# SECURITIES AND EXCHANGE COMMISSION WASHINGTON, D.C. 20549

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[x] Quarterly report pursuant to Section 13 or 15(d) of the Securities and Exchange Act of 1934

For the quarterly period ended September 30, 1998

OF

[ ] 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 000-19319

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

25,341,169

Class

Outstanding at November 10, 1998

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#### Report of Independent Accountants

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

We have reviewed the condensed consolidated balance sheet of Vertex Pharmaceuticals Incorporated as of September 30, 1998, and the related condensed consolidated statements of operations and cash flows for the three month and nine month periods ended September 30, 1998 and 1997. 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, 1997, and the related consolidated statements of operations, stockholders' equity, and cash flows for the year then ended (not presented herein); and in our report dated February 23, 1998, 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, 1997, is fairly stated, in all material respects, in relation to the consolidated balance sheet from which it has been derived.

PricewaterhouseCoopers LLP

Boston, Massachusetts October 21, 1998

# CONDENSED CONSOLIDATED BALANCE SHEETS

(In thousands)
 (Unaudited)

	September 30, 1998	December 31, 1997
ASSETS		
Current assets:    Cash and cash equivalents    Short-term investments    Prepaid expenses and other current assets	\$ 49,652 209,261 1,972	\$ 71,454 208,217 1,952
Total current assets	260,885	
Restricted cash Property and equipment, net Other assets	2,316 13,709 961	11,095
Total assets	\$ 277,871 	
LIABILITIES AND STOCKHOLDERS' EQUITY  Current liabilities:   Obligations under capital lease and debt   Accounts payable and accrued expenses   Deferred revenue	\$ 2,840 8,320 	10,632 556
Total current liabilities	11,160	13,698
Obligations under capital leases and debt, excluding current portion  Total liabilities	7,629  18,789	19,603
Stockholders' equity:    Common stock    Additional paid-in capital    Accumulated other comprehensive income    Accumulated deficit	253 394,373 1,720 (137,264)	392,372 152
Total stockholders' equity	259,082	
Total liabilities and stockholders' equity	\$ 277,871	

# CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS (Unaudited) (In thousands, except per share data)

	Three Months Ended	September 30,
	1998	
Revenues:		
Collaborative and other research and development	\$ 14,633	\$ 9 739
Investment income	3,784	3,808
Total revenues	18,417	13,547
Ocata and company		
Costs and expenses:  Research and development	15,741	16,449
General and administrative		2,813
Interest	177	141
Total costs and expenses	20,690	19,403
Net loss	\$ (2,273)	
100 1000		
Basic and diluted net loss per common share	\$ (0.09)	\$ (0.23)
Basic and diluted weighted average number of		
common shares outstanding	25,308	25,119

# CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS (Unaudited)

(In thousands, except per share amounts)

Nine Months Ended September 30, 1998 1997 Revenues: Collaborative and other research and development \$ 21,053 \$ 22,719 Investment income 11,685 9,901 32,738 32,620 Total revenues Costs and expenses: 37,561 7,654 40,554 Research and development 40,55 12,189 General and administrative Interest 438 -----Total costs and expenses 53,227 45,653 -----------Net loss \$(20,489) \$ (13,033) -----\$ (0.81) \$ (0.54) Basic and diluted net loss per common share ----------Basic and diluted weighted average number of 25,282 23,950 common shares outstanding 23,950 -----

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

	Nine months ended September 30,	
	1008	1997
Cash flows from operating activities: Net loss Adjustment to reconcile net loss to	\$ (20,489)	\$ (13,033)
net cash used by operating activities: Depreciation and amortization Changes in assets and liabilities: Prepaid expenses and other	3,116	2,565
current assets Accounts payable and accrued	(20)	(392)
expenses Deferred revenue	(2,312) (556)	4,379 556
Net cash provided (used) by operating activities	(20,261)	
Cash flows from investing activities: Short-term investments Expenditures for property and equipment Other assets	514 (5,730) (391)	(4,084) (393)
Net cash provided (used) by investing activities	(5,607)	(14,945)
Cash flows from financing activities:  Proceeds from public offering of common stock  Proceeds from private placement of common stock  Other issuances of common stock  Proceeds from equipment sale/leaseback  Repayment of capital lease obligations	  2,002 4,084 (2,030)	148,810 10,000 4,776 1,855 (2,217)
Net cash provided (used) by financing activities	4,056	
Effect of exchange rate changes on cash	10	(14)
Increase (decrease) in cash and cash equivalents Cash and cash equivalents at beginning of period	(21,802) 71,454	142,340 34,851  \$ 177,191
Cash and cash equivalents at end of period	\$ 49,652	\$ 177,191 

#### NOTES TO CONDENSED FINANCIAL STATEMENTS

#### 1. Basis of Presentation

The accompanying condensed consolidated financial statements are unaudited and have been prepared by the Company in accordance with generally accepted accounting principles.

Certain information and footnote disclosures normally included in the Company's annual financial statements 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, 1998 and 1997.

