

4.10. No royalties will be collected or paid hereunder to The Regents on Products sold to the account of the U.S. Government. Licensee and its sublicensee will reduce the amount charged for Products distributed to the United States Government by an amount equal to the royalty for such Products otherwise due The Regents as provided herein.

4.11. No more that one royalty payment shall be due with respect to a sale of a particular Product. No multiple royalties shall be payable because any Product or its manufacture, sale, or use is covered by more than one patent application or patent



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within the Patent Rights or both the Patent Rights and Property Rights. No royalty shall be payable under Section 4.1 above with respect to sales of Products among Licensee and its sublicensees where such sales are not for end use by such Licensee or its sublicensees, nor shall a royalty be payable under this Article 4. (Royalties) with respect to Products distributed for use in research and/or development in clinical trials, or as promotional samples.

## 5. Due Diligence

5.1. Licensee, upon execution of this Agreement, will diligently proceed to develop and provide Services, and to develop, manufacture, and sell Research Reagents and will earnestly and diligently market the same after execution of this Agreement and in quantities sufficient to meet the market demands therefor.

5.2. Licensee will be entitled to exercise prudent and reasonable business judgment in the manner in which it meets its due diligence obligations hereunder. In no case, however, will Licensee be relieved of its obligations to meet the due diligence provisions of this Article 5. (Due Diligence).

5.3. Licensee will obtain all necessary governmental approvals in each country in which Licensee elects to manufacture or commercialize Research Reagents and provide Services.

5.4. If Licensee is unable to perform any of the following:

5.4.1. obtain at least Ten Million Dollars ($10M) in funding by August 31, 1996 and

5.4.2. complete at least one corporate alliance with a pharmaceutical or biotechnology company for Services to identify Identified Products using Patent Rights and Property Rights before April 1, 1997; and

5.4.3. fill the market demand for Services and Identified Products that are marketed by Licensee following commencement of marketing at any time during the exclusive period of this Agreement.



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then The Regents will have the right and option, subject to Section 5.7 below, to terminate this Agreement or reduce the exclusive licenses granted to Licensee to non-exclusive licenses in accordance with Section 5.6 hereof. The exercise of this right and option by The Regents will supersede the rights granted in Article 2 (Grant).

5.5. In addition to the provisions of Section 5.4 above, Licensee shall also market each of the Research Reagents listed on Appendix E attached hereto to nonprofit/academic institutions solely for their internal, noncommercial research use either within: (i) two years following the Effective Date of this Agreement; or (ii) six months following the publication of the first paper describing the use of the Research Reagent, whichever is earlier. This Section 5.5 may be satisified by Licensee or its sublicenseees.

5.6. If Licensee fails to market a particular Research Reagent in accordance with Section 5.5 above, then The Regents will have the right and option, subject to Section 5.7 below, to terminate all rights granted to Licensee under this Agreement with respect to that particular Research Reagent. This termination includes Licensee's right to use the particular Research Reagent for its own internal use. The Regents will thereafter be free to dispose of the particular Research Reagent as it wishes. The exercise of this right and option by The Regents will supersede the rights granted in Article 2 (Grant).

5.7. To exercise either the right to terminate this Agreement in whole or with respect to any portion of Patent Rights or Property Rights, or reduce the exclusive licenses granted to Licensee to non-exclusive licenses for lack of diligence required in this Article 5. (Due Diligence), The Regents will give Licensee written notice of the deficiency stating its intent to terminate this Agreement in whole or with respect to any portion of Patent Rights or Property Rights, or to reduce the licenses to non-exclusive licenses. Licensee thereafter shall have 60 days to cure the deficiency. If The Regents

has not received written tangible evidence satisfactory to The Regents that the deficiency has been cured by the end of the 60-day period, then The Regents may, at its option, terminate this Agreement in whole or with respect to any portion of Patent Rights or Property Rights, or reduce the exclusive licenses granted to Licensee to non-exclusive licenses by giving written notice to Licensee. These notices will be subject to Article 20. (Notices).

## 6. Progress and Royalty Reports

6.1. Beginning August 31, 1996, and semi-annually thereafter, Licensee will submit to The Regents a progress report covering activities by Licensee and its sublicensees related to the development and testing of all their Products and the obtaining of the governmental approvals necessary for marketing them, but Licensee will not be required to report on Products for which a royalty is not due The Regents. These progress reports will be provided to The Regents to cover the progress of the research and development of the Products until the first commercial sale of Products in the United States.

6.2. The progress reports submitted under Section 6.1 will include, but not be limited to, the following topics so that The Regents may be able to determine the progress of the development of Products on which a royalty is due The Regents and may also be able to determine whether or not Licensee has met its diligence obligations set forth in Article 5. (Due Diligence) above:

- summary of work in progress in anticipation of providing Services and Research Reagents
- summary of work completed in anticipation of providing Services and Research Reagents
- summary of Services completed
- current schedule of anticipated events or milestones specified in Section 5.4 and 5.5

- anticipated market introduction date of Products on which a royalty is due The Regents
- sublicenses granted, if any

6.3. Licensee also will report to The Regents in its immediately subsequent progress and royalty report the date of first commercial sale of each Product for which a royalty is due to The Regents in each country.

6.4. After the first commercial sale of a Product on which a royalty is due The Regents, Licensee will provide The Regents with quarterly royalty reports to The Regents on or before each February 28, May 31, August 31, and November 30 of each year. Each such royalty report will cover the most recently completed calendar quarter of Licensee (October through December, January through March, April through June, and July through September) and will show:

6.4.1. the gross sales and Net Sales of such Products sold by Licensee and reported to Licensee as sold by its sublicensees during the most recently completed calendar quarter;

6.4.2. the number of such Products sold or distributed by Licensee and reported to Licensee as sold or distributed by its sublicensees;

6.4.3. the royalties, in U.S. dollars, payable hereunder with respect to Net Sales; and

6.4.4. the exchange rates used, if any.

6.5. If no sales of Products for which a royalty is due to The Regents have been made during any reporting period after the first commercial sale of such Product, then a statement to this effect is required.

## 7. Books and Records

7.1. Licensee will keep books and records accurately showing all Products manufactured, used, and/or sold with respect to which Licensee owes royalties to The Regents under the terms of this Agreement. Such books and records will be preserved

for at least five years after the date of the royalty payment to which they pertain and will be open to inspection by representatives or agents of The Regents during normal business hours at agreed upon times to determine the accuracy of the books and records and to determine compliance by Licensee with the terms of this Agreement. Such independent certified public accountant shall be bound to hold all information in confidence except as necessary to communicate Licensee's non-compliance with this Agreement to The Regents. The only purpose of any inspection and audit pursuant to this Paragraph 7.1 shall be to verify Licensee's royalty statement or payment under this Agreement and to determine Licensee's compliance with the other provisions thereunder.

7.2. The fees and expenses of representatives of The Regents performing such an examination will be borne by The Regents. However, if an error in royalties of more than five percent (5%) of the total royalties due for any year is discovered, then the fees and expenses of these representatives will be borne by Licensee.

## 8. Life of the Agreement

8.1. Unless otherwise terminated by operation of law or by acts of the parties in accordance with the terms of this Agreement, this Agreement will be in force from the Effective Date and will remain in effect for the life of the last-to-expire patent licensed under this Agreement, or until the last patent application licensed under this Agreement is abandoned, or in the event no patent issues, for a period of fifteen (15) years from market introduction for the last to be introduced Proprietary Product in the United States.

8.2. In the event this Agreement remains in effect for the entire term specified in Paragraph 8.1 above, and is not otherwise terminated under the provisions of Articles 5. (Due Diligence), 9. (Termination by The Regents), or 10. (Termination by Licensee), Licensee is hereby granted an option for renewal of this Agreement for a period of twenty (20) years from the date of its termination. Said option for renewal shall be

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automatically exercised provided that the Licensee has not notified The Regents to the contrary prior to the option renewal date. The renewal licenses will be for the same terms and conditions as set forth in this Agreement, except that such licenses shall be royalty-free.

8.3. Any termination of this Agreement will not affect the rights and obligations set forth in the following Articles:

| | |
|---|---|
| Article 7 | Books and Records |
| Article 13 | Disposition of Products on Hand Upon Termination |
| Article 14 | Use of Names and Trademarks |
| Article 19 | Indemnification |
| Article 22 | Late Payments |
| Article 24 | Failure to Perform |
| Article 29 | Confidentiality |

8.4. Termination of this Agreement for any reason shall not release any party hereto from any liability which, at the time of such termination, has already accrued to the other party or which is attributable to a period prior to such termination, or preclude either party from pursuing any rights and remedies it may have hereunder or at law or in equity which accrued or are based upon any event occurring prior to such termination.

## 9. Termination by The Regents

9.1. If Licensee should violate or fail to perform any term or covenant of this Agreement, then The Regents may give written notice of such default ("Notice of Default") to Licensee. If Licensee should fail to repair such default within 60 days after the date of such notice takes effect, The Regents will have the right to terminate this Agreement and the licenses herein by a second written notice ("Notice of Termination") to Licensee. If a Notice of Termination is sent to Licensee, this Agreement will

automatically terminate on the date such notice takes effect. Such termination will not relieve Licensee of its obligation to pay any royalty or license fees owing at the time of such termination and will not impair any accrued right of The Regents. These notices will be subject to Article 20. (Notices).

## 10. Termination by Licensee

10.1. Licensee will have the right at any time to terminate this Agreement in whole or as to any portion of Patent Rights or Property Rights by giving notice in writing to The Regents. Such Notice of Termination will be subject to Article 20. (Notices) and termination of this Agreement in whole or with respect to any portion of the Patent Rights or Property Rights will be effective 60 days after the effective date thereof.

10.2. Any termination pursuant to the above paragraph will not relieve Licensee of any obligation or liability accrued hereunder prior to such termination or rescind anything done by Licensee or any payments made to The Regents hereunder prior to the time such termination becomes effective, and such termination will not affect in any manner any rights of The Regents arising under this Agreement prior to such termination.

## 11. Supply of the Biological Materials and Biological Products

11.1. The Regents will initially supply Licensee with viable samples of the Biological Materials set forth in Appendix D within thirty (30) days of the Effective Date or as soon as reasonably practicable, and additional Biological Materials elected by Licensee pursuant to Section 2.11 promptly after Licensee's notice to The Regents pursuant to such Section. To the extent Licensee requires and requests additional samples from The Regents during the term hereof (due to failure of the initial supply of Biological Material(s)), and The Regents has such additional samples in its possession,

The Regents agrees to supply such additional samples. Licensee will pay the actual handling and shipping costs for any additional samples provided.

## 12. Maintenance of the Biological Materials

12.1. The Regents shall instruct Dr. Roger Tsien that if The Regents circulates any of the Biological Materials to third parties for noncommercial research purposes, it shall only do so under the terms and conditions set forth in the biological material transmission letter attached hereto as Appendix A. The Regents expressly reserves the right to transfer the Biological Materials to non-profit entities strictly for noncommercial research purposes in the manner set forth above. The Regents agrees that it will not otherwise transfer the Biological Materials. The Licensee acknowledges that The Regents' right to so transfer the Biological Materials could lead to the inadvertent loss or diminution of the proprietary commercial value of the Biological Materials.

## 13. Disposition of the Biological Materials, Biological Products, and Products on Hand Upon Termination

13.1. Upon termination of this Agreement prior to the expiration of its full term, the Licensee shall have the privilege of disposing all previously made or partially made Products, but no more, for a period of one hundred and twenty (120) days following the effective date of termination, provided, however, that the sale of such Products shall be subject to the terms of this Agreement including, but not limited to, the payment of royalties at the rate and at the time provided herein and the rendering of reports in connection therewith.

13.2. Upon termination of this Agreement for any reason, Licensee, at its sole discretion, shall destroy or transfer to The Regents any Biological Materials in its possession within thirty (30) days following the effective date of termination. Licensee

shall provide The Regents within sixty (60) days following said termination date with written notice that the Biological Materials have been destroyed.

