

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-Q

- Quarterly report pursuant to Section 13 or 15(d) of the Securities and Exchange Act of 1934
For the quarterly period ended September 30, 1997
OR
 Transition report pursuant to Section 13 or 15(d) of the Securities and Exchange Act of 1934
For the transition period from _____ to _____

Commission File Number 0-19319

Vertex Pharmaceuticals Incorporated
(Exact name of registrant as specified in its charter)

Massachusetts

(State or other jurisdiction of
incorporation or organization)

04-3039129

(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 X NO
----- -----

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 -----	25,196,342 -----
Class	Outstanding at November 6, 1997

VERTEX PHARMACEUTICALS INCORPORATED

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Report of Independent Accountants

To the Board of Directors and Stockholders of Vertex Pharmaceuticals Incorporated:

We have reviewed the accompanying condensed consolidated balance sheet of Vertex Pharmaceuticals Incorporated as of September 30, 1997, and the related condensed consolidated statements of operations and cash flows for the three month and the nine month periods ended September 30, 1997 and 1996. These financial statements are the responsibility of the company's management.

We conducted our review in accordance with standards established by the American Institute of Certified Public Accountants. A review of interim financial information consists principally of applying analytical procedures to financial data and making inquiries of persons responsible for financial and accounting matters. It is substantially less in scope than an audit conducted in accordance with generally accepted auditing standards, the objective of which is the expression of an opinion regarding the financial statements taken as a whole. Accordingly, we do not express such an opinion.

Based on our review, we are not aware of any material modifications that should be made to the condensed consolidated financial statements referred to above for them to be in conformity with generally accepted accounting principles.

We have previously audited, in accordance with generally accepted auditing standards, the consolidated balance sheet as of December 31, 1996, and the related consolidated statements of operations, retained earnings, and cash flows for the year then ended (not presented herein); and in our report dated February 18, 1997, we expressed an unqualified opinion on those consolidated financial statements. In our opinion, the information set forth in the accompanying condensed consolidated balance sheet as of December 31, 1996, is fairly stated, in all material respects, in relation to the consolidated balance sheet from which it has been derived.

/s/ COOPERS & LYBRAND L.L.P.

Boston, Massachusetts
October 21, 1997

VERTEX PHARMACEUTICALS INCORPORATED
CONDENSED CONSOLIDATED BALANCE SHEETS
(Unaudited)
(In thousands)

	September 30, 1997	December 31, 1996
	-----	-----
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 177,191	\$ 34,851
Short-term investments	106,092	95,508
Prepaid expenses and other current assets	2,183	1,791
	-----	-----
Total current assets	285,466	132,150
Restricted cash	2,316	2,316
Property and equipment, net	10,182	8,663
Other assets	763	370
	-----	-----
Total assets	\$ 298,727	\$ 143,499
	-----	-----
	-----	-----
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Obligations under capital lease and debt	\$ 2,677	\$ 2,910
Accounts payable and accrued expenses	8,525	4,146
Deferred revenue	556	---
	-----	-----
Total current liabilities	11,758	7,056
	-----	-----
Obligations under capital leases and debt, excluding current portion	5,488	5,617
	-----	-----
Total liabilities	17,246	12,673
	-----	-----
Stockholders' equity:		
Common stock	251	211
Additional paid-in capital	391,056	227,510
Equity adjustments	151	49
Accumulated deficit	(109,977)	(96,944)
	-----	-----
Total stockholders' equity	281,481	130,826
	-----	-----
Total liabilities and stockholders' equity	\$ 298,727	\$ 143,499
	-----	-----
	-----	-----

The accompanying notes are an integral part of
these condensed consolidated financial statements.

VERTEX PHARMACEUTICALS INCORPORATED
 CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
 (Unaudited)
 (In thousands, except per share data)

	Three Months Ended September 30,	
	1997	1996
	-----	-----
Revenues:		
Collaborative and other research and development	\$ 9,739	\$ 2,930
Interest income	3,808	1,190
	-----	-----
Total revenues	13,547	4,120
	-----	-----
Costs and expenses:		
Research and development	16,449	8,525
General and administrative	2,813	1,832
Interest	141	109
	-----	-----
Total costs and expenses	19,403	10,466
	-----	-----
Net loss	\$ (5,856)	\$ (6,346)
	-----	-----
	-----	-----
Net loss per common share	\$ (0.23)	\$ (0.33)
	-----	-----
	-----	-----
Weighted average number of common shares outstanding	25,119	19,364
	-----	-----
	-----	-----

The accompanying notes are an integral part of these condensed consolidated financial statements.

VERTEX PHARMACEUTICALS INCORPORATED
 CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
 (Unaudited)
 (In thousands, except per share amounts)

	Nine Months Ended September 30,	
	1997	1996
Revenues:		
Collaborative and other research and development	\$ 22,719	\$ 8,519
Interest income	9,901	3,498
	32,620	12,017
Costs and expenses:		
Research and development	37,561	27,352
General and administrative	7,654	5,473
License payment	---	15,000
Interest	438	331
	45,653	48,156
Net loss	\$(13,033)	\$(36,139)
Net loss per common share	\$ (0.54)	\$ (2.00)
Weighted average number of common shares outstanding	23,950	18,036

The accompanying notes are an integral part of
 these condensed consolidated financial statements.

VERTEX PHARMACEUTICALS INCORPORATED

CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(Unaudited)
(In thousands)

	Nine Months Ended September 30,	
	1997	1996
	-----	-----
Cash flows from operating activities:		
Net loss	\$(13,033)	\$(36,139)
Adjustments to reconcile net loss to net cash used by operating activities:		
Depreciation and amortization	2,565	2,534
Changes in assets and liabilities:		
Prepaid expenses and other current assets	(392)	18
Accounts payable and accrued expenses	4,379	(3,607)
Deferred revenue	556	(197)
	-----	-----
Net cash provided (used) by operating activities	(5,925)	(37,391)
	-----	-----
Cash flows from investing activities:		
Net purchases and sales of short-term investments	(10,468)	(33,767)
Expenditures for property and equipment	(4,084)	(1,708)
Other assets	(393)	(869)
	-----	-----
Net cash provided (used) by investing activities	(14,945)	(36,344)
	-----	-----
Cash flows from financing activities:		
Net proceeds from public offerings of common stock	148,810	77,539
Proceeds from private placement of common stock	10,000	5,000
Other issuances of common stock	4,776	2,039
Proceeds from equipment sale/leaseback and debt	1,855	1,488
Repayment of capital lease obligations	(2,217)	(1,598)
	-----	-----
Net cash provided (used) by financing activities	163,224	84,468
	-----	-----
Effect of exchange rate changes on cash	(14)	1
	-----	-----
Increase (decrease) in cash and cash equivalents	142,340	10,734
Cash and cash equivalents at beginning of period	34,851	28,390
	-----	-----
Cash and cash equivalents at end of period	\$177,191	\$ 39,124
	-----	-----
	-----	-----

The accompanying notes are an integral part of these condensed consolidated financial statements.