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, 1998. These interim financial statements should be read in conjunction with the audited financial statements for the year ended December 31, 1997, which are contained in the Company's 1997 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. Basic and Diluted Loss per Common Share

Basic earnings per share is based upon the weighted average number of common shares outstanding during the period. Diluted earnings per share is based upon the weighted average number of common shares outstanding during the period plus additional weighted average common equivalent shares outstanding during the period when the effect is not anti-dilutive. Common equivalent shares result from the assumed exercise of outstanding stock options, the proceeds of which are then assumed to have been used to repurchase outstanding stock using the treasury stock method. Common equivalent shares have not been included in the per share calculations as the effect would be anti-dilutive. Potential common equivalent shares consist of 5,311,300 stock options outstanding with a weighted average exercise price of \$22.15 as of September 30, 1998.

#### NOTES TO CONDENSED FINANCIAL STATEMENTS

#### 4. Comprehensive Income

The Company has adopted SFAS No. 130, "Reporting Comprehensive Income," which requires that all components of comprehensive income and total comprehensive income be reported and that changes be shown in a financial statement displayed with the same prominence as other financial statements. The Company has elected to disclose this information in its statement of stockholders' equity. For the nine months ended September 30, 1998 and 1997 total comprehensive loss was as follows (in thousands):

	September 30, 1998	September 30, 1997
Net loss	\$ (20,489)	\$ (13,033)
Other comprehensive income (loss): Unrealized holding gains (losses) on investments Foreign currency translation adjustment	1,559 10	116 (14)
Total other comprehensive income (loss)	1,569	102
Total comprehensive loss	\$ (18,920) 	\$ (12,931) 

#### 5. Subsequent Event

In October 1998, the Company earned a \$3,000,000 milestone payment from Glaxo Wellcome on the submission of a New Drug Application (NDA) for the new HIV protease inhibitor Agenerase-TM- (amprenavir).

#### Recent Collaborative Agreements

In August 1998, the Company and Schering AG, Germany entered into an agreement to collaborate on the research, development and commercialization of novel, orally active neurophilin compounds to promote nerve regeneration for the treatment of a number of neurological diseases. Under the terms of the agreement, Schering AG will pay the Company up to \$88,000,000 composed of a \$6,000,000 upfront license payment paid in September 1998, \$22,000,000 of product research funding over five years and \$60,000,000 of development and commercialization milestone payments. Under terms of the agreement, Vertex and Schering AG will have an equal role in management of neurophilin research and product development. In North America, Vertex will have manufacturing rights, and Vertex and Schering AG will share equally in the marketing expenses and profits from commercialized compounds. In addition to having manufacturing rights in North America, the Company retains the option to manufacture bulk drug substance for sales and marketing in territories outside Europe, the Middle East and Africa. Schering AG will have the right to manufacture and market any commercialized compounds in Europe, the Middle East and Africa, and pay Vertex a royalty on product sales. Schering AG has the right to terminate the research agreement without cause upon three months' notice after December 1998, but will be obligated to make the payments for the period January to December 1999. After December 2000, Schering AG has the right to terminate without cause upon a six months' written notice.

#### 7. Recently Issued Accounting Standards

In July 1997, the Financial Accounting Standards Board (FASB) issued SFAS No. 131, "Disclosures about Segments of an Enterprise and Related Information," which is effective for fiscal years beginning after December 15, 1997. The interim reporting disclosures are not required in the first year of adoption. SFAS 131 specifies revised guidelines for determining an entity's operating segments and the type and level of financial information to be disclosed. SFAS 131 changes current practice under SFAS No. 14 by establishing a new framework on which to base segment reporting. The "management" approach expands the required disclosures for each segment. The Company will adopt SFAS 131 in the fourth quarter ending December 31, 1998 and has not yet determined the impact of such adoption on its segment reporting.

In June 1998, the FASB issued SFAS No. 133, "Accounting for Derivative Instruments and Hedging Activities". SFAS 133 is effective for all fiscal quarters of all fiscal years beginning after June 15, 1999. SFAS 133 requires that all derivative instruments be recorded on the balance sheet at their fair value. Changes in the fair value of derivatives are recorded each period in current earnings or other comprehensive income, depending on whether a derivative is designated as part of a hedge transaction and if it is, the type of hedge transaction. The Company is currently assessing the impact of this SFAS 133 does not believe that it will have a material impact on the financial statements.

#### Legal Proceedings

Chiron Corporation ("Chiron") filed suit on July 30, 1998 against the Company and Eli Lilly and Company in the United States District Court for the Northern District of California, alleging infringement by the defendants of various U.S. patents issued to Chiron. The infringement action relates to research activities by the defendants in the hepatitis C viral protease field and the alleged use of inventions claimed by Chiron in connection with that research and development. Chiron has requested damages in an unspecified amount, as well as an order permanently enjoining the defendants from unlicensed use of Chiron inventions. The Company intends to vigorously contest the action.

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

This discussion contains forward-looking statements which are subject to certain risks and uncertainties that can cause actual results to differ materially from those described. Factors that may cause such differences include but are not limited to those described in the section of the Company's annual report on Form 10-K entitled "Risk Factors." Readers are cautioned not to place undue reliance on these forward-looking statements which speak only as of the date hereof. The Company undertakes no obligation to publicly update or revise these forward-looking statements to reflect events or circumstances after the date hereof.

