

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-Q/A

QUARTERLY REPORT UNDER SECTION 13 OR 15(D) OF THE
SECURITIES EXCHANGE ACT OF 1934

For Quarter Ended: MARCH 31, 1996

Commission File Number 0-19319

VERTEX PHARMACEUTICALS INCORPORATED
(Exact name of registrant as specified in its charter)

Massachusetts

04-3039129

(State or other jurisdiction of
incorporation or organization)

(I.R.S. Employer
Identification No.)

130 WAVERLY STREET, CAMBRIDGE, MASSACHUSETTS 02139-4242

(Address of principal executive offices, including zip code)

(617) 577-6000

(Registrant's telephone number, including area code)

Indicate by check mark whether the registrant (1) has filed all reports
required to be filed by Section 13 or 15(d) of the Securities Exchange Act of
1934 during the preceding 12 months (or for such shorter period that the
registrant was required to file such reports), and (2) has been subject to such
filing requirements for the past 90 days.

YES NO
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Indicate the number of shares outstanding of each of the issuer's classes
of common stock, as of the latest practicable date.

Common Stock, par value \$.01 per share	17,368,453
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Class	Outstanding at May 9, 1996

PART II.
OTHER INFORMATION

Item 6. Exhibits:

- 10.2 Research and Development Agreement, dated April 13, 1993, between the Registrant and Kissei Pharmaceutical Co., Ltd. (filed herewith with certain confidential information omitted).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this amendment to be signed on its behalf by the undersigned thereunto duly authorized.

VERTEX PHARMACEUTICALS INCORPORATED

Date: May 17, 1996

/s/ Thomas G. Auchincloss, Jr.

Thomas G. Auchincloss, Jr.
Senior Director of Finance and Treasurer
(Principal Financial Officer)

/s/ Hans D. van Houte

Hans D. van Houte
Controller
(Principal Accounting Officer)

RESEARCH AND DEVELOPMENT AGREEMENT

AGREEMENT made and effective this 13th day of April, 1993, between VERTEX PHARMACEUTICALS INCORPORATED, a Massachusetts corporation ("VERTEX"), and KISSEI PHARMACEUTICAL CO., LTD., a Japanese corporation ("KISSEI").

INTRODUCTION

- A. VERTEX is a multidisciplinary biotechnology company focused on the use of structural biology and organic chemistry to design and develop novel human therapeutics. The Company has been involved for some time in research aimed at developing drugs to treat AIDS and HIV infection.
- B. KISSEI is a diversified worldwide pharmaceutical company with substantial expertise in the area of research, product development, the conduct of preclinical and clinical trials, sales and marketing, and is interested in the research, development, marketing and sale of pharmaceuticals for the treatment of AIDS and HIV infection.
- C. Both parties desire to enter into a collaboration specifically targeting the development of small molecule inhibitors of HIV protease as human therapeutics for the treatment of AIDS and HIV infection, utilizing the complementary skills and strengths which each party brings to the transaction. On the effective date of this Agreement, KISSEI has agreed to make a substantial equity investment in VERTEX.
- D. The purpose of this Agreement is to set forth the terms upon which VERTEX together with KISSEI will attempt to design and develop novel compounds for the treatment of AIDS and HIV infection with the financial and technical assistance of KISSEI, for development, manufacture, marketing and sale by KISSEI and/or sublicensees in the Territory (as defined below) upon the terms set forth herein and in the attached form of the Option and Rights Agreement.
- E. KISSEI desires to learn various scientific strategies from VERTEX that can be applied to drug discovery programs outside of the Research Program, and VERTEX is willing to accommodate that desire.

In consideration of the mutual covenants set forth in this Agreement, and other good and valuable consideration, the parties agree as follows:

ARTICLE I

DEFINITIONS

1.1 "Affiliate" shall mean at any time, any person or legal entity then directly or indirectly controlled by, controlling or under common control with the party with respect to which this term is associated, and shall include any person or legal entity which owns, either of record or beneficially, 50% or more of the voting stock of any party hereto, or 50% or more of the voting stock of which is owned by any party hereto.

1.2 "Field" shall mean human use in the diagnosis, prevention and treatment of AIDS and HIV infection caused by HIV-1 and HIV-2 retroviruses, or infection caused by the related retrovirus, HTLV-1.

1.3 "Compounds" shall mean small molecule inhibitors of HIV-1 and HIV-2 protease, as well as inhibitors of the related protease of HTLV-1 discovered or developed by VERTEX or together with KISSEI in the Field in the course of the Research Program, whether discovered or developed by VERTEX or together with KISSEI prior to or after the effective date of this Agreement, or, if the Research Program is not terminated earlier by KISSEI pursuant to Section 7.2 or 7.3, discovered or developed by VERTEX during the period ending six (6) months after the conclusion of the Research Program pursuant to Section 2.1 of this Agreement.

1.4 "Promising Compound" shall mean any Compound which is the subject of or which is discovered during the Research Program which becomes the subject of KISSEI's rights in accordance with the provisions of Article III hereof.

1.5 "Promising Processes" shall mean any technical information resulting from the Research Program discovered or developed by VERTEX or together with KISSEI in the Field in the course of the Research Program, whether discovered or developed by VERTEX or together with KISSEI prior to or after the effective date of this Agreement.

1.6 "Patents" shall mean any existing or later-filed patents or patent applications filed by VERTEX in the Territory or under which VERTEX acquires or has acquired rights in the Territory claiming a Compound, a Promising Process, or a method of manufacturing or using a Compound, including any continuation, continuation-in-part, or division thereof or any substitute application therefore. An up-to-date list of Patents is appended hereto as Schedule I. VERTEX shall keep KISSEI currently informed in writing of additions and amendments thereto.

1.7 "Promising Patents" shall mean any Patents which become the subject of KISSEI's rights in accordance with the provisions of Article III hereof.

1.8 "Research Program" shall mean research activities associated with discovery or creation of Compounds, including in vitro studies of Compounds, in vivo animal studies for research purposes only (rather than for the generation of data for regulatory submission), and related activities, as described in the Summary of Research Activities attached hereto as Schedule II.

1.9 "Development Program" shall mean activities associated with development of Promising Compounds for sale, including but not limited to (a) selection of clinical candidates from among lead Compounds and preparation for preclinical assessment thereof; (b) formulation of Promising Compounds for use in preparation for preclinical studies; (c) preclinical animal studies performed in accordance with "Good Laboratory Practices" (or the applicable equivalent); (d) manufacture of Promising Compounds for preclinical and clinical studies; (e) planning, implementation, evaluation and administration of human clinical trials; (f) manufacturing process development and scale-up; and (g) preparation and submission of applications for regulatory approval.

1.10 "KISSEI Technical Information" shall mean all know-how, proprietary information, or special knowledge of KISSEI relating to the research, development, utilization, manufacture, or use of any Compound or Promising Process, including but not limited to process, techniques, methods, products, materials, and compositions.

1.11 "VERTEX Technical Information" shall mean all know-how, proprietary information, or special knowledge of VERTEX relating to the research, development, utilization, manufacture, or use of any Compound or Promising Process, including but not limited to processes, techniques, methods, products, materials, and compositions.

1.12 "Territory" shall mean Japan and the People's Republic of China in which KISSEI has exclusive option rights under Section 3.1 hereto.

1.13 "Option Territory" shall mean the countries which may be added to the Territory in accordance with the provisions of Section 3.3 hereof, and which are listed on Schedule 1.13 hereto.

1.14 "Effective Date" shall mean the effective date of this Agreement as set forth on the first page hereof.

ARTICLE II

RESEARCH AND DEVELOPMENT

2.1 COMMENCEMENT. VERTEX or together with KISSEI shall commence the Research Program promptly upon the Effective Date and shall use its reasonable best efforts to diligently conduct the Research Program during the term of this Agreement in accordance with the provisions hereof. The Research Program shall be

concluded not later than 31 December 1995, unless extended by agreement of the parties hereto. At the election of KISSEI, subject to mutual agreement including agreement upon any additional funding to be provided to VERTEX by KISSEI, the Research Program may be extended for an additional two-year period, through 31 December 1997.

2.2 PAYMENTS BY KISSEI. KISSEI will provide financial support to the Research Program and Development Program, in a total amount, not exceeding US \$13,800,008.00 in the following installment payments to VERTEX.

1.	Upon execution of this Agreement :	\$3,800,008.00
2.	On 1 October 1993 :	\$1,000,000.00
3.	1994 :	\$2,500,000.00
4.	1995 :	\$2,500,000.00
5.	Demonstration in a primate, using oral administration of a lead compound, of the ability to sustain over a period exceeding four hours a blood level greater than or equal to the IC90 antiviral concentration, as determined in vitro by p24 assay :	\$1,000,000.00
6.	Filing of Japanese equivalent of Investigational New Drug notice with respect to a Promising Compound :	\$1,000,000.00
7.	CONFIDENTIAL INFORMATION OMITTED	
8.	CONFIDENTIAL INFORMATION OMITTED	

The payments due for the years 1994 and 1995 shall be payable in equal quarterly installments on the last day of each calendar quarter of such year, i.e., each March 31, June 30, September 30, and December 31. All payments shall be made by wire transfer in United States dollars to the credit of such bank account as may be designated by VERTEX in writing to KISSEI. Any payment which falls due on a date which is a legal holiday in the Commonwealth of Massachusetts may be made on the next preceding day which is not a legal holiday in the Commonwealth. If any installment payments set forth above remain unpaid upon termination of this Agreement pursuant to Section 7.1 of this Agreement, KISSEI's obligation to make such payments herein as scheduled in Section 2.2 shall survive termination of this Agreement, if upon such termination, the Option and Rights Agreement shall be in effect with respect to a Promising Compound.