## 14. Use of Names and Trademarks

14.1. Nothing contained in this Agreement will be construed as conferring any right to use in advertising, publicity, or other promotional activities any name, trade name, trademark, or other designation of either party hereto by the other (including contraction, abbreviation or simulation of any of the foregoing). Unless required by law, the use by Licensee of the name "The Regents of the University of California" or the name of any campus of the University of California for use in advertising, publicity, or other promotional activities is expressly prohibited.

14.2. It is understood that The Regents will be free to release to the inventors, HHMI, and senior administrative officials employed by The Regents the terms of this Agreement upon their request. If such release is made, The Regents will request that such terms will be kept in confidence in accordance with the provisions of Article 29. (Confidentiality) and not be disclosed to others. It is further understood that should a third party inquire whether a license to Patent Rights is available, The Regents may disclose the existence of this Agreement and the extent of the grant in Article 2. (Grant) to such third party, but will not disclose the name of Licensee, except where The Regents is required to release such information under either the California Public Records Act or other applicable law.

## 15. Limited Warranty

15.1. The Regents warrants to Licensee that it has the lawful right to grant these licenses and bailment.

15.2. This license and the associated Invention, Biological Materials, Products, and Patent Method are provided WITHOUT WARRANTY OF MERCHANTABILITY OR

FITNESS FOR A PARTICULAR PURPOSE OR ANY OTHER WARRANTY, EXPRESS OR IMPLIED. THE REGENTS MAKES NO REPRESENTATION OR WARRANTY THAT THE INVENTION, BIOLOGICAL MATERIALS, PRODUCTS, OR PATENT METHOD WILL NOT INFRINGE ANY PATENT OR OTHER PROPRIETARY RIGHT.

15.3. IN NO EVENT WILL THE REGENTS BE LIABLE FOR ANY INCIDENTAL, SPECIAL, OR CONSEQUENTIAL DAMAGES RESULTING FROM EXERCISE OF THIS LICENSE OR THE USE OF THE INVENTION, BIOLOGICAL MATERIALS, PRODUCTS, OR PATENT METHOD.

15.4. Nothing in this Agreement will be construed as:

15.4.1. a warranty or representation by The Regents as to the validity, enforceability, or scope of any Patent Rights or Property Rights; or

15.4.2. a warranty or representation that anything made, used, sold, or otherwise disposed of under any license granted in this Agreement is or will be free from infringement of patents of third parties; or

15.4.3. an obligation to bring or prosecute actions or suits against third parties for patent infringement except as provided in Article 18. (Patent Infringement); or

15.4.4. conferring by implication, estoppel, or otherwise any license or rights under any patents of The Regents other than Patent Rights as defined herein, regardless of whether such patents are dominant or subordinate to Patent Rights; or

15.4.5. an obligation to furnish any know-how not provided in Patent Rights and Property Rights.

## 16. Patent Prosecution and Maintenance

16.1. The Regents will diligently prosecute and maintain the United States and foreign patents comprising Patent Rights using counsel of its choice. The Regents will promptly provide Licensee with copies of all relevant documentation so that Licensee

may be currently and promptly informed and apprised of the continuing prosecution, and may comment upon such documentation sufficiently in advance of any initial deadline for filing a response, provided, however, that if Licensee has not commented upon such documentation prior to the initial deadline for filing a response with the relevant government patent office or The Regents must act to preserve Patent Rights, The Regents will be free to respond appropriately without consideration of comments by Licensee, if any. Both parties hereto will keep this documentation in confidence in accordance with the provisions of Article 29. (Confidentiality) herein. Counsel for The Regents will take instructions only from The Regents.

16.2. The Regents will use all reasonable efforts to amend any patent application to include claims requested by Licensee and required to protect the Products contemplated to be sold or Patent Method to be practiced under this Agreement.

16.3. The Regents and Licensee will cooperate in applying for an extension of the term of any patent included within Patent Rights, if appropriate, under the Drug Price Competition and Patent Term Restoration Act of 1984. Licensee will prepare all such documents, and The Regents will execute such documents and will take such additional action as Licensee may reasonably request in connection therewith.

16.4. The Regents will, at the request of Licensee, file, prosecute, and maintain patent applications and patents covered by Patent Rights in foreign countries if available. Licensee must notify The Regents within seven months of the filing of the corresponding United States application of its decision to request The Regents to file foreign counterpart patent applications. This notice concerning foreign filing must be in writing and must identify the countries desired. The absence of such a notice from Licensee to The Regents within the seven-month period will be considered an election by Licensee not to request The Regents to secure foreign patent rights on behalf of Licensee; provided, however, that the absence of such notice from Licensee to The

Regents within the seven-month period with respect to United States applications filed within eight months prior to the Effective Date of this Agreement will not be considered an election by licensee not to request The Regents not to secure foreign patent rights. In such event, Licensee must notify The Regents of its decision to request The Regents to file foreign counterpart patent applications within ninety (90) days of the conventional filing date of such applications. The Regents will have the right to file patent applications at its own expense in any country Licensee has not included in its list of desired countries, and such applications and resultant patents, if any, will not be included in the licenses granted under this Agreement.

16.5. All past, present and future costs of preparing, filing, prosecuting and maintaining all United States and foreign patent applications and all costs and fees relating to the preparation and filing of patents covered by Patent Rights in Section 1.1 will be borne by Licensee. This includes patent preparation and prosecution costs for this Invention incurred by The Regents prior to the execution of this Agreement. Such costs will be due upon execution of this Agreement and will be payable at the time that the license issue fee is payable. The costs of all interferences and oppositions will be considered prosecution expenses and also will be borne by Licensee. Licensee will reimburse The Regents for all costs and charges within 30 days following receipt of an itemized invoice from The Regents for same.

16.6. The obligation of Licensee to underwrite and to pay patent preparation, filing, prosecution, maintenance, and related costs will continue for costs incurred until three months after receipt by either party of a Notice of Termination with respect to a particular patent application or patent within the Patent Rights provided, however, that The Regents provides Licensee with written notification, at least three months prior to the effective date of the termination, that such costs are anticipated. Licensee will reimburse The Regents for all patent costs incurred during the term of the Agreement and for three months thereafter whether or not invoices for such costs are received during the three-month period after receipt of a Notice of Termination. Licensee may

with respect to any particular patent application or patent terminate its obligations with the patent application or patent in any or all designated countries upon three months written notice to The Regents. The Regents may continue prosecution and/or maintenance of such application(s) or patent(s) at its sole discretion and expense, provided, however, that Licensee will have no further right or licenses thereunder.

16.7. Licensee will notify The Regents of any change of its status as a small entity (as defined by the United States Patent and Trademark Office) and of the first sublicense granted to an entity that does not qualify as a small entity as defined therein.

16.8. The Regents acknowledges that Licensee will be conducting independent research and development activities with respect to the Biological Materials, Biological Products, and/or the Patent Rights, and recognizes that such independent research and development may result in patentable inventions and other intellectual property owned by Licensee. The Regents hereby consents to the filing of any patent applications, even if any Biological Materials or Biological Products are within the scope of one or more claims of any such patent application.

## 17. Patent Marking

17.1. Licensee will mark all Products made, used, or sold under the terms of this Agreement, or their containers, in accordance with the applicable patent marking laws.

## 18. Patent Infringement

18.1. In the event that Licensee, or The Regents' licensing associate responsible for administering this Agreement, or Resident Counsel of the Regents' Office of Technology Transfer learns of the substantial infringement of any patent licensed under this Agreement, to the extent contractually able to, it will call the attention to the other party hereto in writing and will provide reasonable evidence of

such infringement. Both parties to this Agreement acknowledge that during the period and in a jurisdiction where Licensee has exclusive rights under this Agreement, neither will notify a third party of the infringement of any of Patent Rights without first obtaining consent of the other party, which consent will not be unreasonably withheld. Both parties will use their best efforts in cooperation with each other to terminate such infringement without litigation.

18.2. Licensee may request that The Regents take legal action against the infringement of Patent Rights. Such request must be made in writing and must include reasonable evidence of such infringement and damages to Licensee. If the infringing activity has not been abated within 90 days following the effective date of such request, The Regents will have the right to elect to:

18.2.1. commence suit on its own account; or

18.2.2. refuse to participate in such suit.

18.3. The Regents will give notice of its election in writing to Licensee by the end of the 100th day after receiving notice of such request from Licensee. Licensee may thereafter bring suit for patent infringement if and only if The Regents elects not to commence suit and if the infringement occurred during the period and in a jurisdiction where Licensee had exclusive rights under this Agreement. However, in the event Licensee elects to bring suit in accordance with this paragraph, The Regents may thereafter join such suit at its own expense.

18.4. Such legal action as is decided upon will be at the expense of the party on account of whom suit is brought and all recoveries recovered thereby will belong to such party, provided, however, that legal action brought jointly by The Regents and Licensee and participated in by both will be at the joint expense of the parties and all recoveries will be allocated in the following order: (a) to each party as reimbursement of costs and fees of outside attorneys and other related expenses to the extent each party



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paid for such costs, fees, and expenses until such costs, fees, and expenses are consumed; (b) any remaining amount shared jointly by them; and (c) any remaining amount to be divided by the parties in the following manner: (i) seventy five percent (75%) for Licensee and twenty-five percent (25%) for The Regents of any recoveries based on direct damages; and (ii) fifty percent (50%) for Licensee and fifty percent (50%) for The Regents of any recoveries based on enhanced damages.

18.5. Each party will cooperate with the other in litigation proceedings instituted hereunder but at the expense of the party on account of whom suit is brought. Such litigation will be controlled by the party bringing the suit, except that The Regents may be represented by counsel of its choice in any suit brought by Licensee.

## 19. Indemnification

19.1. Licensee will (and require its sublicensees to) indemnify, hold harmless, and defend The Regents and HHMI, their officers, employees, and agents; the sponsors of the research that led to the Invention; the inventors of any invention covered by patents or patent applications in Patent Rights (including the Products and Patent Method contemplated thereunder) and their employers against any and all claims, suits, losses, damage, costs, fees, and expenses resulting from or arising out of exercise of this license or any sublicense. This indemnification will include, but will not be limited to, any product liability.

19.2. Licensee, at its sole cost and expense, will insure its activities in connection with the work under this Agreement and obtain, keep in force, and maintain insurance as follows: (or an equivalent program of self insurance)

Comprehensive or Commercial Form General Liability Insurance (contractual liability included) with limits as follows:

- Each Occurrence $1,000,000
- Products/Completed Operations Aggregate $1,000,000



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- Personal and Advertising Injury $1,000,000
- General Aggregate (commercial form only) $1,000,000

19.3. As of and following the date of commencement of any clinical trial with respect to a Product marketed by Licensee, Licensee shall increase insurance coverage under Section 19.2 immediately above from $1,000,000 to an aggregate of $3,000,000. As of and following the date of commencement of any sales of such Products, Licensee shall increase insurance coverage under Section 19.2 to an aggregate of $5,000,000. It should be expressly understood, however, that the coverages and limits referred to under the above will not in any way limit the liability of Licensee. Licensee will furnish The Regents with certificates of insurance evidencing compliance with all requirements. Such certificates will:

19.3.1. Provide for 30 day advance written notice to The Regents of any modification;

19.3.2. Indicate that The Regents has been endorsed as an additional Insured under the coverages referred to under the above; and

19.3.3. Include a provision that the coverages will be primary and will not participate with nor will be excess over any valid and collectable insurance or program of self-insurance carried or maintained by The Regents.

19.4. The Regents will promptly notify Licensee in writing of any claim or suit brought against The Regents in respect of which The Regents intends to invoke the provisions of this Article 19. (Indemnification). Licensee will keep The Regents informed on a current basis of its defense of any claims pursuant to this Article 19. (Indemnification). It is understood that Licensee shall have the right to control the defense and settlement of any such claim or suit, except Licensee shall not enter into any settlement which (i) makes any admission of wrongdoing on the part of The Regents, or (ii) admits that any of the Patent Rights of The Regents are invalid, unenforceable, or not infringed without prior written consent of The Regents.