Since its inception in 1989, the Company has been 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 research and development programs to develop pharmaceuticals for the treatment of viral diseases, multidrug resistance in cancer, autoimmune and inflammatory diseases and neurodegenerative disorders.

To date, the Company has not received any revenues from the sale of pharmaceutical products. The Company's lead product candidate, Agenerase-TM-(amprenavir) for the treatment of HIV infection, is presently undergoing Phase III clinical trials. A New Drug Application ("NDA") was submitted to the U.S. Food and Drug Administration in October 1998, and equivalent applications were subsequently submitted to Canadian and European regulatory agencies. If the clinical trials are concluded successfully and if the NDA is approved by the FDA, and product sales commence, the Company will receive a royalty on sales of Agenerase-TM- by its partner Glaxo Wellcome plc ("Glaxo Wellcome"). However, there can be no assurance that Phase III clinical trials will be successfully completed, or that marketing approval will be granted by the FDA. The Company has incurred operating losses since its inception and expects to incur a loss in 1998. The Company believes that operating losses may continue for the next several years even if significant royalties are realized on Agenerase-TM- sales because the Company is planning to make significant investments in research and development for its other potential products. 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, 1998 Compared with Three Months Ended September 30, 1997.

The Company's total revenues increased to \$18,417,000 in the third quarter of 1998 from \$13,547,000 in the third quarter of 1997. In the third quarter of 1998, revenues consisted of \$14,407,000 under the Company's collaborative agreements, \$3,784,000 in investment income and \$226,000 in government grants and other revenue. In the third quarter of 1997, the Company received \$9,380,000 in revenue from its collaborative agreements, \$3,808,000 in investment income and \$359,000 from government grants and other revenue. Revenues for the third quarter in 1998 included \$9,000,000 of payments from Schering AG, under a new collaboration (the "Schering Agreement") signed in August 1998 to research, develop and commercialize novel, orally active neurophilin compounds that promote nerve growth and repair. The payment included \$3,000,000 in research funding for the period from January 1, 1998 to September 30, 1998, and a \$6,000,000 license fee. Also in the third quarter 1998, Vertex received a \$2,000,000 milestone payment from Kissei Pharmaceutical Co., Ltd. ("Kissei") relating to the selection of Vertex's compound VX-745 as a lead drug development candidate targeting the p38 MAP kinase enzyme. Revenues for the third quarter of 1998 increased even though 1997 third quarter revenues included a \$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, and the reimbursement by Hoechst Marion Roussel ("HMR") of certain costs associated with the Company's ICE program.

The Company's total costs and expenses increased to \$20,690,000 in the third quarter of 1998 from \$19,403,000 in the third quarter of 1997. Research and development expenses decreased to \$15,741,000 in the third quarter of 1998 from \$16,449,000 in the third quarter of 1997. In the third quarter of 1998, the Company experienced lower clinical and preclinical development expenses for its MDR program for cancer, the ICE program for inflammatory diseases and the IMPDH program for autoimmune diseases. These decreases were offset in part by headcount growth of the scientific organization and by commencement of research activities at the Company's new U.K. research facility. General and administrative expenses increased to \$4,772,000 in the third quarter of 1998 from \$2,813,000 in the third quarter of 1997. The increase in general and administrative expenses principally reflects the impact of personnel additions and an increase in marketing activities in preparation for the anticipated launch of Agenerase-TM-. Interest expense increased to \$177,000 in the third quarter of 1998 from \$141,000 in the third quarter of 1997 due to higher levels of equipment lease financing during the year. The Company expects that research and development as well as general and administrative expenses will continue to increase as the Company starts new research projects, advances current clinical and preclinical candidates, and expands its marketing and business development activities.

The Company recorded a net loss of \$2,273,000 or \$0.09 per share in the third quarter of 1998 compared to a net loss of \$5,856,000 or \$0.23 per share in the third quarter of 1997.

Nine Months Ended September 30, 1998 Compared with Nine Months Ended September 30, 1997.

The Company's total revenues were \$32,738,000 for the nine months ended September 30, 1998 as compared to \$32,620,000 for the nine months ended September 30, 1997. In 1998, the Company's revenues consisted of \$20,368,000 in collaborative revenues, \$11,685,000 in investment income, and \$685,000 in government grants and other income. In 1997, the Company's revenues consisted of \$21,439,000 earned under the Company's collaborative agreements, \$9,901,000 in investment income and \$1,280,000 in government grants and other income. While the 1998 first three quarters revenue included \$9,000,000 of payments from Schering AG, there was a moderate decline relative to the 1997 period due to the Company's receipt in 1997 of \$4,000,000 in development reimbursements from Kissei for a clinical trial of Agenerase-TM-, \$3,000,000 of upfront payments from Lilly for the Company's Hepatitis C program and \$4,000,000 from Kissei for the p38 MAP Kinase program.

The Company's total costs increased to \$53,227,000 for the nine months ended September 30, 1998 from \$45,653,000 for the nine months ended September 30, 1997. Research and development expenses increased to \$40,554,000 in the first three quarters of 1998 from \$37,561,000 in the first three quarters of 1997, primarily due to the expansion of the Company's research and development activities. General and administrative expenses increased during the first three quarters of 1998 to \$12,189,000 from \$7,654,000 in the first three quarters of 1997 due primarily to increases in personnel and professional expenses, particularly in preparation for the expected market launch of Agenerase-TM- and corporate advertising activities. Interest expense was \$484,000 in the first three quarters of 1998, an increase from \$438,000 in the first three quarters of 1997 as a result of higher levels of equipment financing during the period.