Notwithstanding that more than one Promising Compound, or more than one indication of the same Compound, may achieve as set forth above, KISSEI shall not be required to make more than one payment with respect to each of items 5-8 above, which shall relate to the first indication of the first Compound to achieve each installment.

2.3 RESEARCH COMMITTEE. Upon the execution of this Agreement, VERTEX and KISSEI will establish a Research Committee which shall consist of not more than three persons designated from time to time by each of VERTEX and KISSEI. The Research Committee shall meet formally at least semi-annually, or with such other frequency, and at such time and location, as may be established by the Committee, for the following purposes:

(a) To receive and review reports by VERTEX or together with KISSEI, which shall be prepared and submitted to the Research Committee and to KISSEI or VERTEX on a quarterly basis within fifteen (15) days after the end of the quarter, setting forth in general terms the results of work performed by VERTEX

during the preceding calendar quarter under the Research Program, including any planned or filed patent applications covering Compounds;

(b) To advise VERTEX and KISSEI concerning research strategy, goals and activities, and to consider whether redirection of the Research Program should be recommended to VERTEX and KISSEI under Section 2.5 of this Agreement;

(c) To assist in coordinating scientific interactions between VERTEX and KISSEI during the course of the Research Program;

(d) To discuss matters relating to patents.

2.4 EXCHANGE OF INFORMATION. VERTEX and KISSEI will meet informally on a regular basis to discuss the Research Program, and will freely share technical information in the Field, including VERTEX Technical Information and KISSEI Technical Information, which is not subject to restrictions imposed by a third party on disclosure to or use by the other party. As of the effective date of this Agreement, neither VERTEX nor KISSEI is subject to any such restrictions. VERTEX will provide quarterly written reports on the progress of the Research Program to KISSEI and the Research Committee, within fifteen (15) days after the end of each calendar quarter during the term of the Research Program. VERTEX will enable any of KISSEI's representatives on the Research Committee, or other authorized representatives of KISSEI, to review the ongoing research being conducted by VERTEX under the Research Program and to discuss that research with its officers, all at such reasonable times and as often as may be reasonably requested. Any representatives of VERTEX or KISSEI receiving information from representatives of the other party shall sign appropriate agreements ensuring that information disclosed to them is held in confidence. KISSEI shall be free to apply any scientific strategies learned from VERTEX by it during the course of the Research Program to its own drug discovery efforts outside the Research Program without any further obligation to VERTEX.

2.5 REDIRECTION OF RESEARCH PROGRAM. If at any time during the term of this Agreement, the Research Committee shall determine in good faith that the Research Program or any portion thereof cannot be successfully completed, or if so completed will not produce Compounds that are commercially viable, the Committee may suggest revision or reorientation of the Research Program to each party's own top management, and upon mutual consent VERTEX and KISSEI shall thereafter promptly modify their respective activities in connection with the Research Program accordingly.

2.6 GRANTBACK. KISSEI shall keep VERTEX fully advised of any improvements by KISSEI or its Affiliates or sublicensees relating to Compounds and Promising Processes during the term of the Research Program and the Development Program whether patentable or not ("KISSEI Improvements"). At the request of VERTEX, KISSEI shall grant to VERTEX a non-exclusive, royalty-free license to any such Improvements generated by it, and will seek to obtain similar rights in favor of VERTEX for any such Improvements generated or made available to it by its Affiliates and sublicensees, if any. In such event, (a) VERTEX shall seek to obtain similar non-exclusive, royalty-free rights to be granted to KISSEI in the Territory for any such improvements generated or made available to VERTEX by its other licensees, if any ("VERTEX Improvements"); and (b) VERTEX shall refrain from exploiting its non-exclusive rights to any such KISSEI Improvements in the Territory so long as the Option and Rights Agreement is in effect between VERTEX and KISSEI covering any Promising Compound.

2.7 INFORMATION TRANSFER. At such time as VERTEX and KISSEI, pursuant to Article III hereof, shall enter into the Option and Rights Agreement with respect to Promising Compounds, VERTEX shall deliver to KISSEI all information requested by it which is necessary or useful for further development, manufacture and commercial exploitation and distribution of the Promising Compounds in the Territory. This information shall include copies of all patents, patent applications, copyrights, copyright registrations and applications therefor and all other manifestations of the intellectual property embodied in the Promising Compounds, whether in human or machine readable form.

2.8 DEVELOPMENT. KISSEI will bear the cost of and be responsible for the Development Program of Promising Compound(s) in the Territory, including without limitation completing any preclinical and clinical studies required to obtain regulatory approval of Compound(s) in the Territory, to the extent that such studies and other

development activities are not otherwise required as part of VERTEX's development of Compound(s) outside the Territory. VERTEX will provide KISSEI with any and all preclinical and clinical data generated by VERTEX as part of VERTEX's development of such Compound(s) in North America and Europe. KISSEI shall be free to use such data and information solely for the purpose of developing Promising Compound(s) in the Territory pursuant hereto.

2.9 BULK SUPPLY FOR RESEARCH AND DEVELOPMENT. VERTEX will provide KISSEI with bulk material for research and development in the Territory with respect to Compounds then under development by VERTEX at VERTEX's cost.

2.10 KISSEI RESEARCH. KISSEI agrees that, during the term of the Research Program it will discuss with and obtain consent from VERTEX or the Research Committee prior to engaging in specific research activities in the Field. VERTEX will not unreasonably withhold such consent.

ARTICLE III

KISSEI'S RIGHTS

3.1 SELECTION OF PROMISING COMPOUNDS. KISSEI has an exclusive option right to select from time to time Promising Compounds for development under the Option and Rights Agreement referenced below, from Compounds in which KISSEI has an interest in development, manufacture, marketing and sale in the Territory, as an outcome of KISSEI's financial and technical support of the Research Program and Development Program. KISSEI has the exclusive option right referenced above during the term of the Research Program and for six (6) months after the termination of the Research Program, and for such longer period as the Option and Rights Agreement referenced below shall be in effect with respect to any Promising Compound.

3.2 OPTION AND RIGHTS AGREEMENT. The rights of KISSEI upon exercise of its option under Section 3.1 above shall be as set forth in the Option and Rights Agreement attached hereto as Exhibit A. Promptly upon exercise of any such option by notice in writing from KISSEI to VERTEX, the parties shall execute the Option and Rights Agreement for further development, manufacture, marketing and sale of Promising Compounds in the Territory.

3.3 OPTION TERRITORY. KISSEI shall have the option to include the Option Territory as part of its Territory, in addition to Japan and the People's Republic of China, by written notice given to VERTEX at any time prior to 31 December 1995, together with payment of \$3,000,000, in addition to any and all other amounts payable under this Agreement. From and after the date of exercise of such option, the Option Territory shall be deemed a part of the Territory for all purposes of this Agreement.

3.4 SCIENTIFIC STRATEGIES. KISSEI may apply scientific strategies learned from VERTEX to drug discovery programs in which KISSEI is or may in the future be engaged outside of the Research Program.

ARTICLE IV

CONFIDENTIALITY

4.1 UNDERTAKING. During the term of this Agreement, each party shall keep confidential, and other than as provided herein shall not use or disclose, directly or indirectly, any trade secrets, confidential or proprietary information, or any other knowledge, information, documents or materials, owned, developed or possessed by the other party, whether in tangible or intangible form, the confidentiality of which such other party takes reasonable measures to protect, including but not limited to VERTEX Technical Information and KISSEI Technical Information. Each party shall take any and all lawful measures to prevent the unauthorized use and disclosure of such information, and to prevent unauthorized persons or entities from obtaining or using such information. Each party further agrees to refrain from directly or indirectly taking any action which would constitute or facilitate the unauthorized use or disclosure of such information. Each party may disclose such information to its officers, employees and agents, and to sublicensees under KISSEI's rights pursuant to Section 3.1 hereof, and to subcontractors in connection with the development or manufacture of Promising Compounds, to the extent necessary

to enable such parties to perform their obligations hereunder or under the applicable sublicense or subcontract, as the case may be; provided, that such officers, employees, agents, sublicensees and subcontractors have entered into appropriate confidentiality agreements for secrecy and non-use of such information which by their terms shall be enforceable by injunctive relief at the instance of the disclosing party. Each party shall be liable for any unauthorized use and disclosure of such information by its officers, employees and agents and such sublicensees and subcontractors. For purposes of this Section 4.1, the provisions of this Agreement which relate to the presence of KISSEI researchers or other representatives at VERTEX shall be considered confidential information of VERTEX to be held in strictest confidence by KISSEI and by VERTEX and its representatives without regard to the application of Section 4.2 below.