## 20. Notices

20.1. Any notice or payment required to be given to either party will be deemed to have been properly given and to be effective (a) on the date of delivery if delivered in person or (b) five days after mailing if mailed by first-class certified mail, postage paid, to the respective addresses given below, or to another address as it may designate by written notice given to the other party.

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|---|---|
| In the case of Licensee: | AURORA BIOSCIENCES, CORP.<br>11149 North Torrey Pines Road<br>La Jolla, CA 92037<br>Attention: President<br>(619) 452-5000 |
| In the case of The Regents: | THE REGENTS OF THE UNIVERSITY OF CALIFORNIA<br>1320 Harbor Bay Parkway, Suite 150<br>Alameda, California 94502<br>Tel: (510) 748-6600<br>Fax: (510) 748-6639<br>Attention: Executive Director;<br>Research Administration<br>and Office of Technology Transfer<br>Referring to: U.C. Case Nos. 93-289, 95-110, 95-219, 96-044, 96-160, 96-161, 96-162, and 96-191 |

## 21. Assignability

21.1. This Agreement is binding upon and will inure to the benefit of The Regents, its successors and assigns, but shall be personal to Licensee and assignable by Licensee only with the written consent of The Regents, which consent shall not be unreasonably withheld; provided, however, Licensee may assign this Agreement to an Affiliate or Joint Venture or in connection with the sale or transfer of substantially all the

assets of Licensee relating to the subject matter of this Agreement, without written consent of The Regents.

## 22. Late Payments

22.1. In the event royalty payments or fees or patent prosecution costs are not received by The Regents when due, Licensee will pay to The Regents interest charges at a rate of ten percent (10%) simple interest per annum. Such interest will be calculated from the date payment was due until actually received by The Regents. Acceptance by The Regents of any late payment interest from Licensee under this Section 22.1 will in no way affect the provision of Article 23. (Waiver) herein.

## 23. Waiver

23.1. It is agreed that no waiver by either party hereto of any breach or default of any of the covenants or agreements herein set forth will be deemed a waiver as to any subsequent and/or similar breach or default.

## 24. Failure to Perform

24.1. In the event of a failure of performance due under the terms of this Agreement and if it becomes necessary for either party to undertake legal action against the other on account thereof, then the prevailing party will be entitled to reasonable attorney's fees in addition to costs and necessary disbursements.

## 25. Governing Laws

25.1. THIS AGREEMENT WILL BE INTERPRETED AND CONSTRUED IN ACCORDANCE WITH THE LAWS OF THE STATE OF CALIFORNIA, excluding any choice of law rules that would direct the application of the laws of another jurisdiction,

but the scope and validity of any patent or patent application will be governed by the applicable laws of the country of such patent or patent application.

## 26. Government Approval or Registration

26.1. If this Agreement or any associated transaction is required by the law of any nation to be either approved or registered with any governmental agency, Licensee will assume all legal obligations to do so. Licensee will notify The Regents if it becomes aware that this Agreement is subject to a United States or foreign government reporting or approval requirement. Licensee will make all necessary filings and pay all costs including fees, penalties, and all other out-of-pocket costs associated with such reporting or approval process.

## 27. Export Control Laws

27.1. Licensee will observe all applicable United States and foreign laws with respect to the transfer of Products and related technical data to foreign countries, including, without limitation, the International Traffic in Arms Regulations (ITAR) and the Export Administration Regulations.

## 28. Force Majeure

28.1. The parties to this Agreement will be excused from any performance required hereunder if such performance is rendered impossible or unfeasible due to any acts of God, catastrophes, or other major events beyond their reasonable control, including, without limitation, war, riot, and insurrection; laws, proclamations, edicts, ordinances, or regulations; strikes, lock-outs, or other serious labor disputes; and floods, fires, explosions, or other natural disasters. However, any party to this Agreement will have the right to terminate this Agreement upon 30 days' prior written notice if either party is unable to fulfill its obligations under this Agreement due to any of

the causes mentioned above and such inability continues for a period of one year. Notices will be subject to Article 20. (Notices). When such events have abated, the parties' respective obligations hereunder shall resume.

## 29. Confidentiality

29.1. Licensee and The Regents respectively will treat and maintain the proprietary business, patent prosecution, software, engineering drawings, process and technical information, and other proprietary information ("Proprietary Information") of the other party in confidence using at least the same degree of care as that party uses to protect its own proprietary information of a like nature for a period from the date of disclosure until five years after the date of termination of this Agreement. This confidentiality obligation will apply to the information defined as "Data" under the Secrecy Agreement, and such Data will be treated as Proprietary Information hereunder.

29.2. All Proprietary Information will be labeled or marked confidential or as otherwise similarly appropriate by the disclosing party, or if the Proprietary Information is orally disclosed, it will be reduced to writing or some other physically tangible form, marked and labeled as set forth above by the disclosing party, and delivered to the receiving party within 30 days after the oral disclosure as a record of the disclosure and the confidential nature thereof. Notwithstanding the foregoing, Licensee and The Regents may use and disclose Proprietary Information to its employees, agents, consultants, contractors, and, in the case of Licensee, its sublicensees, provided that any such parties are bound by a like duty of confidentiality.

29.3. Nothing contained herein will in any way restrict or impair the right of Licensee or The Regents to use, disclose, or otherwise deal with any Proprietary Information:

29.3.1. that recipient can demonstrate by written records was previously known to it;

29.3.2. that is now, or becomes in the future, public knowledge other than through acts or omissions of recipient;

29.3.3. that is lawfully obtained without restrictions by recipient from sources independent of the disclosing party;

29.3.4. that is required to be disclosed to a governmental entity or agency in connection with seeking any governmental or regulatory approval, or pursuant to the lawful requirement or request of a governmental entity or agency;

29.3.5. that is furnished to a third party by the recipient with similar confidentiality restrictions imposed on such third party, as evidenced in writing; or

29.3.6. that The Regents is required to disclose pursuant to the California Public Records Act or other applicable law.

29.4. Upon termination of this Agreement, Licensee and The Regents will destroy or return to the disclosing party proprietary information received from the other in its possession within 15 days following the effective date of termination. Licensee and The Regents will provide each other, within 30 days following termination, with a written notice that Proprietary Information has been returned or destroyed. Each party may, however, retain one copy of Proprietary Information for archival purposes in nonworking files.

## 30. Miscellaneous

30.1. The headings of the several sections are inserted for convenience of reference only and are not intended to be a part of or to affect the meaning or interpretation of this Agreement.

30.2. This Agreement will not be binding upon the parties until it has been signed below on behalf of each party, in which event, it will be effective as of the date recited on page one.

30.3. No amendment or modification hereof will be valid or binding upon the parties unless made in writing and signed on behalf of each party.

30.4. This Agreement embodies the entire understanding of the parties and will supersede all previous communications, representations or understandings, either oral or written, between the parties relating to the subject matter hereof. The Letter Agreements, the Option Agreement, and the Secrecy Agreements specified in the Recitals of this Agreement are hereby terminated.

30.5. In case any of the provisions contained in this Agreement are held to be invalid, illegal, or unenforceable in any respect, such invalidity, illegality, or unenforceability will not affect any other provisions hereof, but this Agreement will be construed as if such invalid or illegal or unenforceable provisions had never been contained herein.

The Regents and Licensee execute this Agreement in duplicate originals by their respective, authorized officers on the date indicated.

| Aurora Biosciences Corporation | The Regents of the University of California |
|---|---|
| By Timothy J. Rink (Signature) | By Terence A Feuerborn (Signature) |
| Name TIMOTHY J RINK (Please Print) | Name Terence A. Feuerborn |
| Title PRESIDENT, CEO | Title Executive Director Research Administration and Office of Technology Transfer |
| Date 6/17/96 | Date 6-18-96 |

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Approved as to legal form: Sandra Schmidt, Attorney, Office of Technology Transfer, University of California 6/14/96 Date

## APPENDIX A - PAGE 1A

University of California/San Diego (UCSD)

Instructions for Standard Letter Transmitting
Biological Materials to Universities and
Non-Profit Institutions

The attached letter is authorized for use by University of California, UCSD Principal Investigators and Administrators only with Scientists and other universities and nonprofit research institutions when transmitting cell lines, plasmids and the like for non-commercial research purposes.

1. Choose the appropriate form of university or nonprofit research institution in paragraph 2.

2. Choose whether or not to include the phrase "our cooperative" in paragraph 2.

3. Insert in paragraph 4 the amount of processing charge. If the material is to be shipped at no charge, insert the words "no charge".

4. Send the letter in duplicate to the other scientists.

5. Do not send biological materials until you receive the duplicate copy executed by both the scientist and the other institution.

6. Send a copy of the fully executed letter agreement to:

   Terence A. Feuerborn
   Executive Director
   Research Administration
   and Technology Transfer
   1320 Harbor Bay Parkway
   Suite 150
   Alameda, CA 94501

7. Any changes in the wording of this standard letter must be reviewed by the Executive Director of the Office of Technology Transfer before acceptance.

Note: Do not use this letter for the exchange of living plants. A separate "Testing Agreement for the Plant Varieties" is available for that purpose.

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# SAMPLE LETTER FOR USE PRIOR TO TRANSMISSION OF BIOLOGICAL MATERIALS TO INVESTIGATORS AT UNIVERSITIES OR NON-PROFIT RESEARCH INSTITUTIONS

(date)

IN DUPLICATE

To:_____

This is to (acknowledge receipt of your letter) (confirm our telephone conversation) in which you requested certain research materials developed in this laboratory be sent to you for scientific research purposes. The materials concerned, which belong to The Regents of the University of California/San Diego Campus (UCSD) are _____.

While I cannot transfer ownership of these materials to you, I will be pleased to permit your use of these materials within your (university) (Non-Profit Research Institution) laboratory for (our cooperative) scientific research. However, before forwarding them to you, I require your agreement that the materials will be received by you only for use in (our cooperative work) (scientific research), that you will bear all risk to you or any others resulting from your use, and that you will not pass these materials, their progeny or derivatives, on to any other party or use them for commercial purposes without the express written consent of The Regents of the University of California. You understand that no other right or license to these materials, their progeny or derivatives, is granted or implied as a result of our transmission of these materials to you.

These materials are to be used with caution and prudence in any experimental work, since all of their characteristics are not known.

As you recognize, there is a processing cost to us involved in providing these materials to you. We will bill you for our processing costs, which will amount to $_____.

If you agree to accept these materials under the above conditions, please sign the enclosed duplicate copy of this letter, then have it signed by an authorized representative of your institution, and return it to me. Upon receipt of that confirmation I will forward the material(s) to you.

(Note: other paragraphs discussing the relevant literature, the nature of the work, hazards relating to materials to be sent etc. may be appropriate. These will vary depending on the individual circumstances and the relationship between the two parties previously established. Be sure to retain a signed copy when received and send a photocopy of the completed agreement to the University of California Patent Administrator, Office of Technology Transfer, Systemwide Administration, 1320 Harbor Bay Parkway, Suite 150, Alameda, CA 94502)

Sincerely yours,

ACCEPTED:

RESEARCH INVESTIGATOR

_____
Printed Name

_____
(Signature)

_____
Date

RESEARCH UNIVERSITY OR
NON-PROFIT INSTITUTION

_____
Printed Name

_____
(Signature)

_____
Date

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## APPENDIX B - PAGE 1B

The INVENTORS listed below understand and agree to abide by the terms and conditions of Article 12 (MAINTENANCE OF THE BIOLOGICAL MATERIALS) of the Exclusive License Agreement between The Regents of the University of California and Aurora Biosciences, Corp. effective _____, 1996, and to instruct all relevant personnel working within their laboratory to act accordingly. Said paragraph reads, in part, as follows:

*"12.1 The Regents shall instruct Roger Tsien that if The Regents circulates any of the Biological Materials to third parties for noncommercial research purposes, it shall only do so under the terms and conditions set forth in the biological material transmission letter attached hereto as Appendix A. The Regents expressly reserves the right to transfer the Biological Materials to non-profit entities strictly for noncommercial research purposes in the manner set forth above. The Regents agrees that it will not otherwise transfer the Biological Materials. The Licensee acknowledges that The Regents' right to so transfer the Biological Materials could lead to the inadvertent loss or diminution of the proprietary commercial value of the Biological Materials."*

The Biological Materials is defined in said Agreement as follows:

*"1.2 Biological Materials" means (i) the chemical reagents and biological materials owned by The Regents and listed in Appendix D attached hereto and provided to Licensee by The Regents pursuant to the April 26, 1996 Letter Agreement, and (ii) any other chemical reagents or biological materials elected for inclusion under this Agreement by Licensee pursuant to Section 2.11 below."*

By:

Roger Tsien
(Inventor)

July 3, 1996
Date

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CHANCELLOR APPROVAL OF COMMERCIAL RESTRICTIONS OF TANGIBLE RESEARCH PRODUCTS

In May 1989, the University of California issued the *Guidelines on University-Industry Relations* ("Guidelines"). Guideline 10 entitled "Tangible Research Products" requires that when the commercial availability of tangible research products resulting from the conduct of research are restricted by a license, approval must be obtained from the Chancellor of the campus where the research took place.