For the reasons stated above, the Company incurred a net loss of 20,489,000 or 0.81 per share in the nine months ended September 30, 1998 compared to a net loss of 13,033,000 or 0.54 per share in the nine months ended September 30, 1997.

#### 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 investment income. The Company expects to incur increased research and development and related supporting expenses and, consequently, may continue to experience 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 of approximately \$258,913,000 at September 30, 1998, together with investment income earned thereon, future payments under its existing collaborative agreements, and facilities and equipment financing. In addition, an NDA for Agenerase-TM- was submitted in October which, if approved, will lead to royalty income. 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 new research collaborations for new or existing projects, or other methods of financing. There can be no assurance that such financing will be available on acceptable terms, if at all. The Company believes that its existing cash and investments should be sufficient to meet its anticipated requirements for at least the next two years.

The Company's aggregate cash and investments decreased by \$20,758,000 during the nine months ended September 30, 1998 to \$258,913,000. Cash used by operations, principally to fund research and development activities, was \$20,261,000 during the same period. The Company also expended \$5,730,000 during this period to acquire property and equipment, principally for research equipment and

facilities. During the first three quarters of 1998, the Company entered into equipment financing arrangements in the aggregate amount of \$4,084,000 and repaid \$2,030,000 of its lease obligations.

In addition to the expansion of the research and development activities in the U.S., the Company started the expansion of its U.K. operations to include a research site during the third quarter in 1998. The Company expects that, in general, research and development as well as general and administrative expenses will continue to increase as the Company starts new research projects, advances current clinical and preclinical candidates, and expands its marketing and business development activities.

Under the terms of the Schering Agreement, Schering AG will pay the Company up to \$88,000,000 composed of a \$6,000,000 upfront license payment paid in September 1998, \$22,000,000 of product research funding over five years and \$60,000,000 of development and commercialization milestone payments.

The Company adopted requirements relating to comprehensive income in accordance with the 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.

In July 1997, the Financial Accounting Standards Board (FASB) issued SFAS No. 131, "Disclosures about Segments of an Enterprise and Related Information", which is effective for fiscal years beginning after December 15, 1997. The interim reporting disclosures are not required in the first year of adoption. SFAS 131 specifies revised guidelines for determining an entity's operating segments and the type and level of financial information to be disclosed. SFAS 131 changes current practice under SFAS No. 14 by establishing a new framework on which to base segment reporting. The "management" approach expands the required disclosures for each segment. The Company will adopt SFAS 131 in the fourth quarter ended December 31, 1998 and has not yet determined the impact of such adoption on its segment reporting.

In June 1998, the FASB issued SFAS No. 133, "Accounting for Derivative Instruments and Hedging Activities". SFAS 133 is effective for all fiscal quarters of all fiscal years beginning after June 15, 1999. SFAS 133 requires that all derivative instruments be recorded on the balance sheet at their fair value. Changes in the fair value of derivatives are recorded each period in current earnings or other comprehensive income, depending on whether a derivative is designated as part of a hedge transaction and if it is, the type of hedge transaction. The Company is currently assessing the impact of this FASB and does not believe that it will have a material impact on the financial statements.

#### Year 2000

The Company is currently assessing the potential impact of the Year 2000 on the processing of date-sensitive information by the Company's computerized information systems and products purchased by the Company. The Company's review includes its own computer systems and software ("IT Systems"), embedded systems in its non-computer equipment ("Non-IT Systems"), and relationships with certain third parties.

The Company has completed its evaluation of its business critical IT Systems and has determined the actions necessary in order to ensure that such IT Systems will be able to function without disruption with respect to the application of dating systems in the Year 2000. The Company has begun to upgrade, replace and test certain of its IT Systems based on the results of that evaluation. Evaluation of Non-IT Systems for Year 2000 compliance is under way but has not been completed.

In addition to risks associated with the Company's own computer systems and equipment, the Company has relationships with, and is to varying degrees dependent upon, a number of third parties that provide goods, services and information to the Company. These include contract manufacturers, suppliers,

licensees and licensors, vendors, research partners and financial institutions, whose systems and equipment are outside the control of the Company. If certain of these third parties experience failures in their computer systems or equipment due to Year 2000 non-compliance, it could affect the Company's ability to engage in normal business activities. The Company intends to contact its significant vendors and partners to ascertain their Year 2000 compliance and to determine the extent to which the Company is vulnerable to their non-compliance, if any.

The Company expects to complete its internal evaluation and remediation efforts and its assessment of third party compliance by mid-1999. However, there can be no assurance that these evaluations and any required remedial actions will be able to be completed on a timely basis. The Company believes that its internal IT Systems and Non-IT Systems are either already Year 2000 compliant or will be so prior to the Year 2000 without incurring material costs. There can be no assurance, however, that the Company will not experience unexpected costs in achieving Year 2000 compliance for its internal systems, which could result in a material adverse effect on the Company's future results of operations. The Company believes that it will be able to locate alternate sources for any critical goods or services provided by non-compliant third parties, if any. However, the Company may not be able to timely develop or implement contingency plans to address those business critical systems and third party relationships which may not be Year 2000 compliant.