4.2 EXCEPTIONS. Notwithstanding the foregoing, the provisions of Section 4.1 hereof shall not apply to knowledge, information, documents or materials which the receiving party can conclusively establish: (i) have entered the public domain without such party's breach of any obligation owed to the disclosing party; (ii) have become known to the receiving party prior to the disclosing party's disclosure of such information to such receiving party; (iii) are permitted to be disclosed by the prior written consent of the disclosing party; (iv) have become known to the receiving party from a source other than the disclosing party other than by breach of an obligation of confidentiality owed to the disclosing party; (v) are disclosed by the disclosing party to a third party without restrictions on its disclosure; (vi) are independently developed by the receiving party without breach of this Agreement; or (vii) are required to be disclosed by the receiving party to comply with applicable laws, to defend or prosecute litigation or to comply with governmental regulations, provided that the receiving party provides prior written notice of such disclosure to the disclosing party and takes reasonable and lawful actions to avoid or minimize the degree of such disclosure.

4.3 PUBLICITY. The timing and content of any press releases or other public communications relating to the Agreement and the transactions contemplated herein will, except as otherwise required by law, be determined jointly by KISSEI and VERTEX.

4.4 SURVIVAL. The provisions of this Article IV shall survive the termination of this Agreement.

ARTICLE V

PATENTS

5.1 PREPARATION. VERTEX shall take responsibility for the preparation, filing, prosecution and maintenance of any and all patent applications and patents included in Patents; and shall furnish to KISSEI copies of documents relevant to any such preparation, filing, prosecution or maintenance. VERTEX and KISSEI shall otherwise cooperate fully in the preparation, filing, prosecution and maintenance of all Patents, executing all papers and instruments so as to enable VERTEX to apply for, to prosecute and to maintain patent applications and patents in VERTEX's name in any country in the Territory. The parties acknowledge the importance of maintaining the confidentiality of any inventions or other information relating to potential patent claims prior to the filing of patent applications with respect hereto. Each party shall provide to the other prompt notice as to all matters which may affect the preparation, filing, prosecution or maintenance of any such patent applications or patents.

5.2 COST REIMBURSEMENT. KISSEI shall reimburse VERTEX for all reasonable expenses VERTEX has incurred, or may incur in the future, for the preparation, filing, prosecution and maintenance of Promising Patents in the Territory as set forth in the Option and Rights Agreement. KISSEI will be notified by VERTEX in writing from time to time of its plans with respect to the preparation, filing, prosecution and maintenance of Patents in each country in the Territory (including the Option Territory) which are, or have not yet become, Promising Patents, together with its estimate of the costs of such preparation, filing, prosecution and maintenance. KISSEI shall reimburse VERTEX for all such reasonable costs, unless it shall notify VERTEX in writing, within thirty (30) days after receipt of any such notice from VERTEX, that KISSEI does not wish to proceed with cost reimbursement with respect to a specific Patent in any specified country in the Territory (or the Option Territory); after which time VERTEX may at its option refrain from, or abandon, the preparation, filing, prosecution or maintenance of such Patent in such country in the Territory.

5.3 FAILURE TO REIMBURSE. If KISSEI shall fail to reimburse VERTEX if required under Section 5.2 above with respect to a patent application or patent included within the Patents within sixty (60) days after receipt of a written request for payment from VERTEX, VERTEX may terminate KISSEI's rights hereunder with respect to that patent or patent application upon thirty (30) days written notice thereof to KISSEI, unless KISSEI during such 30 day period shall have submitted payment pursuant to the aforementioned request for payment.

ARTICLE VI

INFRINGEMENT

KISSEI shall notify VERTEX promptly of any possible infringements, imitations or unauthorized possession, knowledge or use, by others in any country in the Territory, of which KISSEI becomes aware, of the intellectual property embodied in any of the Patents. KISSEI shall promptly furnish VERTEX with full details of such infringements, imitations or unauthorized possession, knowledge or use, and shall assist in preventing any recurrence thereof. VERTEX shall be responsible, at its expense, for bringing any action on account of any such infringements, imitations or unauthorized possession, knowledge or use, and KISSEI shall cooperate with VERTEX, as VERTEX may reasonably request, in connection with any such action. If, within sixty (60) days after receipt by VERTEX of a written request from KISSEI that it bring such an action, VERTEX does not do so, KISSEI shall have the right, at its expense and in its own name or in the name of VERTEX, to do so on behalf of VERTEX, and VERTEX shall cooperate with KISSEI, as KISSEI may reasonably request, in connection with such action. Such suit may not be settled by KISSEI without VERTEX's consent, which shall not be unreasonably withheld. Damages recovered in any actions referenced hereunder shall be divided 50% to KISSEI and 50% to VERTEX after reimbursement to each party of their respective expenses in prosecuting such actions as provided hereunder.

ARTICLE VII

TERM AND TERMINATION

7.1 TERM OF AGREEMENT. This Agreement will extend until the termination of the Research Program and thereafter until six (6) months after the termination of the Research Program, unless earlier terminated by either party hereto in accordance with other applicable provisions of this Agreement.

7.2 TERMINATION OF RESEARCH PROGRAM BY KISSEI FOR CAUSE. Upon written notice to VERTEX, KISSEI may at its sole option terminate the Research Program and this Agreement upon the occurrence of any of the following events:

- (a) VERTEX shall materially breach this Agreement, which shall include a failure to use its reasonable best efforts to diligently pursue the Research Program (provided, however, that this shall not be construed as a guarantee by VERTEX that the Research Program will be successfully completed or any Compounds successfully developed), and such material failure to perform shall not have been remedied or steps initiated to remedy the same to KISSEI's reasonable satisfaction, within sixty (60) days after KISSEI sends written notice of failure to perform to VERTEX.
- (b) VERTEX shall cease to function as a going concern by suspending or discontinuing its business for any reason except for interruptions caused by strike, labor dispute or any other events over which it has no control (unless termination of this Agreement is permitted under Section 9.3 hereof); or
- (c) A receiver for VERTEX shall be appointed or applied for, or a general assignment shall be made for the benefit of its creditors or any proceeding involving VERTEX shall be voluntarily commenced by it under any bankruptcy, reorganization, insolvency, readjustment of debt, dissolution or liquidation law or statute of the United States or any state thereof or such proceedings shall be involuntarily instituted against it, and VERTEX by any action shall indicate its approval of or consent to, or acquiescence therein, or the same shall remain undismissed for sixty (60) days.

In the event of any valid termination under this Section 7.2, KISSEI shall not be required to make any payments under Section 2.2 hereof which are not due and payable prior to receipt by VERTEX of the notice of

failure to perform referenced under Section 7.2(a), receipt by VERTEX of the notice of termination pursuant to Section 7.2(b), or the occurrence of the event referenced in Section 7.2(c) giving rise to KISSEI's right to terminate thereunder, as the case may be. Notwithstanding the foregoing, the Options and Rights Agreement then in effect under the provisions of Article III of this Agreement shall continue in effect in accordance with its terms.

7.3 TERMINATION OF THE RESEARCH PROGRAM BY KISSEI WITHOUT CAUSE. By notice in writing delivered to VERTEX at least six (6) months prior to the proposed date of termination, KISSEI may, at its sole discretion and for any reason or no reason, terminate the Research Program and this Agreement effective as of any date after 1 July 1994. In such event, KISSEI shall make all of the payments specified in Section 2.2 hereof which are due and payable before the effective date of such termination, but shall not be required to make any payment which is due and payable on or after the effective date of termination. Notwithstanding the foregoing, all payments that would have been due under Section 2.2, absent termination by Kissei, shall become immediately due and payable to VERTEX if, before the later of (a) two (2) years after termination of this Agreement under Section 7.3, or (b) 31 December 1995, KISSEI proceeds with substantial research relating to, or development of, a compound or pharmaceutical product in the Field. The Option and Rights Agreement then in effect under the provisions of Article III hereof shall automatically terminate upon the effective date of any termination under this Section 7.3.

7.4 TERMINATION BY VERTEX. In addition to rights of termination which may be granted to VERTEX under other provisions of this Agreement, VERTEX may terminate this Agreement upon sixty (60) days prior written notice to KISSEI upon the material breach by KISSEI of any of its obligations under this Agreement, provided that such termination shall become effective only if KISSEI shall fail to remedy or cure the breach within such sixty (60) day period.

7.5 EFFECT OF TERMINATION. Termination of this Agreement for any reason, or expiration of this Agreement, will not affect: (i) obligations which have accrued as of the date of termination or expiration, and (ii) obligations and rights which, from the context thereof, are intended to survive termination or expiration of this Agreement.

ARTICLE VIII

DISPUTE RESOLUTION

8.1 GOVERNING LAW, AND JURISDICTION. This Agreement shall be governed and construed in accordance with the internal laws of the Commonwealth of Massachusetts. Both parties hereto agree to submit to personal jurisdiction in the Commonwealth of Massachusetts and to accept and agree to venue in that State.