The License Agreement between THE REGENTS OF THE UNIVERSITY OF CALIFORNIA ("The Regents") and AURORA BIOSCIENCES, CORP. ("Licensee") entitled "Fluorescent Assay Technologies" contains provisions that restrict the transfer of certain tangible research products to commercial competitors of the Aurora Biosciences, Corp. and requires that tangible research products transferred for educational and research purposes be conveyed under a biological material transfer agreement that permits the University to retain the discretion to publish any results of research at any time and to disseminate the tangible materials for educational and research purposes.

Approval of the provisions of the License Agreement that restrict the commercial availability of tangible research products is indicated below.

Approval:

Robert C. Dynes
Chancellor

7/22/96
Date

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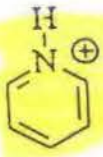
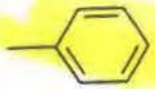
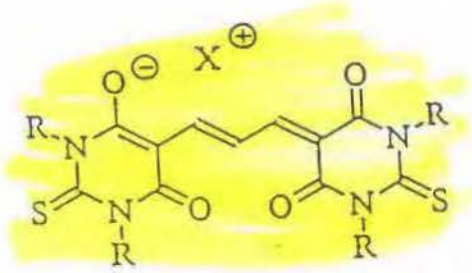
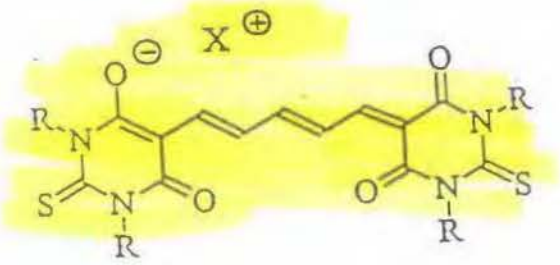
# Fast Voltage-Sensitive Oxonols

X:  , $Na^+$, $K^+$

R: n-butyl
n-hexyl
n-decyl







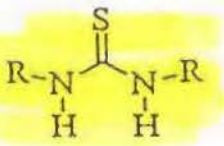
R: n-butyl
n-hexyl

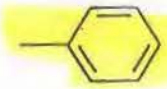
CONFIDENTIAL TREATMENT REQUESTED

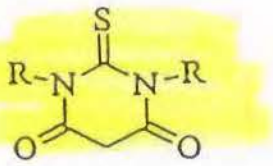
# Thioureas and Thiobarbituric Acids For Preparation of Fast Oxonols

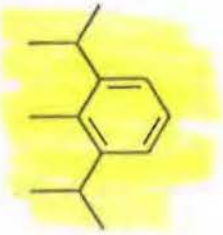
Symmetric

R: n-butyl
n-hexyl
n-decyl

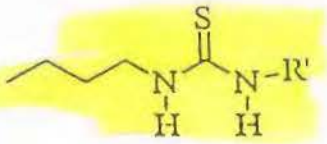




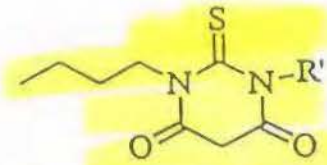




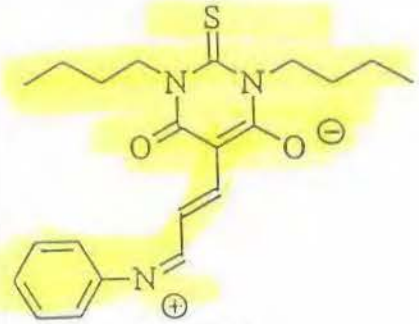
Asymmetric



R': 

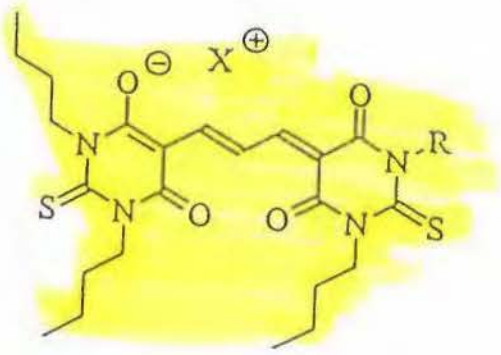


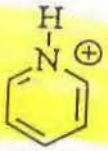
Intermediate for Asymmetric Oxonol



CONFIDENTIAL TREATMENT REQUESTED

# Functionalized Thiobarbituric Oxonols

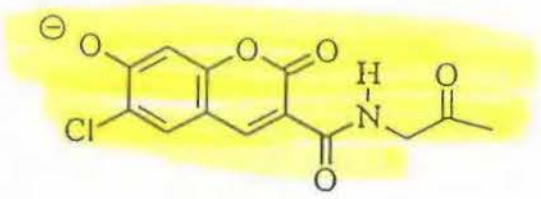


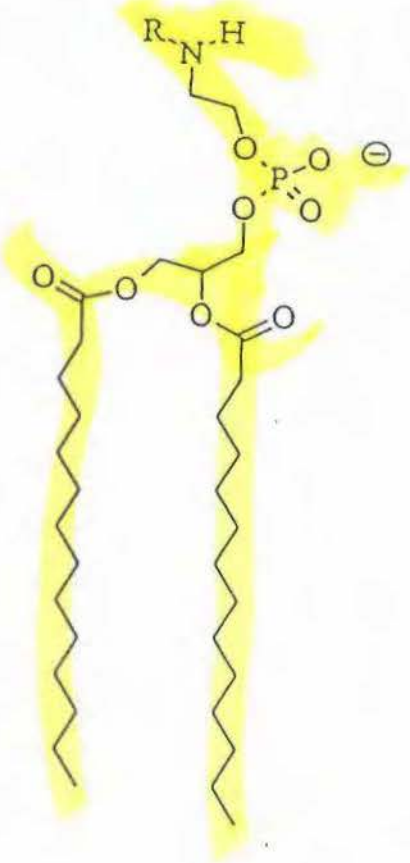
X:  , $Na^+$, $K^+$

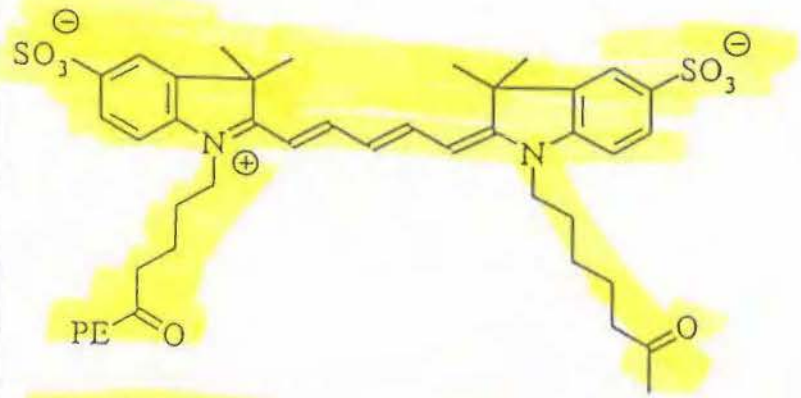
R: listed below

CONFIDENTIAL TREATMENT REQUESTED

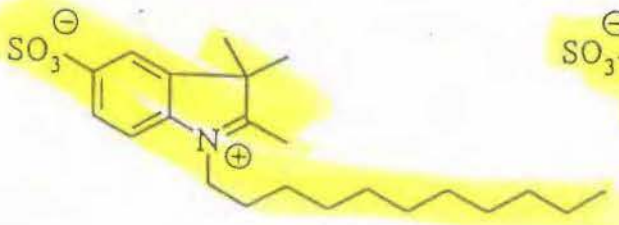
# Donor and Acceptor Fluorescent Lipids for FRET with Oxonols

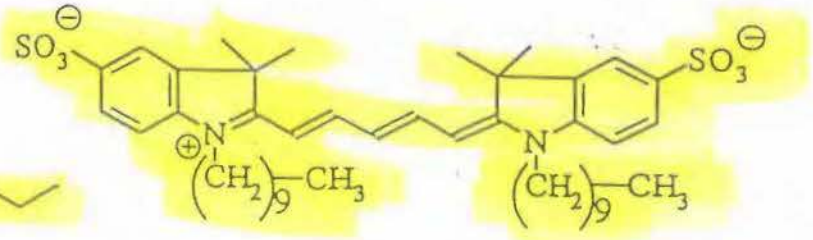






PE: phosphatidylethanolamine



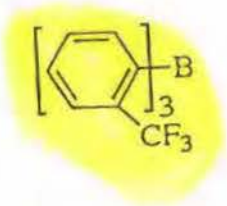


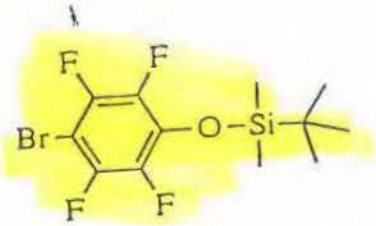
ll Lines Used for Testing FRET Based Voltage-Sensitive Dyes

LM-TK-
Astrocytoma

CONFIDENTIAL TREATMENT REQUESTED

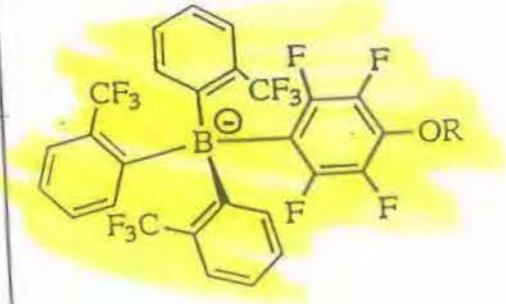
# Voltage-Sensitive Fluorescent Borate Conjugates

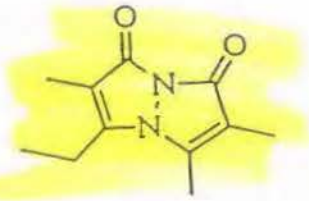




R: H




CONFIDENTIAL TREATMENT REQUESTED

List of plasmids

pMLΔ (RTEM)
pML (RTEM)
pXEX-bla (RTEM)
pCDNA3-bla (RTEM)
pCDNA3-bla (bacillus licheniformis)
pZEO-bla (RTEM)
pNFAT-bla (RTEM)
pCDNA3-Gα15
pCDNA3-Gα16
pCIS-β2R
pCDNA3-GFP
pCDNA3-BFP
pRSET-blip
pCDNA3-blip
pRSET-bla (RTEM)
pRSET-bla (bacillus licheniformis)
pSP72-bla (RTEM)
pCEP4-Gαalpa15
P activator-tet
pZEO-SV40-large T
ptet-CMV-Gα15
ptet-CMV-Gα16
ptet-CMV-luciferase
pCMV-luciferase