#### PART II.

#### OTHER INFORMATION

#### Item 1. Legal Proceedings:

Chiron Corporation ("Chiron") filed suit on July 30, 1998 against the Company and Eli Lilly and Company in the United States District Court for the Northern District of California, alleging infringement by the defendants of various U.S. patents issued to Chiron. The infringement action relates to research activities by the defendants in the hepatitis C viral protease field and the alleged use of inventions claimed by Chiron in connection with that research and development. Chiron has requested damages in an unspecified amount, as well as an order permanently enjoining the defendants from unlicensed use of Chiron inventions. The Company intends to vigorously contest the action.

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 Agreement dated August 24, 1998 between the Company and Schering AG. (Filed herewith with certain confidential information omitted. The omitted portions have been filed separately with the Securities and Exchange Commission pursuant to a request for confidential treatment.)
- 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 13, 1998 /s/ Thomas G. Auchincloss

Thomas G. Auchincloss, Jr.

Vice President of Finance and Treasurer

(Principal Financial Officer)

Date: November 13, 1998 /s/ Hans D. van Houte

-----

Hans D. van Houte

Controller

(Principal Accounting Officer)

Vertex Pharmaceuticals Incorporated 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 this Exhibit for which confidential treatment has been requested are marked with bracketed asterisks ([\*\*\*]), and such confidential portions have been filed separately with the Securities and Exchange Commission.

Research Agreement

between

Vertex Pharmaceuticals Incorporated

and

Schering AG

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Schedule 2.5--Research Plan (including Chemistry Subplan) Schedule 2.7--Development Criteria

Exhibit A--Form of License and Development Agreement

AGREEMENT made and effective this 24th day of August, 1998, between VERTEX PHARMACEUTICALS INCORPORATED ("VERTEX"), a Massachusetts corporation with principal offices at 130 Waverly Street, Cambridge, MA 02139-4242, and SCHERING AG ("SCHERING") a German corporation with principal offices at Muellerstrasse 178, D-13342 Berlin, GERMANY.

#### Introduction

WHEREAS, VERTEX has designed novel, small molecule compounds which it believes may induce or potentiate nerve growth, nerve regeneration or nerve and nerve cell body protection by acting on neurodegenerative, neuroprotective or neurostimulatory mechanisms, and is conducting a research program directed in part toward optimizing those compounds;

WHEREAS, SCHERING and VERTEX have complementary expertise and skills in designing and synthesizing novel compounds and in developing, registering, manufacturing, marketing and selling pharmaceuticals worldwide;

WHEREAS, both parties desire to enter into a collaboration the objective of which will be to design novel compounds for the diagnosis, treatment or prevention of conditions or diseases of the central nervous system and peripheral nervous system, and to develop, market and sell those compounds as drugs upon the terms set forth herein and in a License and Development Agreement substantially in the form of Exhibit A hereto; and

WHEREAS, VERTEX has determined that a compound which it is developing for cancer indications, and which it has designated as VX-853, may be useful in the Field and has agreed to include VX-853 as a Program Compound under the terms of this Agreement; and

NOW THEREFORE, 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, with respect to any Person, any other Person which directly or indirectly, by itself or through one or more intermediaries, controls, or is controlled by, or is under direct or indirect common control with, such Person. The term "control" means the possession, direct or indirect, of the power to direct or cause the direction of the management and policies of a Person, whether through the ownership of voting securities, by contract or otherwise. Control will be presumed if one Person owns, either of record or beneficially, 40% or more of the voting stock of any other Person.
- 1.2 "Base Compound" shall mean a chemical entity falling within the class of compounds described in the patents and patent applications referenced in Schedule 1.2(a), including VX-853 but excluding those compounds and subclasses of compounds (the "Excluded Compounds") which are specifically identified on Schedule 1.2(b) hereto.
- 1.3 "Bulk Drug Substance" shall mean a Drug Product Candidate in bulk crystal, powder or other form suitable for incorporation in a Drug Product.
- 1.4 "Development Criteria" shall have the meaning ascribed to it in Section 2.7 of this Agreement.
- 1.5 "Development Option" shall have the meaning set forth in Article III hereof.
- 1.6 "Development Program" shall mean activities associated with development of a Drug Product Candidate and/or a Drug Product for sale, including but not limited to (a) selection of one or more Drug Product Candidates from among lead Program Compounds, and preparation for preclinical assessment thereof; (b) formulation of the Drug Product Candidate 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 Investigational New Drug application (or the applicable equivalent); (d) manufacture and formulations of Program Compounds and Drug Product Candidates for preclinical and clinical studies; (e) planning, implementation, evaluation and administration of human clinical trials; (f) manufacturing process development and scale-up for the manufacture of Bulk Drug Substance and Drug Product; (g) preparation and submission of applications for Regulatory Approval; and (h) post-market surveillance of approved drug indications, as required or agreed as part of a marketing approval by any governmental regulatory authority.