8.2 ARBITRATION. In the event of any controversy or claim arising out of or relating to any provision of this Agreement or the breach thereof, the parties shall try to settle their differences amicably between themselves. Any such controversy or claim which the parties are unable to resolve shall, upon the written request of one party delivered to the other party, be submitted to and be settled by arbitration in Boston, Massachusetts, in accordance with the rules of the American Arbitration Association (the "AAA") then in effect (except as hereinafter stated), and judgment upon the award rendered by the arbitrators may be entered in any court having jurisdiction thereof. Notwithstanding anything to the contrary which may be contained in the rules of the AAA, the parties further agree as follows:

- (i) Each party will appoint one person approved by the AAA to hear and determine the dispute within fifteen (15) days after receipt of notice of arbitration from the noticing party. The two persons so chosen will select a third impartial arbitrator, and their majority decision will be final and conclusive upon the parties hereto. If either party fails to designate its arbitrator within fifteen (15) days after delivery of the notice provided for herein, then the arbitrator designated by the one party will act as sole arbitrator, and will be deemed to be the single, mutually approved arbitrator to resolve the controversy. In the event the parties are unable to agree upon a rate of compensation for the arbitrators, they will be compensated for their services at a rate to be determined by the AAA.

- (ii) The parties shall enjoy, but are not limited to, the same rights to discovery as they would enjoy under the Federal Rules of Civil Procedure for the district in which the City of Boston is located.
- (iii) Each party will bear its own costs, including attorneys' fees, in the arbitration, and will split equally the cost of the arbitrators.
- (iv) The arbitrators will, upon the request of either party, issue a written opinion of their findings of fact and conclusions of law and shall deliver a copy of such opinion to both parties.
- (v) Upon receipt of said written opinion, either party will have the right, within fifteen (15) days thereof, to file with the arbitrators a motion to reconsider, and the arbitrators thereupon will reconsider the issues raised by said motion and either confirm or alter their decision, which will then be final and conclusive upon both parties hereto. The costs of such a motion for reconsideration and written opinion of the arbitrators, including attorneys' fees, will be paid by the non-prevailing party. Any motion to reconsider shall be sent to the other party at the time it is filed with the arbitrators.

ARTICLE IX

MISCELLANEOUS PROVISIONS

9.1 OFFICIAL LANGUAGE. English shall be the official language of this Agreement and the Option and Rights Agreement, and all communications between the parties hereto shall be conducted in that language.

9.2 WAIVER. Any waiver by either party of the breach of any term or condition of this Agreement will not be considered as a waiver of any subsequent breach of the same or any other term or condition hereof.

9.3 FORCE MAJEURE. Neither party will be in breach hereof by reason of its delay in the performance of or failure to perform any of its obligations hereunder, if that delay or failure is caused by strikes, acts of God or the public enemy, riots, incendiaries, interference by civil or military authorities, compliance with governmental priorities for materials, or any fault beyond its control or without its fault or negligence. Notwithstanding the foregoing, in the event that any delay or failure to perform by VERTEX by reason of force majeure shall extend beyond six months, KISSEI may suspend any payments which would otherwise become due and payable to VERTEX during the next succeeding six month period under Section 2.2 hereof, and may terminate this Agreement upon notice in writing to VERTEX if such delay or failure to perform continues beyond such succeeding six (6) month period; provided, that any suspended payments shall immediately be made by KISSEI upon the earlier of (a) the resumption of normal operations by VERTEX during such succeeding six (6) month period, or (b) if KISSEI does not exercise its right to terminate this Agreement under this Section 9.3 within fifteen (15) days after the conclusion of this one year period. In the case of the occurrence of force majeure beyond six (6) months or anticipated to continue beyond six months, the parties to this Agreement shall meet and discuss the possibility of extending this Agreement, on terms acceptable to both parties.

9.4 SEVERABILITY. In the event that any provision of this Agreement, or any part hereof, is found invalid or unenforceable, the remainder of this Agreement will be binding on the parties hereto, and will be construed as if the invalid or unenforceable provision or part thereof had been deleted from this Agreement.

9.5 GOVERNMENT ACTS. In the event that any act, regulation, directive, or law of a government within the Territory, including its departments, agencies or courts, should make impossible or prohibit, restrain, modify or limit any material act or obligation of KISSEI or VERTEX under this Agreement, the party, if any, not so affected, shall have the right, at its option, to suspend or terminate this Agreement as to such country, or to make such modifications therein as may be necessary.

9.6 GOVERNMENT APPROVALS. KISSEI will obtain any government approval required in the Territory to enable this Agreement to become effective, or to enable any payment hereunder to be made, or any other obligation hereunder to be observed or performed. Each party will keep the other informed of progress in obtaining any such government approval, and will cooperate with the other party in any such efforts.

9.7 EXPORT CONTROLS. This Agreement is made subject to any restrictions concerning the export of Promising Compounds or VERTEX Technical Information from the United States which may be imposed upon or related to either party to this Agreement from time to time by the Government of the United States. Furthermore, KISSEI will not export, directly or indirectly, any VERTEX Technical Information or any Promising Compounds utilizing such Technical Information to any countries for which the United States Government or any agency thereof at the time of export requires an export license or other governmental approval, without first obtaining the written consent to do so from the Department of Commerce or other agency of the United States Government when required by applicable statute or regulation.

9.8 ASSIGNMENT. KISSEI will not have the right to assign this Agreement without the prior written consent of VERTEX, except to one of KISSEI's Affiliates. VERTEX is free to assign this Agreement to any of its Affiliates, and, with KISSEI's written consent, which shall not be unreasonably withheld, to any entity which shall assume any and all of VERTEX's obligations hereunder.

9.9 COUNTERPARTS. This Agreement may be executed in duplicate, each of which shall be deemed to be original and both of which shall constitute one and the same Agreement.

9.10 NO AGENCY. Notwithstanding any of the provisions of this Agreement, neither party to this Agreement shall at any time enter into, incur, or hold itself out to third parties as having authority to enter into or incur, on behalf of the other party, any commitment, expense, or liability whatsoever, and all contracts, expenses and liabilities in connection with or relating to the obligations of each party under this Agreement shall be made, paid, and undertaken exclusively by such party on its own behalf and not as an agent or representative of the other.

9.11 NOTICE. All communications between the parties with respect to any of the provisions of this Agreement will be sent to the addresses set out below or to other addresses as notified by the parties for the purpose of this clause, by prepaid certified air mail (which shall be deemed received by the other party on the seventh business day following deposit in the mails), or by cable, telex, facsimile transmission, or other electronic means of communication (which shall be deemed received when transmitted), with confirmation by first class letter, postage pre-paid, given by the close of business on or before the next following business day:

if to KISSEI, at:

19-48 Yoshino Matsumoto-City
Nagano-Pref. 399 Japan
Attention: Yukiyoishi Ajisawa
Director, Information and Patent R&D

Attention: Director of Legal Department

if to VERTEX, at:

40 Allston Street
Cambridge, MA 02139-4211
Attention: Richard H. Aldrich
Chief Business Officer

9.12 HEADINGS. The paragraph headings are for convenience only and will not be deemed to affect in any way the language of the provisions to which they refer.

9.13 AUTHORITY. The undersigned represent that they are authorized to sign this Agreement on behalf of the parties hereto. The parties each represent that no provision of this Agreement will violate any other agreement that a party may have with any other person or company. Each party has relied on that representation in entering into this Agreement.

9.14 ENTIRE AGREEMENT. This Agreement contains the entire understanding of the parties relating to the matters referred to herein, and may only be amended by a written document, duly executed on behalf of the respective parties.

VERTEX PHARMACEUTICALS INCORPORATED

By: _____

Title: _____

Date of Signature: _____

KISSEI PHARMACEUTICAL CO., LTD.

By: _____

Title: _____

Date of Signature: _____

SCHEDULE I (a)
 LIST OF VERTEX PATENT APPLICATIONS
 RELATED TO HIV PROTEASE INHIBITOR PROGRAM
 U.S. DISCLOSURES

DOCKET NO.	INVENTOR (S)	TITLE	STATUS	FILING DATE OR ISSUE DATE	APPLICATION OR PATENT NO.	EXPIRATION DATE
VP191-01 (AOC)	Tung, Deininger	Tetrahydroxy Alkane and Alkene Derivatives as Inhibitors of HIV Aspartyl Protease	AB	3/20/91	07/672,176	
VP191-01A	Tung, Deininger	Tetrahydroxy Alkane and Alkene Derivatives as Inhibitors of HIV Aspartyl Protease	F	3/20/92	07/856,095	
VP191-02	Meyers, Livingston, Murcko, Tung	Novel Compounds Having Affinity for HIV Aspartyl Protease	F	3/28/91	07/676,897	
VP191-02Z	Meyers, Livingston, Murcko, Tung	Novel Compounds Having Affinity for HIV Aspartyl Protease	F	1/6/93	08/000,966	
VP192-07 (AOC)	Tung	Novel Inhibitors of HIV-1 Aspartyl Protease	F	9/8/92	07/941,982	
VP192-08 (AOC)	Boger, Meyers, Mullican	Novel Inhibitors of HIV Aspartyl Protease	F	12/11/92	07/989,239	

STATUS CODE:

AB =	Abandoned	DP =	Draft Prepared
AD =	Active Disclosure	H =	Hold
AF =	Approved for Filing	I =	Inactive
AS =	Approved for Search	P =	Patented
C =	Combined with	S =	Searched
DI =	Draft in Preparation	F =	Filed

SCHEDULE I (B)

LIST OF VERTEX PATENT APPLICATIONS
RELATED TO HIV PROTEASE INHIBITOR PROGRAM

FOREIGN DISCLOSURES

DOCKET NO.	COUNTRY	INVENTOR (S)	TITLE	STATUS	FILING DATE OR ISSUE DATE	APPLICATION OR PATENT NO.	EXPIRATION DATE
VP191-01A (AOC)	PCT	Tung, Deininger	Tetrahydroxy Alkane and Alkene Derivatives as Inhibitors of HIV Aspartyl Protease	F	3/20/92	PCT/US92/02290	

(Designating all EPO countries; Austria, Belgium, Switzerland/Liechtenstein, Germany, Denmark, Spain, France, United Kingdom, Greece, Italy, Luxembourg, Monaco, Netherlands, Sweden, OAPI and all member countries except US.)