NOTES TO CONDENSED FINANCIAL STATEMENTS

1. Basis of Presentation

The year end condensed balance sheet data was derived from audited financial statements. Certain information and footnote disclosures normally included in the Company's annual financial statements prepared in accordance with generally accepted accounting principles have been condensed or omitted. The interim financial statements, in the opinion of management, reflect all adjustments (including normal recurring accruals) necessary for a fair statement of the results for the interim periods ended September 30, 1997 and 1996.

The results of operations for the interim periods are not necessarily indicative of the results of operations to be expected for the fiscal year, although the Company expects to incur a substantial loss for the year ended December 31, 1997. These interim financial statements should be read in conjunction with the audited financial statements for the year ended December 31, 1996, which are contained in the Company's 1996 Annual Report to its shareholders and in its Form 10-K filed with the Securities and Exchange Commission.

2. Cash and Cash Equivalents

For purposes of the statement of cash flows, the Company considers all highly liquid investments with maturities of three months or less at the date of purchase to be cash equivalents. Changes in cash and cash equivalents may be affected by shifts in investment portfolio maturities as well as by actual net cash receipts or disbursements.

3. Net Loss per Common Share

The net loss per common share is computed based upon the weighted average number of common shares outstanding. Common equivalent shares are not included in the per-share calculations where the effect would be anti-dilutive.

4. Recently Issued Accounting Standards

The Financial Accounting Standards Board ("FASB") has issued Statement of Financial Accounting Standards No. 128 ("SFAS 128"), "Earnings Per Share" which modifies the way in which earnings per share ("EPS") is calculated and disclosed. SFAS 128 requires a dual presentation of basic and diluted EPS for all years presented in the income statements. SFAS 128 is effective for financial statements for periods ending after December 15, 1997. The adoption of SFAS 128 is not expected to have a material impact on the Company's EPS calculation.

The FASB has recently issued Statement of Financial Accounting Standards No. 130 ("SFAS 130"), "Reporting Comprehensive Income". This Statement requires that total comprehensive income be reported and that changes be shown in a financial statement displayed with the same prominence as other financial statements. SFAS 130 is effective for fiscal years beginning after December 15, 1997. Reclassification of financial statements for earlier periods is required for comparative purposes. The Company does not believe that this will have a material impact on results of operations.

5. Recent Collaborative Agreements

In September 1997, the Company and Kissei Pharmaceutical Co. Ltd. ("Kissei") entered into a collaborative agreement to design inhibitors of p38 MAP Kinase and to develop them as novel, orally active drugs for the treatment of inflammatory and neurological diseases. Under the terms of the agreement, Kissei will pay the Company up to \$22 million composed of a \$4 million research funding payment paid in September 1997, \$11 million of product research funding over three years and \$7 million of development and commercialization milestone payments. The Company and Kissei will collaborate to identify and evaluate compounds that target p38 MAP Kinase. Kissei will have the right to develop and commercialize these compounds in its licensed territories. Kissei has exclusive rights to p38 MAP Kinase compounds in Japan and certain Southeast Asian countries and semi-exclusive rights in China, Taiwan and South Korea. The Company retains exclusive marketing rights in the United States, Canada, Europe, and the rest of the world. In addition, the Company will have the right to supply bulk drug material to Kissei for sale in its territory, and will receive royalties and drug supply payments on any product sales. Kissei has the right to terminate the agreement without cause upon six months' notice after June 1998.

In June 1997, the Company and Eli Lilly and Company ("Lilly") entered into a collaborative agreement to design inhibitors of the hepatitis C protease enzyme, and to develop them as novel drugs to treat hepatitis C infection. Under the terms of the agreement, Lilly will pay the Company up to \$51 million composed of a \$3 million research funding payment paid in June 1997, \$33 million of product research funding over six years and \$15 million of development and commercialization milestone payments. The Company and Lilly will jointly manage the research, development, manufacturing and marketing of drug candidates emerging from the collaboration. The Company will have primary responsibility for drug design, process development and pre-commercial drug substance manufacturing, and Lilly will have primary responsibility for formulation, preclinical and clinical development and global marketing. The Company has the option to supply 100 percent of Lilly's commercial drug substance supply needs. The Company will receive royalties on future product sales, if any. If the Company exercises its commercial supply option, the Company will receive drug supply payments in addition to royalties on future product sales, if any. Lilly has the right to terminate the agreement without cause upon six months' notice after June 1999. In connection with this collaboration, Lilly purchased 263,922 shares of the Company's common stock for \$10,000,000.

VERTEX PHARMACEUTICALS INCORPORATED

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL
CONDITION AND RESULTS OF OPERATIONS

The Company is engaged in the discovery, development and commercialization of novel, small molecule pharmaceuticals for the treatment of major diseases for which there are currently limited or no effective treatments. The Company is a leader in the use of structure-based drug design, an approach to drug discovery that integrates advanced biology, biophysics and chemistry. The Company is conducting nine significant pharmaceutical research and development programs to develop pharmaceuticals for the treatment of viral diseases, multidrug resistance in cancer, autoimmune diseases, inflammatory diseases and neurodegenerative disorders. Four of these programs are in the development phase, and the other four are in the research phase. During the third quarter of 1997, the Company's partner, Glaxo Wellcome plc ("Glaxo Wellcome"), advanced Phase III clinical development of VX-478 (141W94), the lead compound in the Company's HIV program, in the United States, Canada and Europe. Kissei is also developing VX-478 as the Company's partner for the HIV program in the Far East. Through a series of Phase II clinical trials underway, the Company and its partner for development and marketing of VX-710 in Canada, BioChem Therapeutics Inc. ("BioChem"), are evaluating VX-710 for the reversal of cancer multidrug resistance in solid tumors. During the quarter, the Company and Alpha Therapeutic ("Alpha") terminated their agreement to develop VX-366, an oral compound for the treatment of inherited hemoglobin disorders, including sickle cell anemia and beta thalassemia. In addition, the Company signed a research, development and commercialization agreement with Kissei to develop new drugs targeting p38 MAP Kinase to treat inflammatory and neurological diseases.