- 1.7 "Drug Product" shall mean a finished dosage form which is prepared from Bulk Drug Substance and is ready for administration to the ultimate consumer as a pharmaceutical.
- 1.8 "Drug Product Candidate" shall mean any Program Compound as to which SCHERING has exercised its Development Option under Article III hereof, and which has become the subject of a License Agreement in accordance with the provisions of Section 3.2 hereof.
- 1.9 "Effective Date" shall mean the effective date of this Agreement as set forth on the first page hereof.
- 1.10 "Excluded Compounds" shall mean (a) those compounds and subclasses of compounds which are specifically identified on Schedule 1.2(b) hereto and which are excluded from the definition of "Base Compounds" as referenced above; and (b) any Program Compounds which are hereafter excluded from the Research Program under Section 7.4(b) hereof.
- 1.11 "Field" shall mean the diagnosis, treatment or prevention in humans of conditions or diseases of the central nervous system and/or peripheral nervous system.
- 1.12 "Foreign Filing" means any application or regulatory filing to be filed hereunder with a foreign regulatory authority for approval to manufacture and sell Drug Product(s) outside the U.S. and any correspondence, approvals or licenses relating thereto.
- 1.13 "GLP" shall mean the current Good Laboratory Practices regulations promulgated by the FDA, published at 21 CFR Part 58, as such regulations may be from time to time amended, and such equivalent foreign regulations or standards as may be applicable with respect to Bulk Drug Substance or Drug Product(s) manufactured or sold outside the United States.
- 1.14 "GMP" shall mean the current Good Manufacturing Practice regulations promulgated by the FDA, published at 21 CFR Part 210 et seq., as such regulations may from time to time be amended, and such equivalent foreign regulations or standards as may be applicable with respect to Bulk Drug Substance or Drug Product(s) manufactured or sold outside the United States.
- 1.15 "Hazardous Materials" includes, but is not limited to, any substance or material which is or contains a substance designated or defined as oil or a hazardous material, hazardous waste, hazardous substance, medical waste, infectious waste, chemical known to cause cancer or reproductive toxicity, air or water pollutant, or asbestos or polychlorinated biphenyl, as such substances are defined under any applicable federal, state or local statute, regulation, rule or ordinance.

- 1.16 "IND" means the investigational new drug application relating to one or more Drug Product Candidates required to be filed with the FDA pursuant to 21 CFR Part 312, including any amendments thereto. References herein to an IND shall include, to the extent applicable, any comparable Foreign Filing (such as a CTX in the European Union).
- 1.17 "Know-How" means all data, technical information, know-how, experience, inventions, discoveries, trade secrets, compositions of matter and methods, whether currently existing or developed or obtained during the course of this Agreement and whether or not patentable or confidential, that are now owned, co-owned (other than with the other Party or its Affiliates) or licensed (with the right to disclose and sublicense) or hereinafter acquired or licensed (with the right to disclose and sublicense) by a Party or its Affiliates and that relate to the research, development, utilization, manufacture or use of any Program Compound, including but not limited to processes, techniques, methods, products, materials and compositions.
- 1.18 "License Agreement" shall mean the License and Development Agreement, substantially in the form of Exhibit A hereto, executed by VERTEX and SCHERING pursuant to exercise by SCHERING of its Development Option under Article III hereof.
- 1.19 "Licensed Patents" shall mean any VERTEX and SCHERING Patents which become the subject of the License Agreement pursuant to exercise of the Development Option under Article III hereof.
- 1.20 "Live Claim" means a claim of any issued, unexpired United States or foreign patent which shall not have been withdrawn, canceled or disclaimed, nor held invalid or unenforceable by a court of competent jurisdiction in an unappealed or unappealable decision.

## 1.21 [\*\*\*]

1.22 "New Compound" shall mean any chemical entity, and members of the same Chemical Class as any such chemical entity, which (i) is synthesized by VERTEX or SCHERING in accordance with the provisions of Section 2.6 hereof, or (ii) which is identified in the course of the Research Program as a diagnostic or therapeutic agent in the Field by means of any biochemical or biological assay developed or applied in the Research Program and which is considered by the Research Committee to have a therapeutic or diagnostic mechanism similar to other Program Compounds. A compound shall be deemed to be in the same "Chemical Class" as another compound if it is [\*\*\*]

- 1.23 "Patents" means all existing patents and patent applications and all patent applications hereafter filed, including any continuation, continuation-in-part, division, provisional or any substitute applications, any patent issued with respect to any such patent applications, any reissue, reexamination, renewal or extension (including any supplemental patent certificate) of any such patent, and any confirmation patent or registration patent or patent of addition based on any such patent, and all foreign counterparts of any of the foregoing and that are now owned, co-owned or licensed (with a right to disclose and sublicense) or hereafter acquired or licensed (with a right to disclose and sublicense) by a Party or its Affiliates.
- 1.24 "Person" means any individual, corporation, partnership, association, joint-stock company, trust, unincorporated organization or government or political subdivision thereof.
- 1.25 "Phase I Clinical Trials" shall mean the initial clinical trials conducted in humans to establish the safety profile of a Drug Product Candidate and to collect initial data on its pharmacokinetics and pharmacological effects.
- 1.26 "Phase II Clinical Trials" shall mean well-controlled human clinical trials conducted in a relatively small number of patients (usually no more than several hundred) to collect preliminary data regarding its efficacy in the particular indication tested, as well as to obtain some indication of the dosage regimen required.
- 1.27 "Program Compound" shall mean a Base Compound or a New Compound.
- 1.28 "Program Process" shall mean any process discovered or developed in the course of the Research Program, or within [\*\*\*] following expiration of the term of the Research Program, which is necessary or useful in the manufacture or development of a Program Compound.
- 1.29 "Refused Compound" shall have the meaning ascribed to it in Article III hereof.