SCHEDULE II

HIV PROTEASE INHIBITOR PROGRAM
SUMMARY OF RESEARCH ACTIVITIES -- 1990 - 1995

CONFIDENTIAL INFORMATION OMITTED

SCHEDULE 1.13

COUNTRIES IN THE OPTION TERRITORY

Brunei
Burma (Myanmar)
Cambodia (Kampuchea)
Hong Kong
Indonesia
Korea, North and South
Laos
Macao
Malaysia
Philippines
Singapore
Taiwan
Thailand
Vietnam

EXHIBIT A

OPTION AND RIGHTS AGREEMENT

This Agreement is made and entered into as of 13 NOVEMBER 1995 between Vertex Pharmaceuticals Incorporated (hereinafter "VERTEX"), a Massachusetts corporation, and Kissei Pharmaceutical Co., Ltd. (hereinafter "KISSEI"), a Japanese corporation.

INTRODUCTION

WHEREAS, VERTEX and KISSEI are parties to a certain Research and Development Agreement dated 13 April 1993 (the "Research and Development Agreement") under which VERTEX is attempting to design and discover novel HIV protease inhibitor compounds with the financial and technical assistance of KISSEI; and

WHEREAS, VERTEX is the owner of the entire right, title and interest in the Promising Patents (as defined below); and

WHEREAS, KISSEI wishes to obtain an exclusive option right to practice the invention covered by the Promising Patents in the Territory (as defined below) and to develop, use and sell in the commercial market the Promising Compounds and the products made in accordance therewith; and

WHEREAS, VERTEX agrees to such exclusive option right of KISSEI in accordance with the terms of this Agreement.

NOW THEREFORE, in consideration of the foregoing premises, the parties agree as follows:

ARTICLE I

DEFINITIONS

1.1 "Affiliate" shall mean at any time, any person or legal entity, then directly or indirectly controlled by, controlling or under common control with the party with respect to which this term is associated, and shall include any person or legal entity which owns, either of record or beneficially, 50% or more of the voting stock of any party hereto, or 50% or more of the voting stock of which is owned by any party hereto.

1.2 "Field" shall mean human use in the diagnosis, prevention and treatment of AIDS and HIV infection caused by HIV-1 and HIV-2 retroviruses, or infection caused by the related retrovirus, HTLV-1.

1.3 "Compounds" shall mean small molecule inhibitors of HIV-1 and HIV-2 protease, as well as inhibitors of the related protease of HTLV-1 discovered or developed by VERTEX or together with KISSEI in the Field in the course of the Research Program, whether discovered or developed by VERTEX or together with KISSEI prior to or after the effective date of the Research and Development Agreement, or, if the Research Program is not terminated earlier by KISSEI pursuant to Section 7.2 or 7.3 of the Research and Development Agreement, discovered or developed by VERTEX or together with KISSEI during the period ending six (6) months after the conclusion of the Research Program pursuant to Section 2.1 of the Research and Development Agreement.

1.4 "Promising Compounds" shall mean any Compounds as to which the option rights granted under Article III of the Research and Development Agreement have been exercised in accordance therewith by KISSEI as identified on Schedule I hereto, as Schedule I may be updated from time to time by reason of the subsequent exercise by KISSEI of such option rights with respect to additional Compounds.

1.5 "Promising Processes" shall mean any processes resulting from the Research Program as to which the option under Article III of the Research and Development Agreement has been exercised in accordance therewith by KISSEI, as identified on Schedule I hereto, as Schedule I may be updated from time to time by reason of the subsequent exercise by KISSEI of such option with respect to additional processes.

1.6 "Promising Patents" shall mean the patents or patent applications claiming a Promising Compound, a Promising Process, or a method of manufacturing or using a Promising Compound, as to which the option under Article III of the Research and Development Agreement has been exercised in accordance therewith by KISSEI, as identified on Schedule I hereto and as Schedule I may be updated from time to time by reason of the subsequent exercise by KISSEI of such option with respect to additional patents, and shall include any continuations, continuations-in-part, or divisions of such patents or patent applications or any substitute applications therefore. VERTEX shall keep KISSEI currently informed in writing of additions and amendments to Schedule I.

1.7 "Research Program" shall have the meaning ascribed to it in the Research and Development Agreement.

1.8 "Research and Development Agreement" shall mean that certain Research and Development Agreement dated 13 April 1993 by and between VERTEX and KISSEI.

1.9 "Development Program" shall mean activities associated with development of Promising Compounds for sale, including but not limited to (a) selection of clinical trial candidates from among lead Compounds and preparation for preclinical assessment thereof; (b) formulation of the Promising Compounds for use in preclinical studies; (c) preclinical animal studies performed in accordance with "Good Laboratory Practices" (or the applicable equivalent) in preparation for the filing of an Investigative New Drug Application (or the applicable equivalent); (d) manufacture and formulation of the Promising Compounds for preclinical and clinical studies; (e) planning, implementation, evaluation and administration of human clinical

trials; (f) manufacturing process development and scale-up; and (g) preparation and submission of applications for regulatory approval.

1.10 "KISSEI Technical Information" shall mean all know-how, proprietary information, or special knowledge of KISSEI relating to the research, development, utilization, manufacture, or use of any Promising Compounds, or Promising Processes, including but not limited to processes, techniques, methods, products, materials, and compositions.

1.11 "VERTEX Technical Information" shall mean all know-how, proprietary information, or special knowledge of VERTEX relating to the research, development, utilization, manufacture, or use of any Promising Compounds, or Promising Processes, including but not limited to processes, techniques, methods, products, materials, and compositions.

1.12 "Territory" shall mean Japan and the People's Republic of China and shall also include, if KISSEI has exercised its option under Section 3.3 of the Research and Development Agreement, the Option Territory as defined therein. Hong Kong shall be included in the Territory from the time that it becomes part of the People's Republic of China.

1.13 "Effective Date" shall mean the date on which this Agreement enters into effect pursuant to Section 3.2 of the Research and Development Agreement.

1.14 "Net Sales" in the twelve months immediately following the first commercial sale of a Promising Compound shall mean the product obtained by multiplying unit sales of the Promising Compound in Japan during each quarterly period by 75% (the "Adjustment Percentage") of the average National Health Insurance price for such Promising Compound during such period; and thereafter the parties shall discuss, at least annually, whether the Adjustment Percentage should be revised to reflect actual experience, to be reported to VERTEX, with respect to the following items of deduction from the National Health Insurance price:

- (a) Customary trade, quantity or cash discounts and non-affiliated brokers' or agents' commissions actually allowed and taken;
- (b) Amounts repaid or credited by reason of rejection or return; and/or
- (c) To the extent separately stated on purchase orders, invoices or other documents of sale, taxes levied on and/or other government charges made as to production, sale, transportation, delivery or use and paid by or on behalf of KISSEI;
- (d) Freight insurance and handling charges.

provided that

- 1.14.1 in the case of any sale or other disposal by a party thereto to an Affiliate, the Net Sales shall be calculated as above on the value

charged or invoiced on the first arm's length sale to a party who is not an Affiliate;

- 1.14.2 in the event of a sublicense as to any Promising Compound, Net Sales will be calculated with respect to sales by the sublicensee.
- 1.14.3 in the case of any other sale or other disposal, such as barter or counter-trade, of any Promising Compounds, or Promising Processes, or part thereof, otherwise than in an arm's length transaction exclusively for money, the Net Sales shall be calculated as above on the fair market price (if higher) in the relevant country of sale or disposal.

ARTICLE II

KISSEI'S RIGHTS

2.1 RIGHTS. KISSEI has the sole and exclusive right even as to VERTEX, under the Promising Patents to develop, make, have made, formulate, use or sell Promising Compounds in the Territory and to practice the Promising Processes to develop, make, have made, formulate, use or sell Promising Compounds in the Territory. KISSEI shall have the right to grant sublicenses under the Promising Patents on terms not inconsistent with this Agreement, provided that KISSEI shall forthwith notify VERTEX of the grant of any such sublicense, together with the name and address of any such sublicensee, shall provide VERTEX with a summary of the terms of any such sublicense, shall promptly take all reasonable steps in the event of the breach of any such sublicense by the sublicensee to enforce the same, and in the event of a breach of any such sublicense shall, if so requested by VERTEX, terminate that sublicense in accordance with the procedures prescribed therein. If VERTEX so requests, KISSEI shall make available to VERTEX for its review a complete copy of any of its agreements that grant a sublicense under the Promising Patents and Promising Processes.