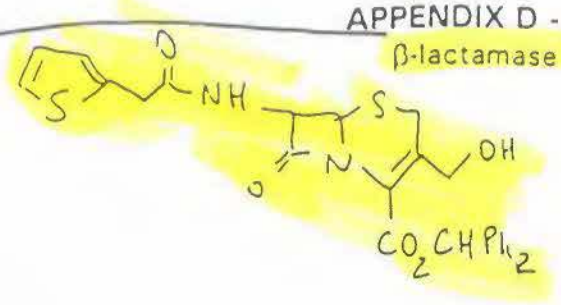
Mike Whitney: primers 101-111

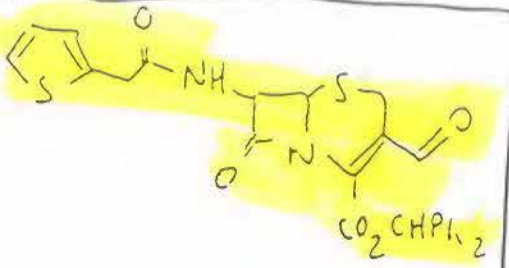
β-lactamase expressing cell lines

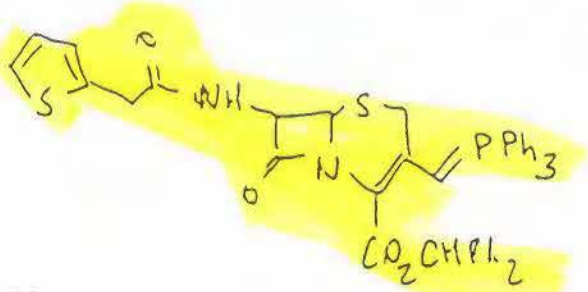
Greg9
G941
CHO-A1
COS7-D5
B3Z-bla-zeo

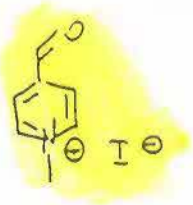
Other cell lines

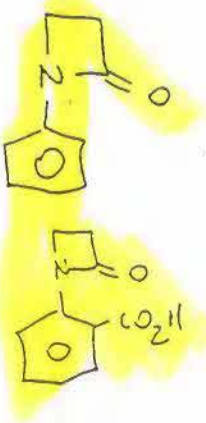
BHK
CHO
COS7
Ref52
Jurkat
Astrocytoma
L cells
Hela
KB5C20
BM3.3
WEHI
P388
EL4
MDCK
B3Z
IE5
HL60

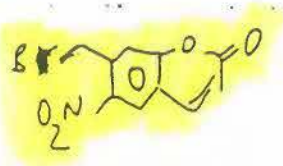


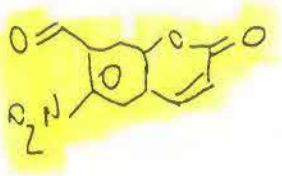


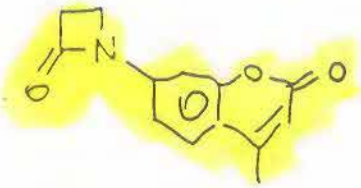


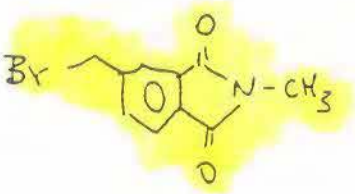


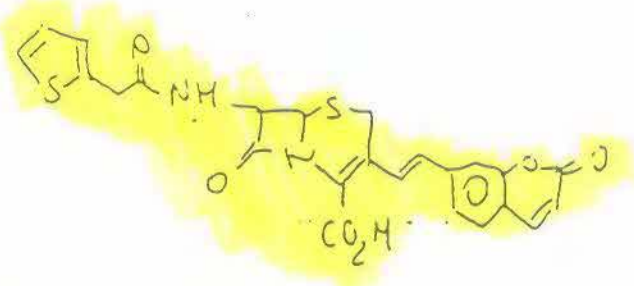


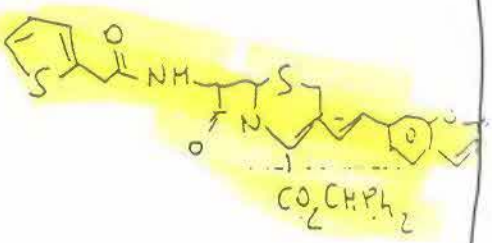






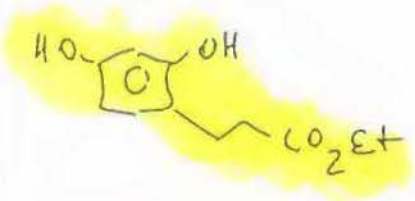


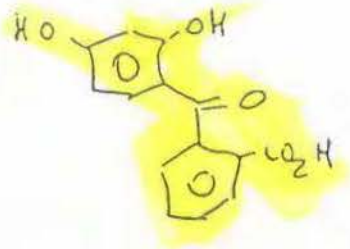


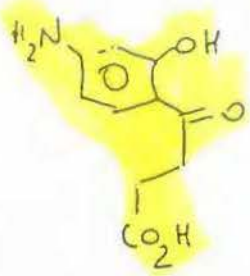


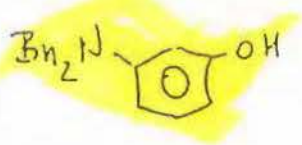
Coumarocephin

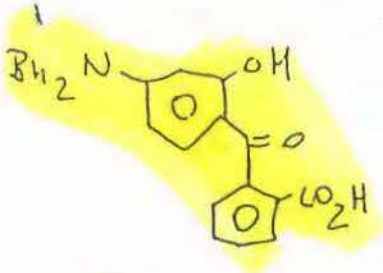
CONFIDENTIAL TREATMENT REQUESTED

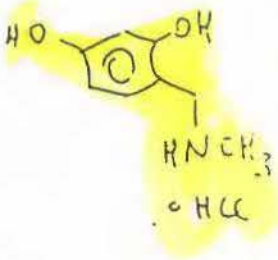


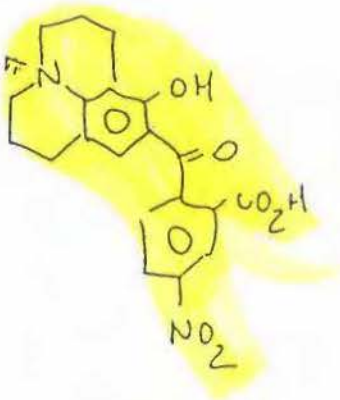


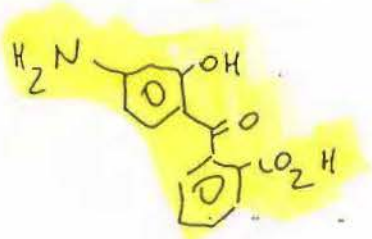


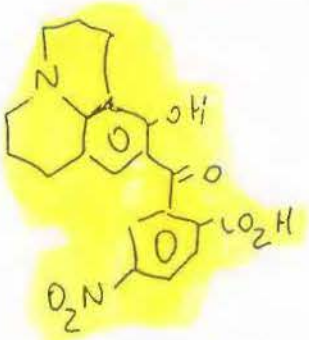


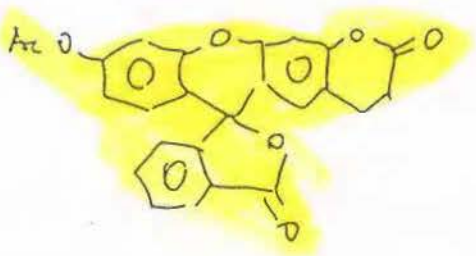


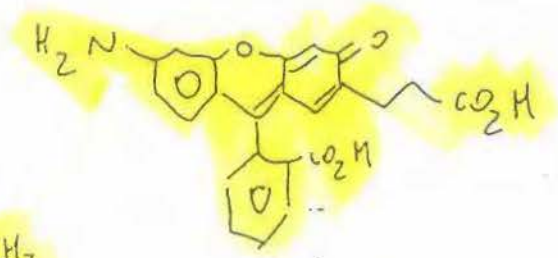


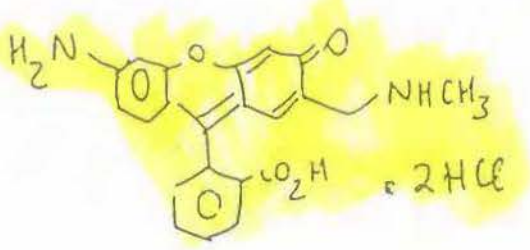


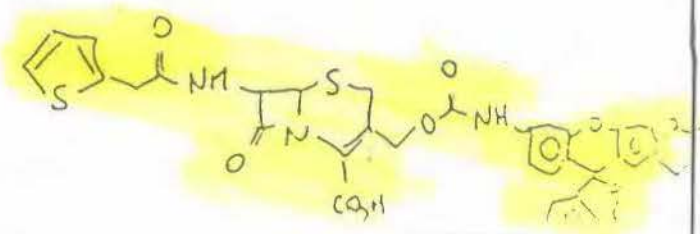












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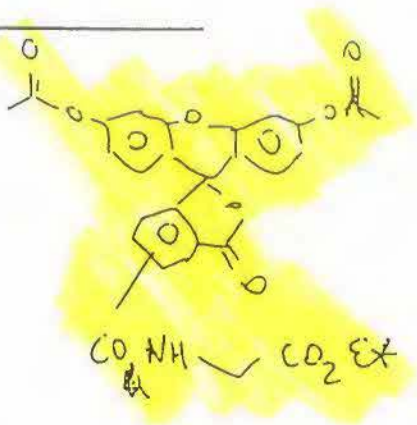

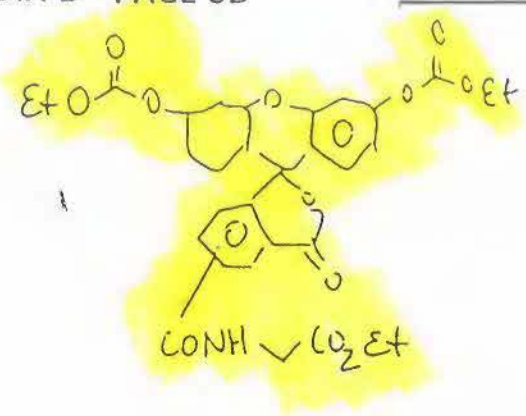

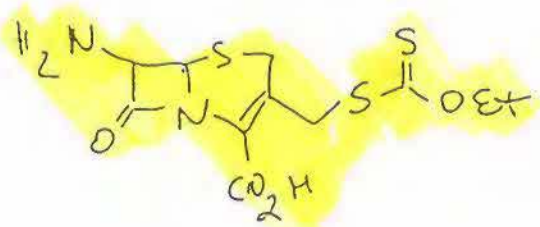

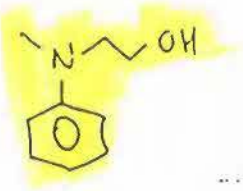

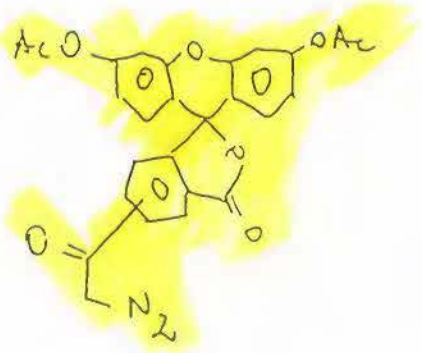

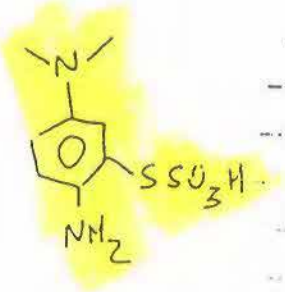

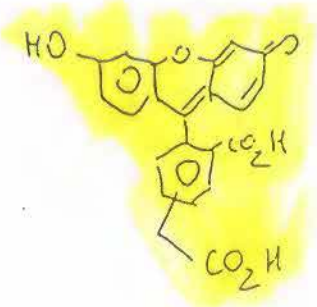

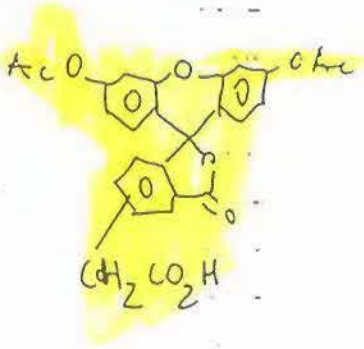

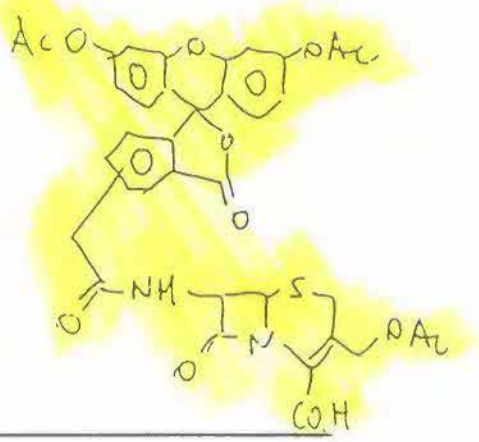



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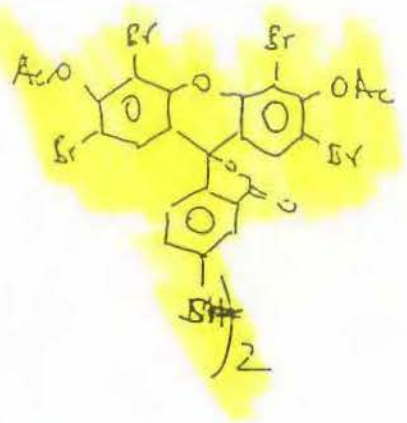