- 1.30 "Research Committee" shall have the meaning ascribed to it in Section 2.4 of this Agreement.
- 1.31 "Research Program" shall mean research activities undertaken pursuant to this Agreement, as described in the Research Plan attached hereto as Schedule 2.5, associated with discovery or creation of Program Compounds, including in vitro studies of Program Compounds, in vivo animal studies for research purposes only (rather than for the generation of data for regulatory submission), and related activities.
- 1.32 "Research Year" means a twelve-month period during the term of the Research Program commencing on January 1 and ending on December 31. The first Research Year hereunder shall be deemed to have commenced on January 1, 1998.
- 1.33 "SCHERING Know-How" shall mean all Know-How of SCHERING.
- 1.34 "SCHERING Patents" shall mean any Patents owned by SCHERING or any of its Affiliates, or under which SCHERING or any of its Affiliates acquires rights (other than under this Agreement or the License Agreement, and unless those acquired rights may not be included under this Agreement by reason of restrictions imposed by a Third Party from which the rights were acquired), claiming (i) a compound discovered or identified during the course of the Research Program, or an improvement to the subject matter of a VERTEX Patent, which, if discovered or developed by VERTEX in the course of the Research Program, would be a Program Compound or otherwise the subject of a VERTEX Patent as defined in this Agreement; (ii) a method of using any such compound; or (iii) any processes (including manufacturing processes) discovered or developed by SCHERING or any of its Affiliates in the course of the Research Program or the Development Program which are or may be useful in the Field, and including any continuation, continuation-in-part, or division of any such Patent. A list of SCHERING Patents will be appended hereto as Schedule 1.34 and updated periodically to reflect additions thereto during the course of the Research Program. SCHERING shall keep VERTEX currently informed in writing of all SCHERING Patents.
- 1.35 "SCHERING Technology" shall mean all SCHERING Patents and SCHERING Know-How.
- 1.36 "Technology" shall mean SCHERING Technology and VERTEX Technology.
- 1.37 "Third Party" shall mean any person or entity which is not a party or Affiliate of any party to this Agreement.
- 1.38 "Third Party Referral" shall mean the procedure for resolution of certain disputes hereunder which is set forth in Section 10.2(b) hereof.

- 1.39 "Total Costs" shall mean the total of all costs incurred by VERTEX associated with the development of a Refused Compound, including [\*\*\*].
- 1.40 "VERTEX Know-How" shall mean all Know-How of VERTEX.
- 1.41 "VERTEX Patents" shall mean any Patents owned by VERTEX or any of its Affiliates or under which VERTEX or any of its Affiliates acquires rights (other than under this Agreement or the License Agreement, and unless those acquired rights may not be included under this Agreement by reason of restrictions imposed by a Third Party from which the rights were acquired), claiming (i) Base Compounds; (ii) a compound discovered or identified during the course of the Research Program, or an improvement to the subject matter of a SCHERING Patent which, if discovered or developed by VERTEX in the course of the Research Program, would be a Program Compound or otherwise the subject of a VERTEX Patent as defined in this Agreement; (iii) a method of using any compound referenced in items (i) and (ii) above; or (iv) any processes (including manufacturing processes) discovered or developed by VERTEX or any of its Affiliates in the course of the Research Program or the Development Program which are or may be useful in the Field, and including any continuation, continuation-in-part, or division of any such Patent. A list of VERTEX Patents will be appended hereto as Schedule 1.41 and updated periodically to reflect additions thereto during the course of the Research Program. VERTEX shall keep SCHERING currently informed in writing of all VERTEX patents.
- 1.42 "VERTEX Technology" shall mean all VERTEX Patents and VERTEX Know-How.
- 1.43 "VX-853" shall mean that chemical compound referenced on Schedule 1.2(a) hereto which is currently under development by VERTEX for cancer multi-drug resistance indications and which is referred to by VERTEX as VX-853.

#### ARTICLE II Research Program

2.1 Commencement. The Research Program shall commence as soon as practicable after the Effective Date. Each party shall use reasonable efforts to discharge its responsibilities

under the Research Program during the term of this Agreement in accordance with the Research Plan. The common objective of the parties is to identify Program compounds which may become Drug Product Candidates for worldwide development and marketing under the terms of the License and Development Agreement, upon exercise by SCHERING of the Development Option. The Research Program will conclude five (5) years from the Effective Date, unless earlier terminated in accordance with the provisions hereof.