To date, the Company has not received any revenues from the sale of pharmaceutical products and does not expect to receive such revenues this fiscal year, if ever. The Company has incurred since its inception, and may incur over the next several years, significant operating losses as a result of expenditures for its research and development programs. The Company expects that losses will fluctuate from quarter to quarter and that such fluctuations may be substantial.

Results of Operations

Three Months Ended September 30, 1997 Compared with Three Months Ended September 30, 1996. For the third quarter of 1997, the Company's total revenues were \$13,547,000 as compared to \$4,120,000 during the same period in 1996. From quarter to quarter, the Company's revenues fluctuate as a result of changes in the timing and amount of partner research support payments, partner reimbursements of Vertex drug development costs, and payments for the achievement of various research and development milestones. In the third quarter of 1997, the Company received \$9,380,000 in revenue from its collaborative agreements, \$3,808,000 in interest received on invested funds and \$359,000 from government grants and other revenue. In the third quarter of 1996, the Company received \$2,678,000 in revenue from its collaborative agreements, \$1,190,000 in interest earned on invested funds and \$252,000 from government grants and other revenue. The increase in collaborative revenue for the third quarter in 1997 is attributable principally to the \$4,000,000 up-front payment and \$750,000 in research funding received from Kissei under the collaborative agreement for the Company's p38 MAP Kinase program, signed in September 1997, the reimbursement by Hoechst Marion Roussel ("HMR") of certain costs associated with the Company's ICE program, and research funding from Lilly under a research collaboration signed in June 1997.

VERTEX PHARMACEUTICALS INCORPORATED

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL
CONDITION AND RESULTS OF OPERATIONS

The Company's total costs and expenses increased to \$19,403,000 in the third quarter of 1997, from \$10,466,000 during the same period in 1996. Research and development expenses were \$16,449,000 in the third quarter of 1997 as compared to \$8,525,000 during the same period in 1996. This increase in expense was principally a result of the continued growth of the Company's research and development organization, ongoing clinical trials in the multidrug resistance program, and preclinical development expenses for the VX-740, the Company's lead compound in the ICE program, and VX-497, the lead compound in the IMPDH program. In addition, during the third quarter of 1997, the Company purchased a portfolio of ten patent application families claiming interleukin 1 beta converting enzyme ("ICE") and its inhibitors from Sanofi S.A. General and administrative expenses increased during the third quarter of 1997 to \$2,813,000 from \$1,832,000 in the third quarter of 1996 due primarily to increases in administrative personnel, increased legal costs associated with patents and other matters, as well as an increase in marketing efforts by the Company and the Company's subsidiary Altus Biologics Inc. ("Altus"). Interest expense increased to \$141,000 in the third quarter of 1997 as compared to \$109,000 during the same period in 1996 due to higher levels of equipment financing.

The Company incurred a net loss of \$5,856,000 or \$0.23 per share in the third quarter of 1997 as compared to a net loss of \$6,346,000 or \$0.33 per share in the third quarter of 1996.

Nine Months Ended September 30, 1997 Compared with Nine Months Ended September 30, 1996. The Company's total revenues increased to \$32,620,000 for the nine months ended September 30, 1997 from \$12,017,000 for the nine months ended September 30, 1996. In 1997, the Company's revenues consisted of \$21,439,000 earned under the Company's collaborative agreements, \$9,901,000 in interest income and \$1,280,000 in government grants and other income. In 1996, the Company's revenues consisted of \$7,825,000 earned under the Company's collaborative agreements, \$3,498,000 in interest income and \$694,000 in government grants and other income. The increase in revenue during 1997 compared to the same period in 1996 was principally due to the new collaborative agreements signed in 1997, an increase in development reimbursements, and higher investment income. The Company received \$4,000,000 from Kissei upon the commencement of the p38 MAP Kinase collaboration in September 1997, an upfront payment of \$3,000,000 from Lilly upon the commencement of the hepatitis C collaboration in June 1997, and reimbursements of certain development costs by Kissei and HMR associated with the Company's HIV and ICE programs including \$4,000,000 from Kissei in the first three quarters of 1997. The increase in investment income was due to higher levels of cash and investments resulting from public offerings of the Company's stock in March 1997 and August 1996.

The Company's total costs decreased to \$45,653,000 for the nine months ended September 30, 1997 from \$48,156,000 for the nine months ended September 30, 1996. In the second quarter of 1996, the Company paid \$15,000,000 to obtain a non-exclusive, worldwide license under certain G.D. Searle and Company patent applications claiming HIV protease inhibitors. Research and development expenses increased to \$37,561,000 in the first nine months of 1997 from \$27,352,000 in the first nine months of 1996, due to additional scientific staffing, ongoing Phase II clinical trials for the Company's multidrug resistance program, purchase of a patent applications portfolio, as well as the commencement of preclinical activities for VX-740, the Company's lead compound in the ICE program, and VX-497, the lead compound in the IMPDH program.

VERTEX PHARMACEUTICALS INCORPORATED

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL
CONDITION AND RESULTS OF OPERATIONS

General and administrative expenses increased during the first nine months of 1997 to \$7,654,000 from \$5,473,000 in the first nine months of 1996 due primarily to increases in administrative personnel, increased legal costs associated with patents and other matters, as well as an increase in marketing efforts of the Company and Altus. Interest expense was \$438,000 in the first nine months of 1997, an increase from \$331,000 in the first nine months of 1996, as a result of higher levels of equipment financing during the period.

For the reasons stated above, the Company incurred a net loss of \$13,033,000 or \$0.54 per share in the nine months ended September 30, 1997 compared to a net loss of \$36,139,000 or \$2.00 per share in the nine months ended September 30, 1996.

Liquidity and Capital Resources

The Company's operations have been funded principally through strategic collaborative agreements, public offerings and private placements of the Company's equity securities, equipment lease financing, government grants and interest income. The Company expects to incur increased research and development and related supporting expenses and, consequently, may incur continued losses on a quarterly and annual basis as it continues to develop existing and future compounds and to conduct clinical trials of potential drugs. The Company also expects to incur substantial administrative and commercialization expenditures in the future and additional expenses related to the filing, prosecution, defense and enforcement of patent and other intellectual property rights.

The Company expects to finance these substantial cash needs with its existing cash and investments at September 30, 1997 of approximately \$283 million, together with interest earned thereon, future payments under its existing collaborative agreements, and facilities and equipment financing. To the extent that funds from these sources are not sufficient to fund the Company's activities, it will be necessary to raise additional funds through public offerings or private placements of securities or other methods of financing. There can be no assurance that such financing will be available on acceptable terms, if at all.