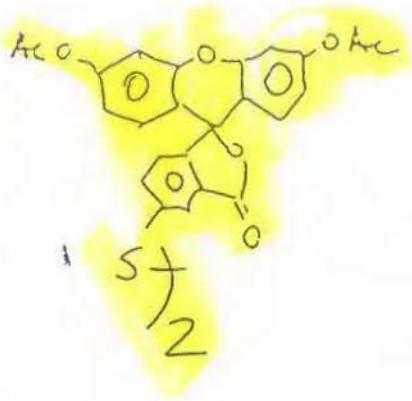

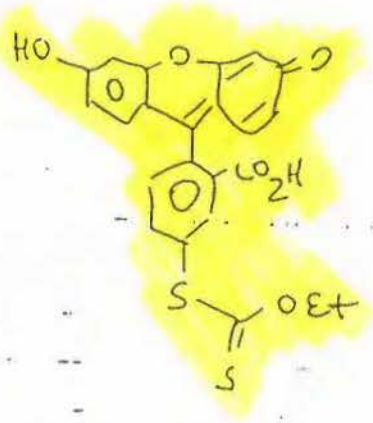

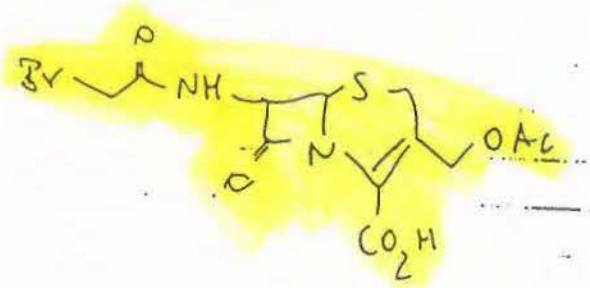

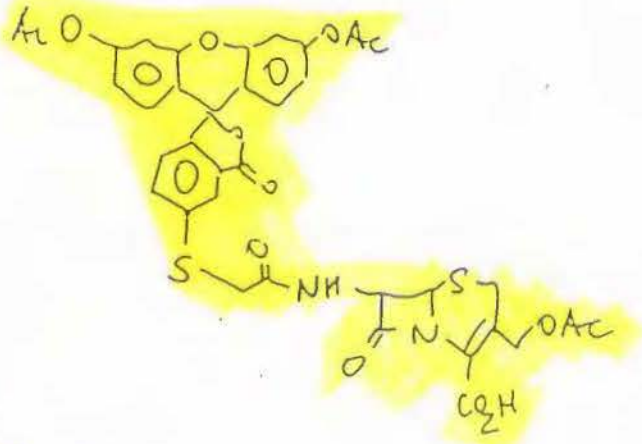

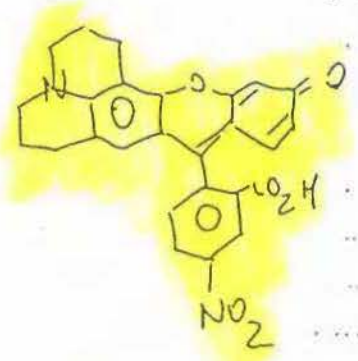

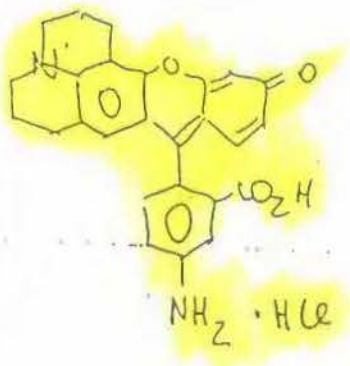

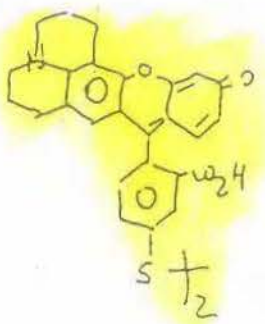

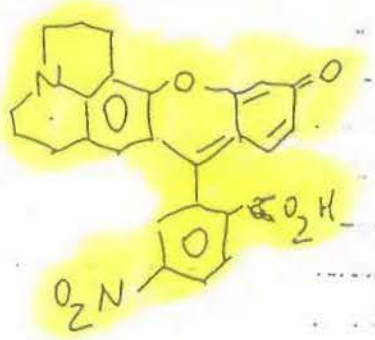

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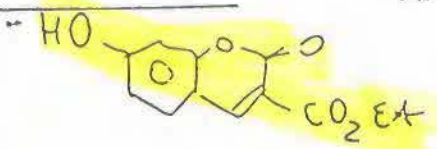

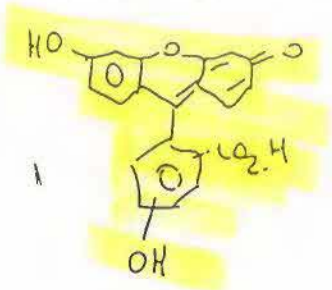

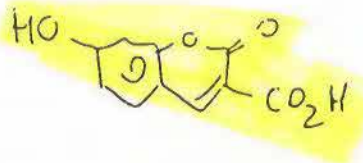

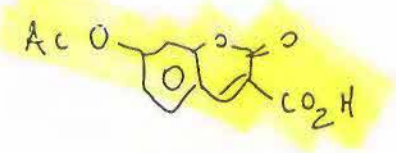

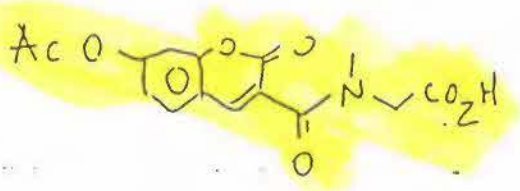

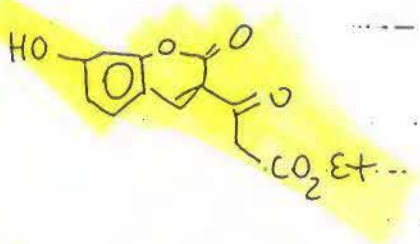

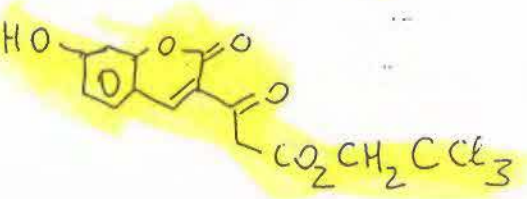

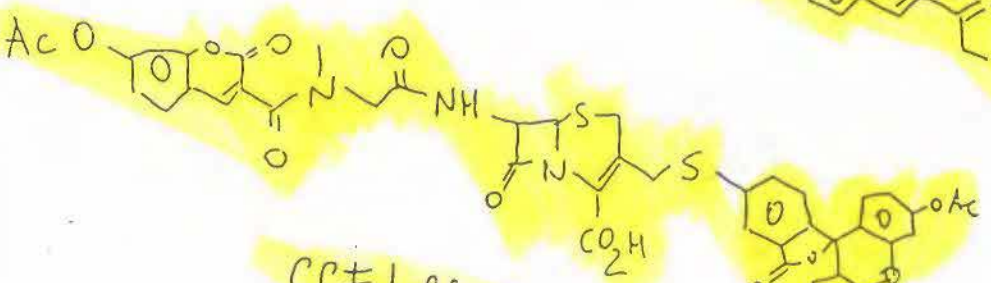

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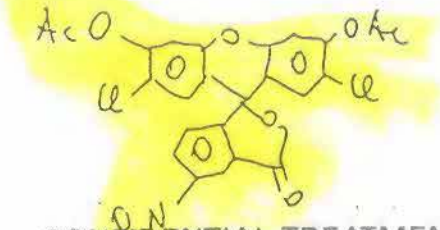

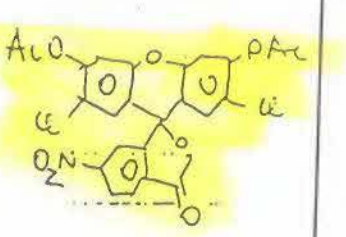

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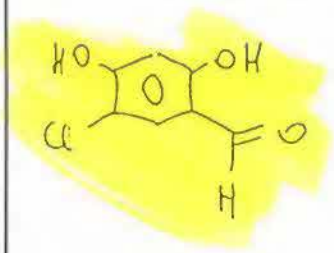