2.2 TECHNICAL INFORMATION. VERTEX hereby grants to KISSEI the exclusive right, even as to VERTEX, to use VERTEX Technical Information throughout the Territory to develop, manufacture, formulate and sell Promising Compounds and to permit any subcontractors or sublicensees to use VERTEX Technical Information for such purposes pursuant to provisions safeguarding confidentiality equivalent to those provided in this Agreement.

2.3 INFORMATION TRANSFER. At such time as VERTEX and KISSEI shall enter into this Agreement with respect to a Promising Compound, VERTEX shall deliver to KISSEI all information accurately and adequately requested by it which is necessary or useful for further development, manufacture, formulation and commercial exploitation and distribution of the Promising Compound in the Territory. This information shall include copies of all patents, patent applications, copyrights, copyright registrations and applications therefor and all other manifestations of the intellectual property embodied in the Promising Compound, whether in

human or machine readable form. Should regulatory authorities in the Territory seek to audit or inspect data or samples from development activities completed outside of the Territory, VERTEX will reasonably cooperate and will seek reasonable cooperation from its collaborative partners outside of the Territory on this matter even if they are no longer involved in the development of this project. KISSEI will provide VERTEX with reasonable notice regarding specific audits and inspections that may be required.

2.4 DUE DILIGENCE. KISSEI shall promptly commence a Development Program with respect to the Promising Compounds and use its best efforts to effect introduction of the Promising Compounds (or other Compounds which become the subject of a KISSEI's rights under the Research and Development Agreement) into the commercial market in the Territory as soon as practicable consistent with the requirements of the Development Program and sound and reasonable business practices and judgment. In the normal course of Development, (including activities in compliance with requirements or instructions of the Japanese government or other public organizations with jurisdiction over KISSEI and its drug development activities), a certain Promising Compound may be dropped from Development and replaced within a reasonable time with an improved or another Promising Compound, and such occurrence in the Development Program shall not constitute a failure of due diligence. And if KISSEI should change its development schedule because of requirements or instructions of the Japanese government or other public organizations with jurisdiction over KISSEI and its drug development activities, such change shall not constitute a failure of due diligence. Thereafter, until the expiration of this Agreement, KISSEI shall endeavor to keep Promising Compounds (or other Compounds which become the subject of KISSEI's rights under Article III of the Research and Development Agreement) reasonably available to the public.

2.5 DEVELOPMENT. KISSEI will bear the cost of and be responsible for the Development Program for Promising Compound(s) in the Territory, including without limitation completing any preclinical and clinical studies required to obtain regulatory approval of Promising Compound(s) in the Territory, to the extent that such studies and other development activities are not otherwise required as part of VERTEX's development of Promising Compound(s) outside the Territory. VERTEX will provide KISSEI with any and all preclinical and clinical data generated by VERTEX as part of VERTEX's development of such Compound(s) in North America and Europe. KISSEI shall be free to use such data and information solely for the purpose of developing Promising Compound(s) in the Territory pursuant hereto.

2.6 TERMINATION. VERTEX shall have the right to terminate or render non-exclusive KISSEI's Rights hereunder upon sixty (60) days' written notice to KISSEI if, in VERTEX's reasonable judgment, KISSEI is not demonstrably and diligently engaged in development, manufacturing, or marketing programs, as appropriate, directed toward placing Promising Compounds hereunder into commercial use in Japan, or, following product introduction in Japan, is not keeping Promising Compounds reasonably available to the public in such country. In making this determination VERTEX shall take into account the normal course of such programs conducted with sound and reasonable business practices and judgment. VERTEX shall also have the right to terminate or render this right non-exclusive in any other country in the territory at any time upon sixty (60) days' written notice to KISSEI if, within two (2) years from the date of

regulatory approval for the sale of the Promising Compound(s) in Japan, KISSEI has not put the Promising Compound(s) into commercial use in such country, or following initial product introduction in such country is not keeping the Promising Compound(s) matter reasonably available to the public, unless KISSEI is demonstrably and diligently engaged in development, manufacturing or marketing programs as appropriate, directed toward placing the Promising Compound(s) into commercial use in such country as aforesaid.

2.7 GRANTBACK. KISSEI shall keep VERTEX fully advised of any improvements by KISSEI or its Affiliates or sublicensees relating to Compounds and Promising Processes during the term of the Research Program and the Development Program, whether patentable or not ("KISSEI Improvements"). At the request of VERTEX, KISSEI shall grant to VERTEX a non-exclusive royalty-free license to any such Improvements generated by it, and will seek to obtain similar rights in favor of VERTEX for any such Improvements generated or made available to it by its Affiliates and sublicensees, if any. In such event, (a) VERTEX shall seek to obtain similar non-exclusive, royalty-free rights to be granted to KISSEI in the Territory for any such Improvements generated or made available to VERTEX by its other licensees, if any ("VERTEX Improvements"); and (b) VERTEX shall refrain from exploiting its non-exclusive rights to any such KISSEI Improvements in the Territory so long as this Agreement is in effect between VERTEX and KISSEI covering Promising Compounds.

ARTICLE III

SUPPLY

3.1 MANUFACTURING AND SUPPLY. Based on mutual agreement, VERTEX will manufacture and supply for KISSEI and KISSEI shall purchase all of KISSEI's requirements of bulk Promising Compound(s) then under development or being marketed by VERTEX at VERTEX's cost plus a reasonable profit consistent with industry practices and an arm's length transaction, and upon such further terms and conditions as shall be agreed upon by the parties, negotiating in good faith, not less than twelve (12) months prior to the anticipated date of first commercial sale of a Promising Compound in the Territory. Moreover, the supplying price in the Territory other than Japan should be consulted on and be fixed again before the first launch outside Japan. VERTEX plans to use the most efficient and cost effective manufacturing process available at the time it establishes its manufacturing capacity and will use commercially reasonable efforts to incorporate KISSEI's process development recommendations into its production processes, to the extent that those recommendations are submitted to VERTEX in a timely manner and would result, if implemented, in substantially lower bulk production costs and a substantially lower cost of material to KISSEI.

KISSEI may formulate Promising Compounds for sale and use in the Territory, and VERTEX will provide KISSEI, including but not limited to, formulation information and technology relating to Promising Compounds that it receives from partners and collaborators outside of the Territory which is not subject to restriction on distribution to or use by KISSEI. VERTEX and KISSEI will coordinate their respective activities with a goal of developing and marketing Promising Compounds using the same formulation in the Territory and outside of the Territory.

Should VERTEX be unable to produce bulk Promising Compound(s) at a price that allows KISSEI to sell products profitably in any particular country in the Territory, and if KISSEI can demonstrate to the reasonable satisfaction of VERTEX that it can produce bulk Promising Compound(s) of comparable quality and consistency at a substantially more favorable cost for commercial sale in that country in the Territory, VERTEX and KISSEI may agree that KISSEI can produce its own bulk Promising Compound(s) sole for sale and use in that country. In such case, KISSEI will pay a higher royalty to VERTEX, based on the profits VERTEX will lose by not selling bulk Promising Compound(s) to KISSEI solely for sale and use in that country.

ARTICLE IV

REPORTING

4.1 DEVELOPMENT REPORTS. KISSEI shall prepare and submit to VERTEX, on a quarterly basis, reports which set forth in reasonable detail the progress of the Development Program and the results of work performed thereunder during the preceding quarter. Vertex shall also report to KISSEI on a quarterly basis the results of any development work which it may have undertaken with respect to Promising Compounds during the preceding quarter.

4.2 EXCHANGE OF INFORMATION. VERTEX and KISSEI will freely share technical information in the Field, including VERTEX Technical Information and KISSEI Technical Information, which is not subject to restrictions imposed by a third party on disclosure to or use by the other party. KISSEI will enable VERTEX to review the ongoing development being conducted under the Development Program and to discuss that information with its officers, all at such reasonable times and as often as may be reasonably requested. VERTEX and KISSEI will seek to form a committee or other such body, when appropriate, to coordinate development activities between KISSEI, VERTEX and any of their respective licensees or sublicensees. Any representatives of VERTEX or KISSEI receiving information from representatives of the other party shall sign appropriate agreements ensuring that information disclosed to them is held in confidence.

ARTICLE V

ROYALTIES

5.1 ROYALTY. Subject to the following paragraphs, KISSEI shall pay to VERTEX a royalty of [CONFIDENTIAL INFORMATION OMITTED] percent of the Net Sales of all Promising Compounds in Japan. On sales between KISSEI and its Affiliates for resale, the royalty shall be computed and paid on the resale. The parties will agree on a method of calculation of return to VERTEX from sales of Promising Compounds in the Territory outside Japan which will reflect the principles set forth in this Agreement with respect to royalties on Net Sales in Japan, but with formulations and measures appropriate to the particular circumstances. Prior to the initial commercial launch of a Promising Compound in the Territory, and thereafter as requested by

either party, VERTEX and KISSEI will discuss in good faith market factors expected upon sale of the Promising Compounds. If KISSEI can establish the existence, to VERTEX's reasonable satisfaction, of extraordinary cost/price factors involving reimbursement and manufacturing in a country in the Territory, then VERTEX and KISSEI shall negotiate in good faith a downward revision in the royalty rate for the Promising Compounds for the relevant country or countries in the Territory, but any such revision shall not reduce the royalty rate to less than [CONFIDENTIAL INFORMATION OMITTED] percent.