In September 1997, the Company entered into a collaborative agreement for up to \$22 million with Kissei for the research, development and commercialization of compounds in connection with the Company's p38 MAP Kinase program. The Company will supply bulk drug material to Kissei for sale in its territory, and will receive royalties and drug supply payments on product sales, if any.

In August 1997, the Company and Alpha terminated their agreement to develop VX-366, an oral compound for the treatment of inherited hemoglobin disorders, including sickle cell anemia and beta thalassemia. This termination does not have a material effect on the liquidity and capital resources of the Company.

In June 1997, the Company and Lilly entered into a collaborative agreement to design inhibitors of the hepatitis C protease enzyme, and to develop them as novel drugs to treat hepatitis C infection. The Company has the option to supply 100 percent of Lilly's commercial drug substance supply needs. The Company will receive royalties on future product sales, if any. If the Company exercises its commercial supply option, the Company will receive drug supply payments in addition to royalties on future product sales, if any. In connection with this collaboration, Lilly purchased 263,922 shares of the Company's common stock for \$10,000,000.

VERTEX PHARMACEUTICALS INCORPORATED

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL
CONDITION AND RESULTS OF OPERATIONS

The Company's aggregate cash and investments increased by \$152,924,000 during the nine months ended September 30, 1997 to \$283,283,000, principally due to a public offering of common stock completed in March 1997, with net proceeds of approximately \$148,810,000, and an equity investment by Lilly in June 1997 of \$10,000,000. Cash used by operations, principally to fund research and development activities, was \$5,925,000 during the same period. The Company also expended \$4,084,000 during this period to acquire property and equipment, principally for research equipment and facilities. During the first nine months of 1997, the Company entered into equipment lease financing in the aggregate amount of \$1,855,000 and repaid \$2,217,000 of its lease obligations.

The Financial Accounting Standards Board ("FASB") has issued Statement of Financial Accounting Standards No. 128 ("SFAS 128"), "Earnings Per Share" which modifies the way in which earnings per share ("EPS") is calculated and disclosed. SFAS 128 requires a dual presentation of basic and diluted EPS for all years presented in the income statements. SFAS 128 is effective for financial statements for periods ending after December 15, 1997. The adoption of SFAS 128 is not expected to have a material impact on the Company's EPS calculation. The FASB has also issued Statement of Financial Accounting Standards No. 130 ("SFAS 130"), "Reporting Comprehensive Income". This Statement requires that total comprehensive income be reported and that changes be shown in a financial statement displayed with the same prominence as other financial statements. SFAS 130 is effective for fiscal years beginning after December 15, 1997. Reclassification of financial statements for earlier periods is required for comparative purposes. The Company does not believe that this will have a material impact on results of operations.

PART II.
OTHER INFORMATION

Item 1. Legal Proceedings:

None

Item 2. Changes in Securities:

None

Item 3. Defaults Upon Senior Securities:

None

Item 4. Submission of Matters to a Vote of Security Holders:

None

Item 5. Other Information:

None

Item 6. Exhibits:

10.1 Research and Development Agreement between the Company and Kissei Pharmaceutical Co. Ltd and the Company effective September 10, 1997 (filed herewith with certain confidential information deleted).

27 Financial Data Schedule. (Exhibit 27 is submitted as an exhibit only in the electronic format of this Quarterly Report on Form 10-Q submitted to the Securities and Exchange Commission.).

99 Letter of Independent Accountants.

Reports on Form 8-K:

None

SIGNATURES

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

VERTEX PHARMACEUTICALS INCORPORATED

Date: November 12, 1997

/s/ Thomas G. Auchincloss, Jr.

Thomas G. Auchincloss, Jr.
Vice President of Finance and Treasurer
(Principal Financial Officer)

Date: November 12, 1997

/s/ Hans D. van Houte

Hans D. van Houte
Controller
(Principal Accounting Officer)

EXHIBIT 10.1

The Company has omitted from this Exhibit 10.1 portions of the Agreement for which the Company has requested confidential treatment from the Securities and Exchange Commission. The portions of the Agreement for which confidential treatment has been requested have been deleted and marked with an asterisk surrounded by brackets ([*]) and have been filed separately with the Securities and Exchange Commission.

Research and Development Agreement

between

Vertex Pharmaceuticals Incorporated

and

Kissei Pharmaceutical Co., Ltd.

Cambridge, Massachusetts, U.S.A.

Matsumoto-City, Nagano Pref., Japan

RESEARCH AND DEVELOPMENT AGREEMENT
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Research and Development Agreement

AGREEMENT made and effective this 10th day of September, 1997, between VERTEX PHARMACEUTICALS INCORPORATED, a Massachusetts corporation ("VERTEX"), and KISSEI PHARMACEUTICAL CO., LTD., a Japanese corporation ("KISSEI").

Introduction

- A. VERTEX is a multidisciplinary biopharmaceutical company focused on the use of structural biology, biophysics 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 acute and chronic inflammation and neurodegeneration.
- B. KISSEI is a diversified 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 acute and chronic inflammation and neurodegeneration.
- C. Both parties desire to enter into a collaboration specifically targeting an area in which VERTEX has been working for some time -- the development of small molecule inhibitors of the p38 enzyme, a member of the MAP kinase family -- applying the complementary skills and strengths which each party brings to the transaction.
- 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 small molecule inhibitors of the p38 enzyme for the treatment of acute and chronic inflammation and neurodegeneration, 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 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 acute and chronic inflammation and neurodegeneration.

1.3 "Compounds" shall mean small molecule inhibitors of the p38 enzyme discovered or developed by VERTEX, or by VERTEX together with KISSEI, in the Field in the course of the Research Program, whether discovered or developed by VERTEX or by VERTEX together with KISSEI (i) prior to or after the effective date of this Agreement, or (ii) unless the Research Program is terminated earlier by KISSEI pursuant to Section 7.2 or 7.3 hereof, during [*] Research Program pursuant to Section 2.1 of this Agreement.

1.4 "Core Development Activities" shall have the meaning ascribed to it in Section 2.8(c) hereof.

1.5. "Core Development Costs" shall have the meaning ascribed to it in Section 2.8(c) hereof.

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

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

1.8 "Patents" shall mean any existing or later-filed patents or patent applications filed by VERTEX or under which VERTEX acquires or has acquired rights (including rights acquired under Section 2.6 hereof) 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 therefor. 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.

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

1.10 "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.

1.11 "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.

1.12 "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 processes, techniques, methods, products, materials, and compositions.

1.13 "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.

1.14 "Exclusive Territory" shall mean those countries identified on Schedule III hereto as comprising the exclusive territory.