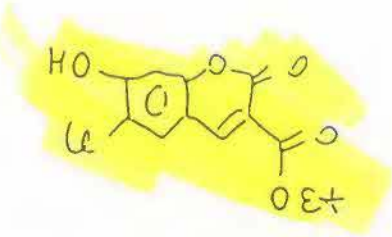

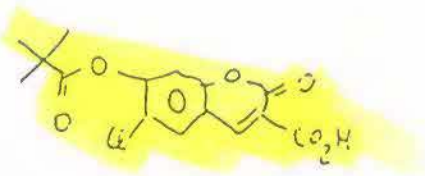

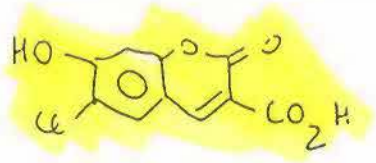

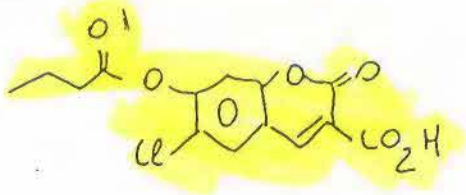

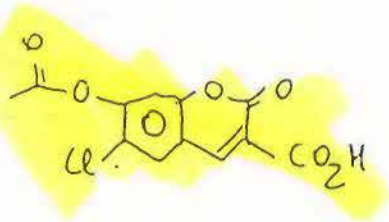

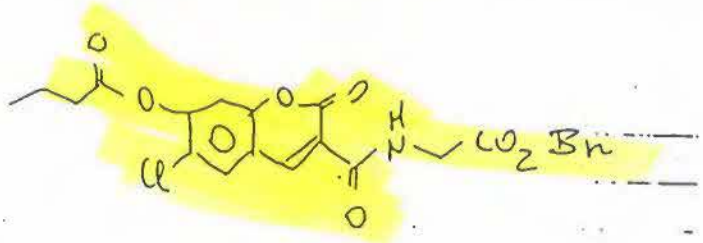

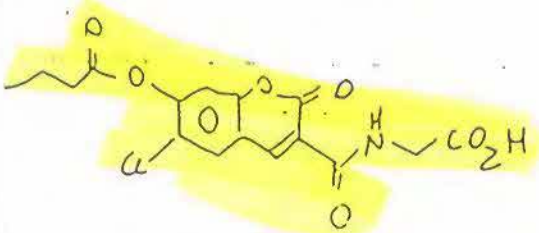

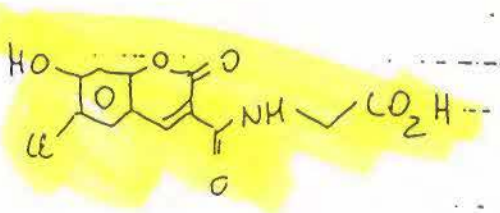

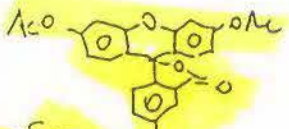

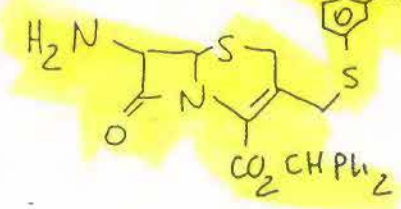

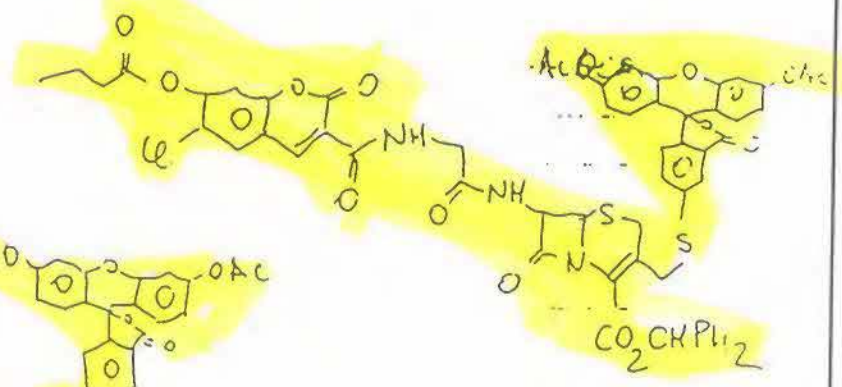

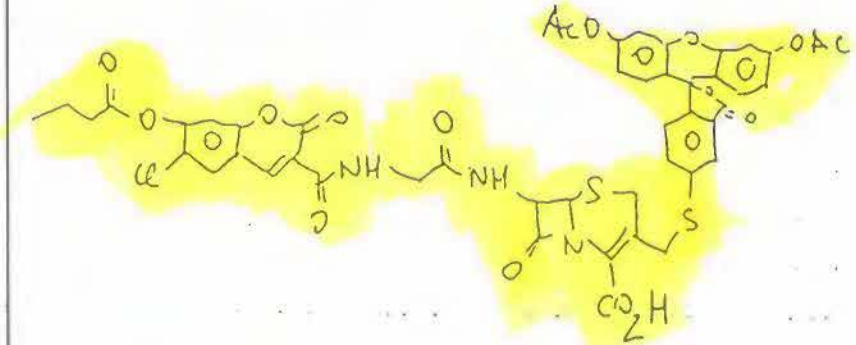

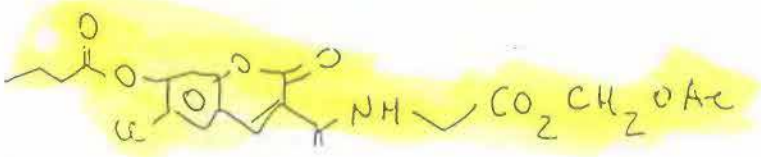

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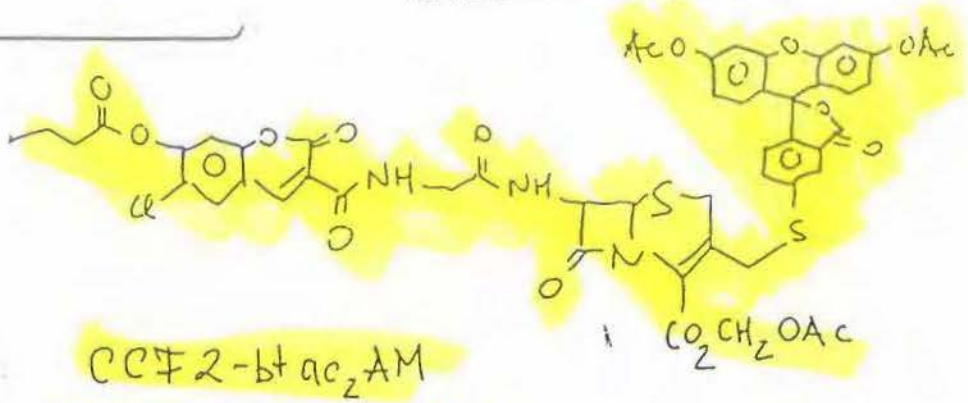

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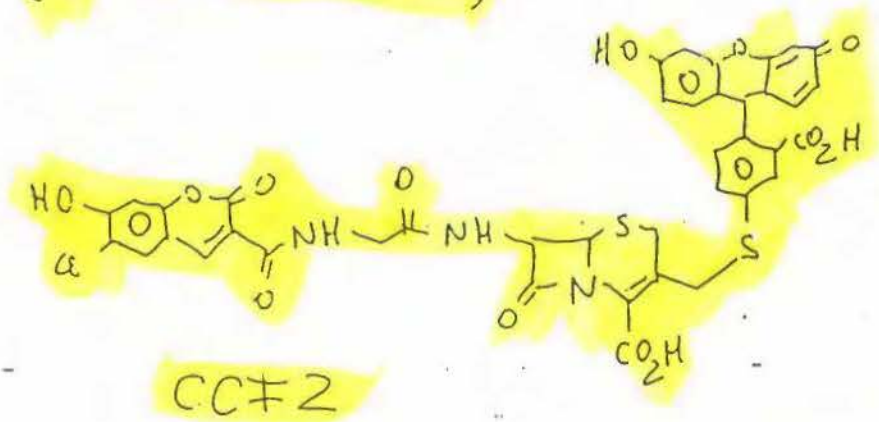
(also: CCF2-AM)



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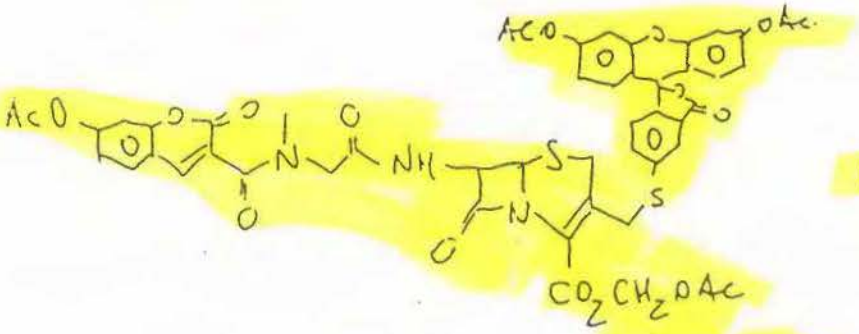

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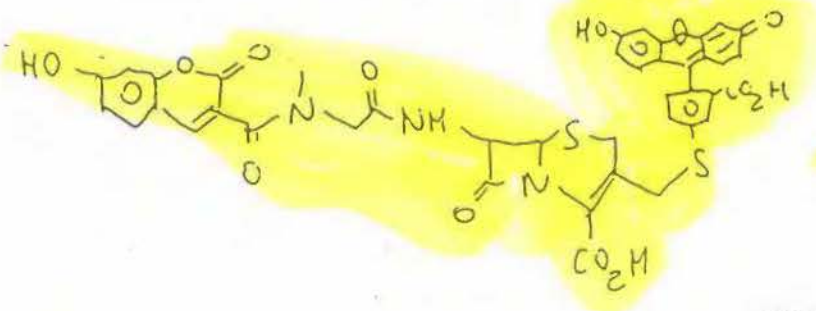

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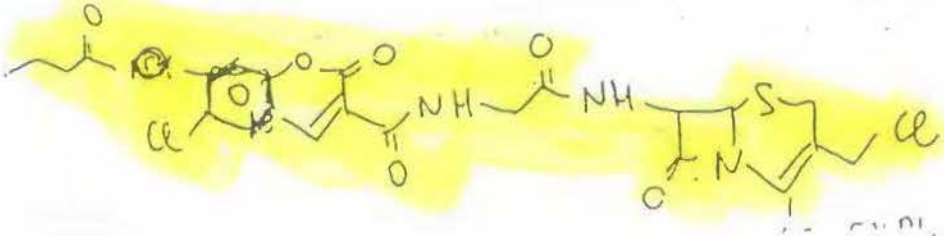

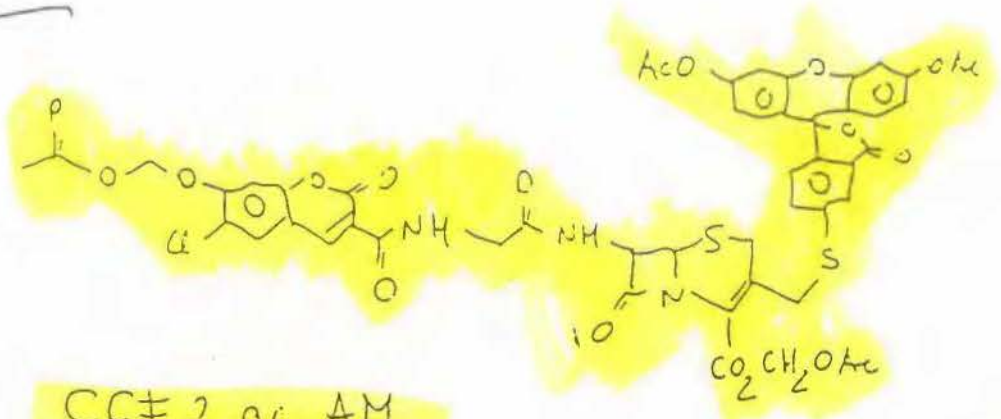

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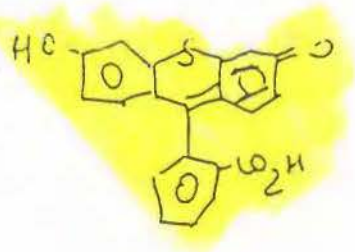

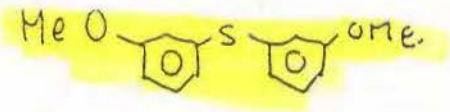

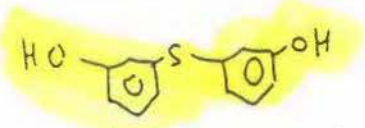

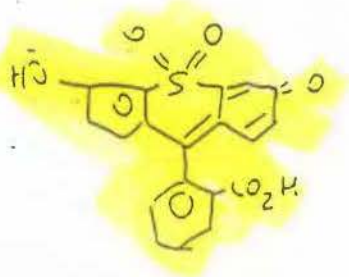

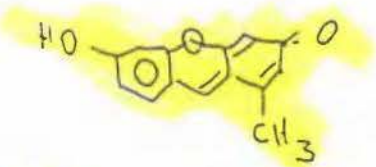

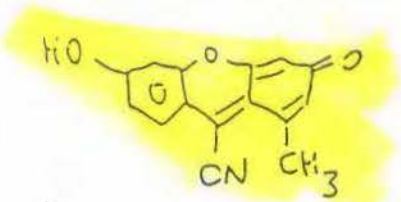

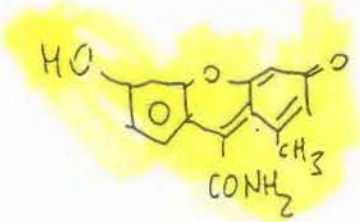

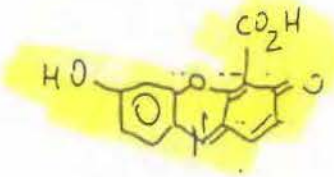

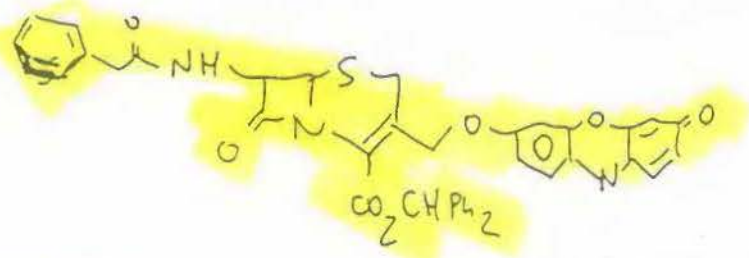

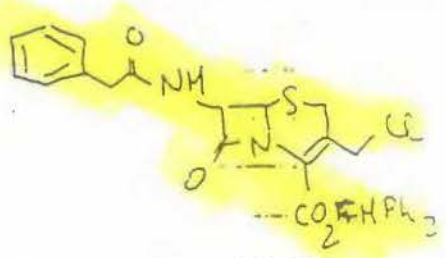

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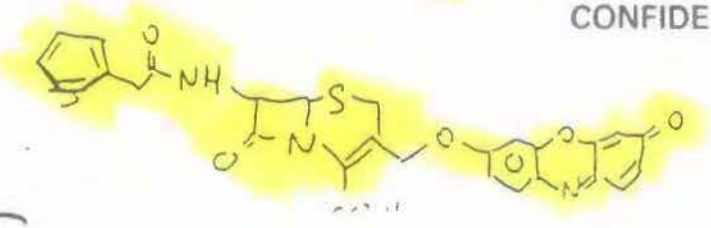