5.2 CURRENCY OF PAYMENT. All payments from KISSEI to VERTEX shall be made by wire transfer in U.S. dollars. The rates of exchange for such payments shall be the Telegraphic Transfer Selling rate ("TTS") of the Sumitomo Bank in Tokyo, Japan on the day and time of remittance.

5.3 REPORTS, PAYMENTS, AND RECORDS. KISSEI shall deliver to VERTEX within 45 days after the end of each calendar quarter a written report showing its computation of royalties due under this Agreement on Net Sales by KISSEI, its Affiliates and sublicensees during such calendar quarter. All Net Sales shall be divided in each such report into sales by KISSEI and each Affiliate and sublicensee, as well as on a country-by-country basis, and shall state the rates of exchange used to convert the royalties into United States dollars from the currency in which such sales were made. Simultaneously with the delivery of each such report, KISSEI shall tender payment to VERTEX of all royalties shown to be due thereon. KISSEI will keep complete, true and accurate books of account and records for the purpose of showing the derivation of all royalties payable to VERTEX under this Agreement. Such books and records will be kept at KISSEI's principal place of business for at least three (3) years following the end of the calendar quarter to which they pertain, and will be open at all reasonable times for inspection by representatives of VERTEX for the purpose of verifying KISSEI's royalty statements, or KISSEI's compliance in other respects with this Agreement. Such inspections shall be at the expense of VERTEX, unless a variation or error exceeding U.S. \$1,000, or the equivalent, is discovered in the course of any such inspection, whereupon the costs relating thereto shall be for the account of KISSEI. KISSEI will promptly pay to VERTEX the full amount of any underpayment, together with interest thereon at the rate of twelve percent (12%) per annum, compounded monthly from the date payment was due.

5.4 PAYMENT DELAY. In case of any delay in payment by KISSEI to VERTEX not occasioned by force majeure, interest at the rate of one percent (1%) per month, assessed from the thirty-first day after the due date of the said payment, shall be due by KISSEI without any special notice.

ARTICLE VI

CONFIDENTIALITY

6.1 UNDERTAKING. During the term of this Agreement, each party shall keep confidential, and other than as provided herein shall not use or disclose, directly or indirectly, any trade secrets, confidential or proprietary information, or any other knowledge, information,

documents or materials, owned, developed or possessed by the other party, whether in tangible or intangible form, the confidentiality of which such other party takes reasonable measures to protect, including but not limited to VERTEX Technical Information and KISSEI Technical Information. Each party shall take any and all lawful measures to prevent the unauthorized use and disclosure of such information, and to prevent unauthorized persons or entities from obtaining or using such information. Each party further agrees to refrain from directly or indirectly taking any action which would constitute or facilitate the unauthorized use or disclosure of such information. Each party may disclose such information to its officers, employees and agents, and to sublicensees under the right pursuant to Section 2.1 and 2.2 hereof and to subcontractors in connection with its development or manufacturing of Promising Compounds to the extent necessary to enable such parties to perform their obligations hereunder or under the applicable sublicense or subcontract, as the case may be; provided that such officers, employees, agents, sublicensees and subcontractors have entered into appropriate confidentiality agreements for secrecy and non-use of such information which by their terms shall be enforceable by injunctive relief at the instance of the disclosing party. Each party shall be liable for any unauthorized use and disclosure of such information by its officers, employees, agents, sublicensees and subcontractors.

6.2 EXCEPTIONS. Notwithstanding the foregoing, the provisions of section 6.1 hereof shall not apply to knowledge, information, documents or materials which the receiving party can conclusively establish: (i) have entered the public domain without such party's breach of any obligation owed to the disclosing party; (ii) have become known to the receiving party prior to the disclosing party's disclosure of such information to such receiving party; (iii) are permitted to be disclosed by the prior written consent of the disclosing party; (iv) have become known to the receiving party from a source other than the disclosing party other than by breach of an obligation of confidentiality owed to the disclosing party; (v) are disclosed by the disclosing party to a third party without restrictions on its disclosure; (vi) are independently developed by the receiving party without breach of this Agreement; or (vii) are required to be disclosed by the receiving party to comply with applicable laws, to defend or prosecute litigation or to comply with governmental regulations, provided that the receiving party provides prior written notice of such disclosure to the other party and takes reasonable and lawful actions to avoid or minimize the degree of such disclosure.

6.3 SURVIVAL. The provisions of this Article VI shall survive the termination of this Agreement.

ARTICLE VII

PATENTS

7.1 PREPARATION. VERTEX shall take responsibility for the preparation, filing, prosecution and maintenance of any and all patent applications and patents included in Promising Patents; and shall furnish to KISSEI copies of documents relevant to any such preparation, filing, prosecution or maintenance. VERTEX and KISSEI shall otherwise cooperate fully in the preparation, filing, prosecution and maintenance of all Promising Patents, executing all papers

and instruments so as to enable VERTEX to apply for, to prosecute and to maintain patent applications and patents in VERTEX's name in any country in the Territory. Each party shall provide to the other prompt notice as to all matters which may affect the preparation, filing, prosecution or maintenance of any such patent applications or patents.

7.2 COST REIMBURSEMENT. KISSEI shall reimburse VERTEX for all reasonable expenses VERTEX has incurred, or may incur in the future, for the preparation, filing, prosecution and maintenance of Promising Patents in the Territory, including with respect to the Option Territory, if applicable, and shall reimburse VERTEX for all such future expenses.

7.3 FAILURE TO REIMBURSE. If KISSEI shall fail to reimburse VERTEX as required under Section 7.2 above with respect to a patent application or patent included within the Promising Patents within sixty (60) days after receipt of a written request for payment from VERTEX, VERTEX may terminate KISSEI's rights hereunder and under the Research and Development Agreement with respect to that patent or patent application upon thirty (30) days' written notice thereof to KISSEI, unless KISSEI during such 30-day period shall have submitted payment pursuant to the aforementioned request for payment.

ARTICLE VIII

INFRINGEMENT

KISSEI shall notify VERTEX promptly of any possible infringements, unauthorized possession, knowledge or use of the intellectual property embodied in any of the Promising Patents by others in any country in the Territory, of which KISSEI becomes aware. KISSEI shall promptly furnish VERTEX with full details of such infringements, unauthorized possession, knowledge or use, and shall assist in preventing any recurrence thereof. VERTEX shall be responsible, at its expense, for bringing any action on account of any such infringements, unauthorized possessions, knowledge or use, and KISSEI shall cooperate with VERTEX, as VERTEX may request, in connection with any such action. If, within sixty (60) days after receipt by VERTEX of a written request from KISSEI that it bring such action VERTEX does not do so, KISSEI shall have the right, at its expense and in its own name or in the name of VERTEX, to do so on behalf of VERTEX, and VERTEX shall cooperate with KISSEI, as KISSEI may reasonably request, in connection with such action. Such suit may not be settled by KISSEI without VERTEX's consent, which shall not be unreasonably withheld. Damages recovered in any actions referenced hereunder shall be divided 50% to KISSEI and 50% to VERTEX, after reimbursement to each party of their respective expenses in prosecuting such actions as provided hereunder. If such expenses incurred by KISSEI exceed any damages recovered in any actions, 50% of such excess may be deducted from royalties thereafter payable to VERTEX on Net Sales in such country, provided that total royalties otherwise due to VERTEX on Net Sales in such country in any year shall not be reduced by more than 50% as a result of such deduction.

ARTICLE IX

DISPUTE RESOLUTION

9.1 GOVERNING LAW; JURISDICTION. This Agreement shall be governed and construed in accordance with the internal laws of the Commonwealth of Massachusetts. Both parties hereto agree to submit to personal jurisdiction in the Commonwealth of Massachusetts and to accept and agree to venue in that State.

9.2 ARBITRATION. In the event of any controversy or claim arising out of or relating to any provision of this Agreement or the breach thereof, the parties shall try to settle their differences amicably between themselves. Any such controversy or claim which the parties are unable to resolve shall, upon the written request of one party delivered to the other party, be submitted to and be settled by arbitration in Boston, Massachusetts, in accordance with the rules of the American Arbitration Association (the "AAA") then in effect (except as hereinafter stated), and judgment upon the award rendered by the arbitrators may be entered in any court having jurisdiction thereof. Notwithstanding anything to the contrary which may be contained in the rules of the AAA, the parties further agree as follows:

- (i) Each party will appoint one person approved by the AAA to hear and determine the dispute within fifteen (15) days after receipt of notice of arbitration from the noticing party. The two persons so chosen will select a third impartial arbitrator, and their majority decision will be final and conclusive upon the parties hereon. If either party fails to designate its arbitrator within fifteen (15) days after delivery of the notice provided for herein, then the arbitrator designated by the one party will act as sole arbitrator, and will be deemed to be the single, mutually approved arbitrator to resolve the controversy. In the event the parties are unable to agree upon a rate of compensation for the arbitrators, they will be compensated for their services at a rate to be determined by the AAA.
- (ii) The parties shall enjoy, but are not limited to, the same rights to discovery as they would enjoy under the Federal Rules of Civil Procedure for the district in which the City of Boston is located.
- (iii) Each party will bear its own costs, including attorneys' fees, in the arbitration, and will split equally the cost of the arbitrators.
- (iv) The arbitrators will, upon the request of either party, issue a written opinion of their findings of fact and conclusions of law and shall deliver a copy of such opinion to both parties.
- (v) Upon receipt of said written opinion, either party will have the right, within fifteen (15) days thereof, to file with the arbitrators a motion to reconsider, and the arbitrators thereupon will reconsider the issues raised by said motion and either confirm or alter their decision, which will then be final and conclusive upon both parties hereto. The costs of such a motion for reconsideration and written opinion of the arbitrators, including attorneys' fees, will be paid by the non-prevailing party. Any motion to reconsider shall be sent to the other party at the time it is filed with the arbitrators.