1.15 "Semi-Exclusive Territory" shall mean those countries identified on Schedule III hereto as comprising the semi-exclusive territory.

1.16 "Territory" shall mean the Exclusive Territory and the Semi-Exclusive Territory.

1.17 "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 VERTEX 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 30 June 2000, 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 through 31 December 2001.

2.2 Payments by KISSEI. KISSEI will provide financial support to the Research Program and Development Program in the form of the following payments to VERTEX.

1. As soon as practicable but in any event not more than fourteen (14) days after execution of this Agreement : \$4,000,000.00
2. July 1, 1997 - June 30, 1998: [*]
3. July 1, 1998 - June 30, 1999: [*]
4. July 1, 1999 - June 30, 2000: [*]

KISSEI will make additional research support payments to VERTEX in the amounts stated below upon the occurrence of any of the following events with respect to each Promising Compound.

5. [*] [*]
6. [*] [*]
7. [*] [*]

The payments referenced in each of items 2, 3 and 4 above shall be made in equal quarterly installments on the first day of each three month period during the year referenced in each item, i.e., each July 1, October 1, January 1 and April 1. The payment due on July 1, 1997 shall be made within fourteen (14) days after the execution of this Agreement. 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 succeeding day which is not a legal holiday in the Commonwealth. If any installment payments set forth above are not then due and remain unpaid upon termination of this Agreement pursuant to Section 7.1 here of, 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.

KISSEI shall be required to make the payments referenced in items 5, 6 and 7 above with respect to each Promising Compound developed hereunder and under the Option and Rights Agreement, provided that in the event that a Promising Compound fails in development, any of items 5, 6 and 7 previously paid with respect to such Promising Compound shall be made fully creditable toward the same item due with respect to a subsequent Promising Compound, and provided further that if two (or more) Promising Compounds are being developed at the same time, items 5, 6 and 7 will be applicable to each such Promising Compound. On the date any one of the payments under items 5, 6 and 7 above is earned with respect to a particular Promising Compound, any of the other lower numbered items 5, 6 and 7 which have not yet been earned with respect to that Promising Compound shall be deemed to have been achieved and therefore payable with respect to that Promising Compound.

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 five 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 and KISSEI, which shall be prepared by each party and submitted to the Research Committee and to the other party 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 the reporting party and its Affiliates and sublicensees 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 and KISSEI will each provide quarterly written reports to the other on the progress of the Research Program within fifteen (15) days after the end of each calendar quarter during the term of the Research Program. Each party will enable any of the other party's representatives on the Research Committee (or other authorized representatives), to review the ongoing research being conducted by it 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, and not the subject of patent claims, 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 Compounds designed or discovered by KISSEI or any of its Affiliates, sublicensees and subcontractors as a result of work under the Research Program ("KISSEI Research Compound"), and any improvements made 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"). KISSEI shall assign to VERTEX all of its rights to any such KISSEI Research Compounds and KISSEI Improvements, and any such KISSEI Research Compounds and KISSEI Improvements shall be considered Compounds and/or VERTEX Technical Information and subject to KISSEI's rights hereunder. KISSEI will seek to obtain similar rights in favor of VERTEX for any KISSEI Improvements generated or made available to it by its Affiliates and sublicensees, if any. VERTEX shall seek to obtain rights hereunder for KISSEI in the Territory for any such improvements generated or made available to VERTEX by its other licensees, if any.

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 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. (a) KISSEI will have the exclusive right and obligation to develop and sell Promising Compounds in the Exclusive Territory, including without limitation the obligation to initiate and complete any preclinical and clinical studies required to obtain regulatory approval of Promising Compounds in the Exclusive Territory, and shall bear all costs of the Development Program for Promising Compounds in the Exclusive Territory.

(b) KISSEI will have exclusive rights to develop, manufacture and sell Promising Compounds in the Semi-Exclusive Territory, but subject to the right of VERTEX, or not more than one licensee of VERTEX in any country in the Semi-Exclusive Territory, also to develop, manufacture or sell Promising Compounds in the Semi-Exclusive Territory. The parties will attempt to coordinate their respective development activities in the Semi-Exclusive Territory but shall have the right to pursue development of Promising Compounds independently if effective coordination is not possible. Absent any agreement to the contrary, each party will bear the cost of its own development activities in the Semi-Exclusive Territory, except as set forth below with respect to Core Development Activities, and will have the right to market and sell in the Semi-Exclusive Territory, for its own account, products incorporating Promising Compounds.

(c) VERTEX will be undertaking development activities, including preclinical and clinical studies and process research, necessary for the development of Promising Compounds outside the Territory. Prior to the commencement of the Development Program with respect to a Promising Compound, VERTEX and KISSEI will meet to discuss the worldwide development plan with respect to that Promising Compound, and will attempt to identify those development activities being undertaken for development of the Promising Compound outside the Territory (including preclinical and clinical studies and process research and development) which will be necessary or useful for the registration of products incorporating that Promising Compound in Japan. Any such agreed activities are hereinafter referred to as "Core Development Activities." VERTEX expects that those activities will be undertaken applying standards (which KISSEI will specifically note to VERTEX if in variance with usual and customary development practices and standards in the United States) which will allow the results of those activities to be used by KISSEI in its regulatory filings in Japan. VERTEX will provide KISSEI with any and all preclinical and clinical data generated by VERTEX from Core Development Activities in North America and Europe, and KISSEI shall be free to use such data and information solely for the purpose of developing Promising Compound(s) in the Territory pursuant hereto. If KISSEI should undertake Core Development Activities with the agreement of VERTEX, VERTEX shall be free to use any data and information generated by KISSEI in connection therewith solely for the purpose of developing Promising Compounds outside the Exclusive Territory. KISSEI shall pay [*] Core Development Activities.

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 Promising Compounds then under development by VERTEX, at [*].