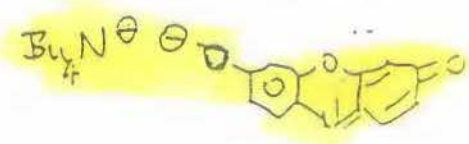

Green fluorescent proteins

1) cDNA clones and sequence information on mutants of Aequorea related green fluorescent proteins (GFP) with altered fluorescent properties. Specifically those that contain mutations:

In or around the chromophore such as mutations of:

S65 to thr,cys,leu,val,ile,ala,gly and met

Y66 to his,trp and phe

Mutations distal to the chromophore such as:

I167 to thr,ser,ala,leu,val,cys,met

S203 to ile.val,leu,phe

ox S65T Y66H
S65C Y66W
S65L Y66F
S65V
S65I
S65A
S65G
S65M

2) Mutants of GFP with altered folding characteristics. These include mutants of GFP which display enhanced folding, or expression at 37C without exhibiting changes in spectral properties as well as those containing additional mutations which alter the fluorescent properties of GFP such as Y66H as well as having enhanced folding characteristics. Specifically GFP clones containing some or all of the following mutations.
Y145F,N146I,M153T or A,V163A,N212K,I123V,H148R,T44A,S205T,F64L,S72A

I167T
I167S
I167A
I167V
I167C
I167M

3) Fusion of GFP and or mutants of GFP with proteins or protein domains such as:

proteolytically sensitive linkers
calcium binding domains
PH (inositol phosphate binding )domains
calmodulin
calineurin

S203I
S203V
S203L
S203F
S203Y
S203H
S203W

* specific sequences available

5) Sequence and or peptide sequence data of novel non-Aequorea related fluorescent proteins such as the Renilla green fluorescent protein.

Y14FF
N146I
M153T
M153A
V163A
N212K
I123V
H148R
T44A
S205T
F64L

6) X-ray crystallography and NMR structural information and data sets of GFP

7) Molecular simulations of the 3-dimensional structure of GFP and mutants of GFP

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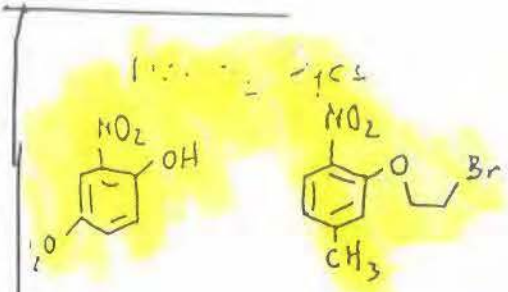

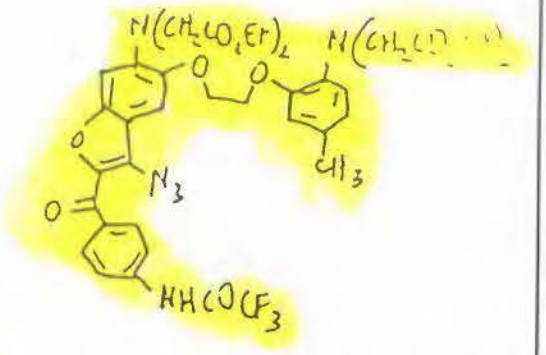

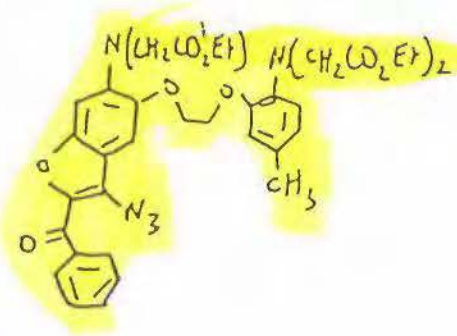

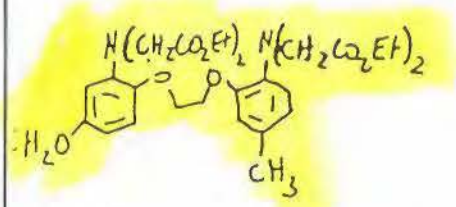

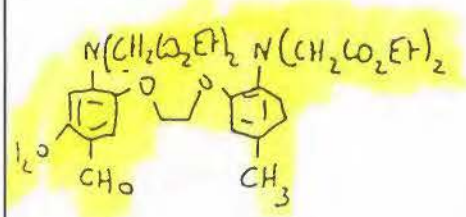

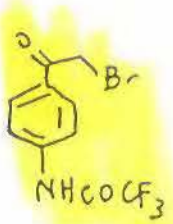

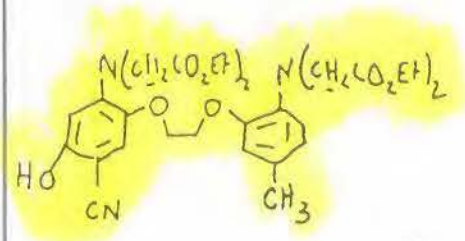

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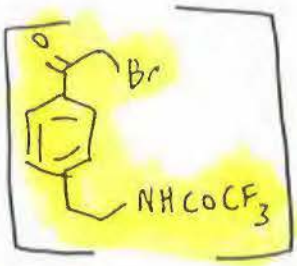


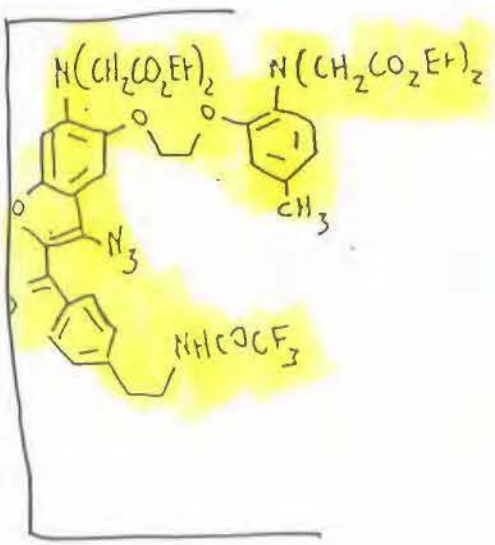


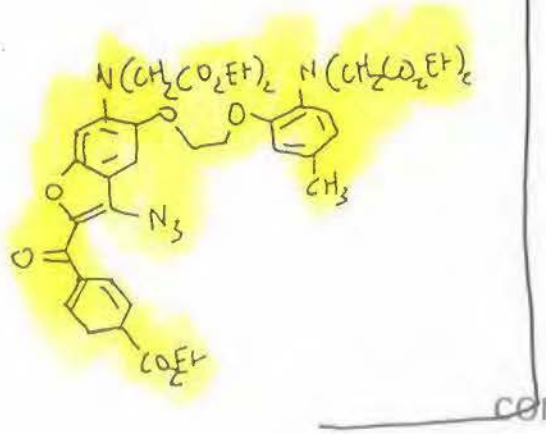


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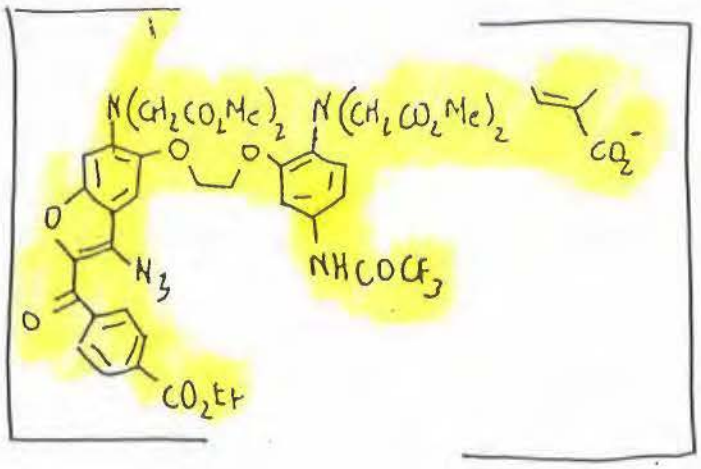

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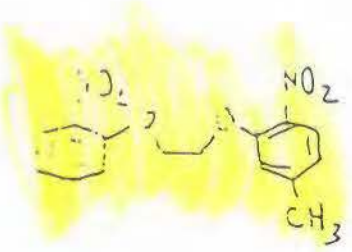

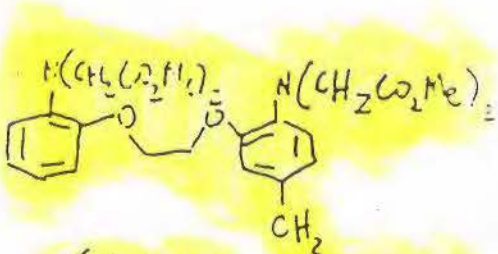

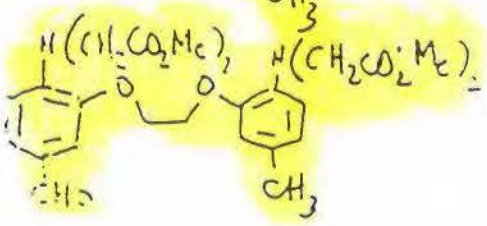

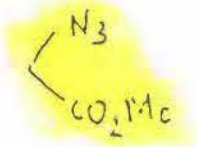

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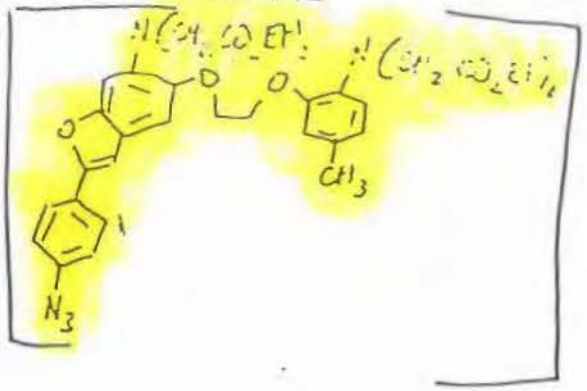

Research Reagents

1) GFP cDNAs encoding S65T, P4-3 (=Y66H/Y145F), W7 (=Y66W/N146I/M153T/ V163A/N212K)

2) β-lactamase substrate CCF2 and its membrane-permeable ester CCF2-btAMac$_2$

3) diSBA-$C_4$-(3), di-SBA-$C_6$-(3)

4) An indicator that memorize $Ca^{2+}$ set-forth in UC Case 96-191-1 and provided to Licensee under Section 11.1 herein.

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