ARTICLE X

TERM AND TERMINATION

10.1 TERM. The term of this Agreement shall extend until the later of the last to expire of the Promising Patents or ten (10) years from the date of first commercial sale of the Promising Compound in the last country in the Territory in which commercial sales are initiated.

10.2 TERMINATION. In addition to rights of termination which may be granted to either party under other provisions of this Agreement, either party may terminate this Agreement upon sixty (60) days' prior written notice to the other party upon the material breach by such other party of any of its obligations under this Agreement, provided that such termination shall become effective only if the breaching party shall fail to remedy or cure the breach within such sixty (60) day period.

10.3 EFFECT OF TERMINATION. Termination of this Agreement for any reason, or expiration of this Agreement, will not affect: (i) obligations, including the payment of any royalties, which have accrued as of the date of termination or expiration, and (ii) rights and obligations which, from the context thereof, are intended to survive termination or expiration of this Agreement.

ARTICLE XI

MISCELLANEOUS PROVISIONS

11.1 NO WARRANTY. VERTEX makes no warranty of any kind whatsoever, either express or implied, to KISSEI, or any customer of KISSEI, as to the ability of KISSEI to understand and utilize the Promising Patents or VERTEX Technical Information. KISSEI shall indemnify and shall hold VERTEX harmless against and from any and all claims of third parties for damages due to personal injury arising out of the actions of KISSEI, its Affiliates, agents, employees, sublicensees or subcontractors, including but not limited to claims arising in connection with the development, manufacturing, assembly, or sale of Promising Compounds by KISSEI. Notwithstanding the foregoing, should VERTEX manufacture Promising Compounds for KISSEI, it will warrant that such manufacture will be accomplished strictly in accordance with KISSEI's manufacturing specifications and will indemnify KISSEI against any damages caused by VERTEX's failure to meet such specifications. In addition, VERTEX and KISSEI will each promptly notify the other should the notifying party become aware of any unexpected adverse reactions to any Promising Compounds administered to humans or animals.

11.2 THIRD PARTY ACTIONS. To VERTEX's knowledge, the exercise of the rights by KISSEI hereunder will not result in the infringement of valid patents of third parties. Nevertheless, each party will promptly notify the other in the event any relevant third party patents come to its notice. VERTEX gives no warranty regarding the infringement of third party rights by practice of the Promising Patents, and gives no indemnity against costs, damages,

expenses or other losses arising out of proceedings brought against KISSEI or any other person by any third party. In the event KISSEI is sued for infringement of any rights of any third party in the course of its development, manufacture, marketing and sale of Promising Compounds or its use of Promising Patents in connection therewith, VERTEX shall extend to KISSEI, at no charge, good faith assistance and support in defending such action, and may participate in the conduct of the suit at its own expense, but shall otherwise be under no obligation in respect thereof. Legal expenses and fees arising from such a legal action shall be paid by KISSEI.

11.3 WAIVER. Any waiver by either party of the breach of any term or condition of this Agreement will not be considered as a waiver of any subsequent breach of the same or any other term or condition hereof.

11.4 FORCE MAJEURE. Neither party will be in breach hereof by reason of its delay in the performance of or failure to perform any of its obligations hereunder, if that delay or failure is caused by strikes, acts of God or the public enemy, riots, incendiaries, interference by civil or military authorities, compliance with governmental priorities for materials, or any fault beyond its control or without its fault or negligence.

11.5 SEVERABILITY. In the event that any provision of this Agreement, or any part hereof, is found invalid or unenforceable, the remainder of this Agreement will be binding on the parties hereto, and will be construed as if the invalid or unenforceable provision or part thereof had been deleted from this Agreement.

11.6 GOVERNMENT ACTS. In the event that any act, regulation, directive, or law of a government within the Territory, including its departments, agencies or courts, should make impossible or prohibit, restrain, modify or limit any material act or obligation of KISSEI or VERTEX under this Agreement, the party, if any, not so affected, shall have the right, at its option, to suspend or terminate this Agreement as to such country, or to make such modifications therein as may be necessary.

11.7 GOVERNMENT APPROVALS. KISSEI will obtain any government approval required in the Territory to enable this Agreement to become effective, or to enable any payment hereunder to be made, or any other obligation hereunder to be observed or performed. Each party will keep the other informed of progress in obtaining any such approvals.

11.8 EXPORT CONTROLS. This Agreement is made subject to any restrictions concerning the export of Promising Compounds, or VERTEX Technical Information from the United States which may be imposed upon or related to either party to this Agreement from time to time by the Government of the United States. Furthermore, KISSEI will not export, directly or indirectly, any VERTEX Technical Information or any Promising Compounds utilizing such Technical Information to any countries for which the United States Government or any agency thereof at the time of export requires an export license or other governmental approval, without first obtaining the written consent to do so from the Department of Commerce or other agency of the United States Government when required by applicable statute or regulation.

11.9 ASSIGNMENT. KISSEI will not have the right to assign this Agreement without the prior written consent of VERTEX, except to one of KISSEI's Affiliates. VERTEX is free to assign this Agreement to any of its Affiliates, and, with KISSEI's written consent, which shall not be unreasonably withheld, to any entity which shall assume any and all of VERTEX's obligations hereunder.

11.10 COUNTERPARTS. This Agreement may be executed in duplicate both of which shall be deemed to be originals, and both of which shall constitute one and the same Agreement.

11.11 NO AGENCY. Notwithstanding any of the provisions of this Agreement, KISSEI at no time will enter into, incur, or hold itself out to third parties as having authority to enter into or incur, on behalf of VERTEX, any commitment, expense, or liability whatsoever, and all contracts, expenses and liabilities in connection with or relating to the development, manufacture or sale of the Promising Compounds shall be made, paid, and undertaken exclusively by KISSEI, and not as an agent or representative of VERTEX.

11.12 COMPETITION. During the term of this Agreement, KISSEI, including its Affiliates, will not manufacture, sell, or cause to be manufactured or sold anywhere in the Territory, products directly competing with the Promising Compounds without the specific prior written approval of VERTEX. If this Agreement is terminated for breach by or nonfeasance of KISSEI, neither KISSEI or its Affiliates will manufacture or sell products within the Field for two (2) years after such termination.

11.13 NOTICE. All communications between the parties with respect to any of the provisions of this Agreement will be sent to the addresses set out below, or to other addresses as notified by the parties for the purpose of this clause, by prepaid, registered or certified air mail which shall be deemed received by the other party on the seventh business day following deposit in the mails, or by cable, telex, facsimile transmission, or other electronic means of communication (which shall be deemed received when transmitted), with confirmation by letter given by the close of business on the next following business day:

if to KISSEI, at:

19-48 Yoshino Matsumoto-City
Nagano Pref. 399 Japan
Attention: Yukiyoshi Ajisawa
Board Director
Discovery Research, R&D

if to VERTEX, at:

40 Allston Street
Cambridge, Massachusetts 02139-4211
Attention: Richard H. Aldrich
Chief Business Officer

11.14 HEADINGS. The paragraph headings are for convenience only and will not be deemed to affect in any way the language of the provisions to which they refer.

11.15 AUTHORITY. The undersigned represent that they are authorized to sign this Agreement on behalf of the parties hereto. The parties each represent that no provision of this Agreement will violate any other agreement that a party may have with any other person or company. Each party has relied on that representation in entering into this Agreement.

This Agreement contains the entire understanding of the parties relating to the matters referred to herein, and may only be amended by a written document, duly executed on behalf of the respective parties.

VERTEX PHARMACEUTICALS INCORPORATED

By: _____

Title: _____

Date of Signature: _____

KISSEI PHARMACEUTICAL CO., LTD.

By: _____

Title: _____

Date of Signature: _____

SCHEDULE I

PROMISING COMPOUNDS, PROCESSES AND PATENTS

"Promising Compound"	VX-478 (also known as 141W94 and KVX-478) IUPAC Chemical Name (3S)-tetrahydro-3-furyl N-[(1S,2R)-3-(4-amino-Nisobutylbenzenesulfonamido)-1-benzyl-2-hydroxypropyl]carbamate mesylate
"Promising Process"	None
"Promising Patent"	PCT Patent Application Serial Number PCT/US93/08458 (WO 94/05639), "Novel Sulfonamide Inhibitors of Aspartyl Protease", Tung, et al., filed September 7, 1993 (VPI/92-07 CIP)