2.10 KISSEI Research. During the term of the Research Program, KISSEI 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 for development under the Option and Rights Agreement referenced below, from Compounds designated by VERTEX for development, Promising Compounds in which KISSEI has an interest in development, manufacture, marketing and sale in the Territory as a result of KISSEI's financial and technical support of the Research Program and the Development Program. During the course of the Research Program and [*], VERTEX will notify KISSEI if and when it has selected a Compound for development in the Field outside the Exclusive Territory, and KISSEI shall have ninety (90) days after receipt of such notice (the "Option Notice") from VERTEX in which to exercise its option to develop that Compound hereunder. VERTEX shall include in any such notice to KISSEI a draft development plan for that Compound outside the Territory and an estimate of related development costs. KISSEI's option, if unexercised within the 90-day period, shall expire with respect to that Compound; provided that if, at the time of receipt of an Option Notice from VERTEX with respect to a Compound, KISSEI is then developing a Promising Compound under the Option and Rights Agreement (but only for so long as it continues such development), then its option under this Section 3.1 with respect to the additional Compound shall extend beyond the 90-day period and shall expire only upon the expiration or termination of KISSEI's option rights under this Article III. If KISSEI should exercise its option with respect to the additional Compound during the extended option period, at a time when, by reason of development activities undertaken by VERTEX or its partners outside the Territory subsequent to the original option period, the development risks with respect to that Compound have been substantially reduced, the parties will discuss an appropriate premium to be paid to VERTEX by reason of the accrual of this benefit to KISSEI. Upon exercise of its development option with respect to any such Promising Compound, KISSEI will develop that Promising Compound in the countries of the Territory in accordance with the terms of the Option and Rights Agreement. KISSEI's option rights under this Article III shall expire [*].

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 (the "Option and Rights Agreement"). 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 in the Territory of the Promising Compound to which the option exercise was directed.

3.3 Scientific Strategies. KISSEI may apply scientific strategies learned from VERTEX, which are not the subject of patent claims, 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 any such sublicensees and subcontractors.

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 in the Territory 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 the following patent costs with respect to Patents: (a) [*] its "general patent preparation and maintenance costs;" (b) [*] the reasonable expenses (other than "general patent prosecution and maintenance" costs) which VERTEX has incurred, or may in the future incur, for the preparation, filing, prosecution and maintenance of Patents in the Semi-Exclusive Territory; and (c) [*] the reasonable expenses (other than "general patent prosecution and maintenance" costs) which VERTEX has incurred, or may in the future incur, for the preparation, filing, prosecution and maintenance of Patents in the Exclusive Territory. "General patent preparation and maintenance costs" shall include the costs of preparation, filing and prosecution of any patent application from which a patent application filed in any country of the Territory claims priority, and any patent application filed under the Patent Cooperation Treaty (PCT). VERTEX shall notify KISSEI 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 which are, or have not yet become, Promising Patents, together with its estimate of the costs of such preparation, filing, prosecution and maintenance and an estimate of VERTEX's general patent preparation and maintenance costs. KISSEI shall reimburse VERTEX for [*] 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; 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. In any event, the provisions of Section 5.3 will

apply to any patent which is the object of the foregoing notice from KISSEI and which VERTEX continues to prosecute or maintain.

5.3 Failure to Reimburse. If KISSEI shall fail to reimburse VERTEX as 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, unauthorized possession, knowledge or use of the intellectual property embodied in any of the Patents by third parties in any country in the Territory, of which KISSEI becomes aware. 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 initially responsible, at its expense, for bringing any action on account of any such infringements, 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 [*].

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 pursue the Research Program diligently (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, any Option 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. KISSEI may, at its sole discretion and for any reason or no reason, terminate the Research Program and this Agreement by six months' prior written notice delivered to VERTEX at any time on or after 30 June 1998. 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, [*] KISSEI proceeds with substantial research relating to, or development of, a compound or pharmaceutical product for the treatment of chronic inflammation or neurodegeneration which acts in whole or in part through inhibition of a MAP kinase enzyme. Any 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 who may be 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 share 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 which extends or is anticipated to extend beyond six (6) months, both parties to this Agreement, so far as circumstances will permit, will 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 the government of a country 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.

9.6 Government Approvals. KISSEI and its sublicensees 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, which shall not be unreasonably withheld, 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: Yuki Yoshi Ajisawa
Board Director
Discovery Research, R&D

Attention: Director of Legal Department

if to VERTEX, at:

130 Waverly Street
Cambridge, MA 02139-4242
Attention: Richard H. Aldrich
Senior Vice President and 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.

9.15 Competition. During the term of this Agreement, neither VERTEX (in the Territory) nor KISSEI (worldwide) will develop, manufacture or sell small molecule compounds or pharmaceutical products containing small molecule compounds which have as their principal

mode of action inhibition of the p38 kinase enzyme, other than under the terms of this Agreement.

VERTEX PHARMACEUTICALS INCORPORATED

By: /s/ Joshua Boger

Title: Chairman, President & CEO

Date of Signature: September 10, 1997

KISSEI PHARMACEUTICAL CO., LTD.

By: /s/ Mutosuo Kanzawa

Title: President C.E.O.

Date of Signature: September 10, 1997

SCHEDULE I

LIST OF VERTEX PATENT APPLICATIONS AND PATENTS
RELATED TO P38 MAP KINASE PROGRAM

U.S. DISCLOSURES

DOCKET NO.	INVENTOR(S)	TITLE	STATUS	FILING DATE OR ISSUE DATE	APPLICATION OR PATENT NO.	EXPIRATION DATE
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[*]

[*]

[*]

[*]

[*]

Schedule II

p38 MAP Kinase Inhibitor Program
Summary of Research Activities -- 1996 - 1999

[*]

Schedule III

Countries in the Territory

A. The Exclusive Territory:

[*]

Japan

[*]

B. The Semi-Exclusive Territory

China

Korea

Taiwan

Exhibit A
Option and Rights Agreement

between

Vertex Pharmaceuticals Incorporated

and

Kissei Pharmaceutical Co., Ltd.

Option and Rights Agreement
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Exhibit A

Option and Rights Agreement

This Agreement is made and entered into as of _____ 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 10 September 1997 (the "Research and Development Agreement") under which VERTEX is attempting to design and discover novel small molecule inhibitors of the p38 enzyme, 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 of Compounds in the diagnosis, prevention and treatment of acute and chronic inflammation and neurodegeneration.

1.3. "Compounds" shall have the meaning ascribed to it in 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 rights 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 therefor. 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 10 September 1997 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 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 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. "Exclusive Territory" shall mean those countries identified on Schedule III of the Research and Development Agreement as comprising the exclusive territory.

1.13. "Semi-Exclusive Territory" shall mean those countries identified on Schedule III of the Research and Development Agreement as comprising the semi-exclusive territory.

1.14. "Territory" shall mean the Exclusive Territory and the Semi-Exclusive Territory.

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

1.16. "Net Sales" shall mean

[*]

- (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

- 1.16.1. 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;
- 1.16.2. in the event of a sublicense as to any Promising Compound, Net Sales will be calculated with respect to arms-length sales by the sublicensee.

1.16.3. 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.]

1.17. "Manufacturing Cost" shall mean

[*]

Article II

KISSEI's Rights

2.1. Rights. KISSEI has the sole and exclusive right, even as to VERTEX (but subject to the rights of VERTEX under Article III hereof), under the Promising Patents to develop, make, have made, use or sell Promising Compounds in the Exclusive Territory and to practice the Promising Processes to develop, make, have made, use or sell Promising Compounds in the Exclusive Territory. KISSEI shall have the sole and exclusive right, except as to VERTEX, under the Promising Patents to develop, make, have made, use or sell Promising Compounds in the Semi-Exclusive Territory and to practice the Promising Processes to develop, make, have made, use or sell Promising Compounds in the Semi-Exclusive Territory. VERTEX shall retain the right to develop, make, have made, use or sell Promising Compounds, and to practice the Promising Processes in connection therewith, in the Semi-Exclusive Territory. KISSEI shall have the right to grant sublicenses under the Promising Patents to not more than one sublicensee in each country in the Territory, to develop, use and sell Promising Compounds in the Territory 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, and any consideration received therefor, 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. Any such sublicense shall be entered into by KISSEI and the sublicensee on an arms-length basis. If VERTEX so requests, KISSEI shall make available to VERTEX for its review a complete copy of any of KISSEI's agreements that grant a sublicense under the Promising Patents and Promising Processes. VERTEX shall have the right to grant a sublicense of its rights under the Promising Patents to not more than one sublicensee in each country in the Semi-Exclusive Territory. Prior to the grant of any such sublicense, VERTEX will discuss the proposed sublicense and the suitability of the proposed sublicensee with KISSEI.

2.2. Technical Information. VERTEX hereby grants to KISSEI the right to use VERTEX Technical Information throughout the Territory to develop, manufacture, and sell Promising Compounds and to permit any sublicensees or subcontractors to use VERTEX Technical Information for such purposes pursuant to provisions safeguarding confidentiality equivalent to those provided in this Agreement. If VERTEX or KISSEI become aware of any technical information which may be useful in the development, manufacture or sale of Promising Compounds, they will cooperate in a mutual attempt to gain access to that information.

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 which is necessary or useful for further development, manufacture and commercial exploitation and distribution of the Promising Compound in the Exclusive 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.

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 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, 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. 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 through the commercial market.

2.5. Development. (a) KISSEI will have the exclusive right and obligation to develop and sell Promising Compounds in the Exclusive Territory, including without limitation the obligation to initiate and complete any preclinical and clinical studies required to obtain regulatory approval of Promising Compounds in the Exclusive Territory and shall bear all costs of the Development Program for Promising Compounds in the Exclusive Territory.

(b) KISSEI will have exclusive rights to develop, manufacture and sell Promising Compounds in the Semi-Exclusive Territory, but subject to the right of VERTEX, or not more than one licensee of VERTEX in any country in the Semi-Exclusive Territory, also to develop, manufacture or sell Promising Compounds in the Semi-Exclusive Territory. The parties will seek to coordinate their respective development activities in the Semi-Exclusive Territory under a mutually agreeable co-development arrangement. Except as otherwise stated in a mutually agreeable co-development agreement, each party will bear the cost of its own development activities in the Semi-Exclusive Territory, except as set forth below with respect to Core Development Activities, and will have the right to market and sell in the Semi-Exclusive Territory, for its own account, products incorporating Promising Compounds.

(c) VERTEX will be undertaking development activities, including preclinical and clinical studies and process research, necessary for the development of Promising Compounds outside the Territory. Prior to the commencement of the Development Program with respect to a Promising Compound, VERTEX and KISSEI will meet to discuss the worldwide development plan with respect to that Promising Compound, and will attempt to identify those development activities being undertaken for development of the Promising Compound outside the Territory (including preclinical and clinical studies and process research and development) which will be necessary or useful for the registration of products incorporating that Promising Compound in Japan. Any such agreed activities are hereinafter referred to as "Core Development Activities." VERTEX expects those activities will be undertaken applying standards (which KISSEI will specifically note to VERTEX if in variance with usual and customary development practices and standards in the United States) which will allow the results of those activities to be used by KISSEI in its regulatory filings in Japan. VERTEX will provide KISSEI with any and all preclinical and clinical data generated by VERTEX from Core Development Activities in North America and Europe, and KISSEI shall be free to use such data and information solely for the purpose of developing Promising Compound(s) in the Territory pursuant hereto. If KISSEI should undertake Core Development Activities with the agreement of VERTEX, VERTEX shall be free to use any data and information generated by KISSEI in connection therewith solely for the purpose of developing Promising Compounds outside the Exclusive Territory. KISSEI shall pay [*] Core Development Activities.

2.6. Termination. VERTEX shall have the right to terminate or render non-exclusive KISSEI's Rights hereunder upon thirty (30) 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 thirty (30) days written notice to KISSEI if, within [*] 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 other country, or following initial product introduction in such country is not keeping the Promising Compound(s) 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 made by KISSEI or any of its Affiliates, sublicensees and subcontractors relating to Promising Compounds and Promising Processes during the term of the Research Program and the Development Program, whether patentable or not ("KISSEI Improvements"). KISSEI shall assign to VERTEX all of its rights to any such KISSEI Improvements and any such KISSEI Improvements shall be considered Promising Compounds and/or VERTEX Technical Information and subject to KISSEI's rights hereunder with respect thereto, and KISSEI will seek to obtain similar rights in favor of VERTEX for any such Improvements generated or made available to it by its Affiliates, sublicensees and subcontractors, if any. VERTEX shall seek to

obtain rights hereunder for KISSEI in the Territory for any such improvements generated or made available to VERTEX by its other licensees, if any.

Article III

Supply

3.1. Commercial Supply Option. VERTEX shall have the option to manufacture or have manufactured and to supply KISSEI and its sublicensees with their entire commercial requirements for bulk Promising Compound in the Territory (the "Commercial Supply Option"). The Commercial Supply Option with respect to a particular Promising Compound will be exercisable upon written notice delivered by VERTEX to KISSEI no later than (a) the date of [*] with respect to such Promising Compound, following written notice of such commencement date delivered to VERTEX by KISSEI not less than six (6) months prior thereto which makes specific mention of this Commercial Supply Option, and (b) the delivery to VERTEX by KISSEI of a reasonably detailed general plan for the final development and marketing of the Promising Compound in each country in the Territory. If VERTEX exercises the Commercial Supply Option, KISSEI, its Affiliates and sublicensees shall purchase all of their respective requirements of bulk Promising Compound from VERTEX for manufacture of products containing Promising Compounds for sale in the Territory.

3.2. Supply Price for Commercial Material. If VERTEX exercises the Commercial Supply Option set forth in Section 3.1: (a) the supply price for a unit of bulk Promising Compound supplied by VERTEX for the manufacture of products sold in Japan shall be

[*]

[*]

Annual Net Sales shall be calculated on a calendar year basis.

(b) the purchase price for each unit of bulk Promising Compound supplied to KISSEI for sale in Japan shall initially be calculated during any year based on [*], which shall be provided by KISSEI to VERTEX within sixty (60) days prior to commencement of that year and which shall be reasonably acceptable to VERTEX. Forecasts shall be updated quarterly to reflect actual experience, and prices for bulk Promising Compound for sale in Japan will be recalculated accordingly, based on any material changes in the forecast. Payments due to VERTEX based upon that forecasted price shall be made within thirty days of receipt from VERTEX of an invoice for bulk promising Compound purchased by KISSEI, and annual adjustments shall be made within such time periods and applying such procedures as the parties may agree to reflect the actual Net Sales in the Territory and the actual Applicable Percentage for that year. Any net adjustments shall be remitted forthwith to the party to whom the adjustment is due.

(c) the supply price for a unit of bulk Promising Compound supplied by VERTEX for the manufacture of products by KISSEI, its Affiliates or sublicensees sold in countries of the Territory other than Japan shall equal [*].

(d) all bulk Promising Compound supplied by VERTEX to KISSEI hereunder shall be provided under the terms of a supply agreement containing terms and conditions, in addition to those provided herein, which are usual and customary in the trade, as shall be agreed in good faith between the parties hereto.

(e) the amounts payable under this Article III are net of any applicable duties, government charges, withholding taxes or similar items, if any.

Article IV

Royalties

4.1. Royalty. KISSEI shall pay VERTEX a [*] royalty on Net Sales of products containing Promising Compounds sold during the effective time of this Agreement in the countries of the Territory other than Japan. In countries other than Japan where KISSEI obtains a royalty (or equivalent) from a sublicensee in excess of [*] sold during the effective time of this Agreement, KISSEI shall pay VERTEX [*] excess amount, as an additional royalty. If VERTEX does not exercise its commercial supply option with respect to a Promising Compound, VERTEX will provide KISSEI with all manufacturing information in its possession concerning that Promising Compound, and KISSEI will pay VERTEX a [*] royalty on Net Sales of products sold in Japan during the effective time of this Agreement containing that Promising Compound.

4.2. Payment. All payments from KISSEI to VERTEX under this Article IV shall be made by wire transfer in U.S. dollars on a quarterly basis along with delivery to VERTEX of the Sales Report referenced in Article V hereof. The rates of exchange for such payments shall be the Telegraphic Transfer Selling rate ("TTS") of the Fuji Bank in Tokyo, Japan on the day and time of remittance.

Article V

Reporting

5.1. 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.

5.2. Sales Reports and Records. During the term of this Agreement and after the first commercial sale of a product containing a Promising Compound, KISSEI shall deliver to VERTEX within 45 days after the end of each calendar quarter a written report showing KISSEI's computation of amounts due under this Agreement on Net Sales by KISSEI, its Affiliates and sublicensees during such calendar quarter and on account of the supply of bulk Promising Compound to KISSEI hereunder. 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 payments due to VERTEX into United States dollars from the currency in which such amounts are received by KISSEI. KISSEI will keep complete, true and accurate books of account and records for the purpose of showing the derivation of all amounts 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 sales reports, 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 [*], 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 [*] per annum, compounded monthly from the date payment was due.

5.3. 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 KISSEI's 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.

5.4. Payment Delay. In case of a delay in any payments due from KISSEI to VERTEX hereunder 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 in the Territory 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 [*] the reasonable expenses which VERTEX has incurred, or may in the future incur, for the preparation, filing, prosecution and maintenance of Promising Patents in the Semi-Exclusive Territory; and [*] the reasonable expenses which VERTEX has incurred, or may in the future incur, for the preparation, filing, prosecution and maintenance of Promising Patents in the Exclusive Territory.

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 third parties 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 initially 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 [*]. If such expenses incurred by KISSEI exceed any damages recovered in any actions, [*] may be deducted from amounts thereafter payable to VERTEX under Article III and Article V hereof in respect of Net Sales in such country, provided that total amounts otherwise due to VERTEX under those Sections in any year shall not be reduced by more than [*].

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 share 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 Territory.

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 will promptly notify KISSEI should VERTEX 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.

11.7. Government Approvals. KISSEI and its sublicensees 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 develop, manufacture, sell, or cause to be developed, manufactured or sold anywhere in the Territory, products for the treatment of chronic inflammation or neurodegeneration which act in whole or in part through inhibition of a MAP kinase enzyme, 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 develop, manufacture or sell such products for [*].

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: Yuki Yoshi Ajisawa
Board Director,
Discovery Research, R&D

Attention: Director of Legal Department

if to VERTEX, at:

130 Waverly Street
Cambridge, Massachusetts 02139-4242
Attention: Richard H. Aldrich
Senior Vice President and 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

Option and Rights Agreement -- Confidential

THIS SCHEDULE CONTAINS SUMMARY FINANCIAL INFORMATION EXTRACTED FROM THE COMPANY'S THIRD QUARTER 10-Q FOR THE PERIOD ENDING SEPTEMBER 30, 1997.

1,000
US DOLLARS

9-MOS	DEC-31-1997	JAN-01-1997	SEP-30-1997
		1.0	177,191
			106,092
			0
			0
	285,466		32,784
		22,602	
		298,727	
	11,758		0
	0		0
			251
		281,230	
298,727			0
	32,620		0
		45,215	
		0	
		0	
		438	
		(13,033)	
		0	0
		0	0
		0	0
		(13,033)	0
		(0.54)	
		(0.54)	

Securities and Exchange Commission
450 Fifth Street, N.W.
Washington, D.C. 20549

Re: Vertex Pharmaceuticals Incorporated
Registration on Form S-8

We are aware that our report dated October 21, 1997 on our review of interim financial information of Vertex Pharmaceuticals Incorporated for the three month and nine month periods ended September 30, 1997 and included in the Company's quarterly report on Form 10-Q for the quarter then ended is incorporated by reference in the Company's registration statements on Form S-8 (File Nos. 33-48030, 33-48348, 33-65742, 33-93224, 333-12325 and 333-27011). Pursuant to Rule 436(c) under the Securities Act of 1933, this report should not be considered a part of the registration statement prepared or certified by us within the meaning of Sections 7 and 11 of that Act.

/s/ Coopers & Lybrand L.L.P.

Boston, Massachusetts
November 12, 1997