- 2.2 Signature Payment by SCHERING. Upon execution of this Agreement SCHERING will make a signature payment of \$6,000,000 to VERTEX.
- 2.3 Research Support Payments by SCHERING. With respect to each Research Year hereunder, SCHERING will make the following payments to VERTEX, in support of the Research Program; provided that the payments on account of the Fourth and Fifth Research Years shall be subject to reduction on the basis set forth below:

First Research Year: \$[\*\*\*]
Second Research Year: \$[\*\*\*]
Third Research Year: \$[\*\*\*]
Fourth Research Year: \$[\*\*\*]

Three months before the end of each of the Third and Fourth Research Years, VERTEX and SCHERING together will assess the projected level of research effort by VERTEX for the next Research Year, as provided in the Research Plan as then most recently revised, compared to the actual level of effort by VERTEX during the Third Research Year, measured by [\*\*\*]. If the parties fairly conclude that the level of effort projected for either such Fourth or Fifth Research Year is less than the actual level of effort in the Third Research Year, then the payment provided above for any such Fourth or Fifth Research Year shall be proportionately reduced (but not below \$[\*\*\*]) to reflect the proportionate reduction in level of effort relative to the Third Research Year (subject to further adjustment at the end of the Fourth or Fifth Research Year based on the level of effort actually sustained during such Research Year as compared with the Third Research Year). The First Research Year will be deemed to have commenced on January 1, 1998. Payments due for each Research Year shall be made quarterly in advance on or before January 1, April 1, July 1 and October 1 of each Research Year, except that the quarterly payments due January 1, April 1 and July 1, 1998, shall be made upon execution of this Agreement. All payments shall be made in United States dollars to the credit of such bank account as may be designated by VERTEX in writing to SCHERING. Any payments which fall due on a date which is a legal holiday in the Commonwealth of Massachusetts may be made on the next following day which is not a legal holiday in the Commonwealth. SCHERING has advised that such payments, if made to VERTEX or another party which is a United States domiciliary, are currently not subject to withholding tax in Germany. If during the term of this

Agreement, withholding tax should be required by law to be deducted from such payments, the parties will agree upon an equitable division of liability for any sum which is withheld and for which VERTEX is not compensated or reimbursed by way of usable tax credits or otherwise.

- 2.4 Research Committee. (a) Composition and Purposes. Upon the execution of this Agreement, VERTEX and SCHERING will establish a Research Committee which shall consist of an equal number of persons designated from time to time by each of VERTEX and SCHERING. If the Research Committee chooses to designate a Committee Chair, the Chair will be elected from among the members of the Committee by a majority vote of the Committee, and may be removed in the same manner. The Research Committee shall meet formally at least quarterly, or with such other frequency, and at such time and location, as may be established by the Committee, for the following purposes:
- (i) To coordinate and review research activity and interactions between VERTEX and SCHERING, to review any proposal by either party to revise Development Criteria (as hereinafter defined), to review development candidates proposed by either party for development, and to consider whether redirection of the Research Program should be recommended to VERTEX and SCHERING under Section 2.10 of this Agreement;
- (ii) To receive and review reports by VERTEX and SCHERING, which shall be prepared and submitted to the Research Committee and to the other party hereto on a quarterly basis within fifteen (15) days after the end of each calendar quarter (commencing with the first full quarter after the execution of this Agreement), setting forth in reasonable detail, with supporting data, the results of work performed by VERTEX and SCHERING during the preceding calendar quarter under the Research Program, including any planned or filed patent applications covering Program Compounds;
  - (iii) To review and consider revisions to the Research Plan; and
  - (iv) To discuss matters relating to Patents.
- (b) Decision Making. (i) The objective of the Research Committee shall be to reach agreement by consensus on all matters within the scope of the Research Plan. However, all decisions to be made under this Agreement will be made by majority vote in the Research Committee, and if the Research Committee cannot reach agreement on any matter (a "Disputed Matter"), the Disputed Matter shall be referred to the President of VERTEX and the member of the Vorstand of SCHERING responsible for research and development, to resolve the matter referred to them in a binding, nonappealable manner.

- (ii) Notwithstanding the foregoing, if either VERTEX or SCHERING proposes a change in the Development Criteria based upon a specified material scientific or commercial development and the other party does not agree that a change in the criteria is necessary or appropriate, or the parties disagree as to whether a chemical entity identified as described in Section 1.23(ii) has a diagnostic or therapeutic mechanism similar to other Program Compounds, the matter will be referred to the President of VERTEX and the member of the Vorstand of SCHERING responsible for research and development to resolve the matter referred. If they are unable to resolve the matter satisfactorily, the matter shall be referred for binding resolution under the dispute resolution process referenced in Section 10.2(b) hereof.
- (iii) Each party shall retain the rights, powers, and discretion granted to it under this Agreement, and the Research Committee shall not be delegated or vested with any such rights, powers or discretion except as expressly provided in this Agreement. The Research Committee shall not have the power to amend or modify this Agreement, which may only be amended or modified as provided in Section 11.15.
- 2.5 Research Plan. VERTEX and SCHERING have agreed upon (i) an outline five-year research plan (the "Research Plan") for identifying, conceiving, synthesizing, structurally characterizing and/or otherwise discovering one or more Program Compounds that are commercially viable candidates for development; (ii) as a component of the Research Plan, a detailed research plan for the first twelve (12) months of the Research Program; and (iii) an overall plan for the chemistry work (the "Chemistry Subplan") which the parties expect will be performed under the Research Program. All of these plans are attached hereto as Schedule 2.5. The Research Committee will be responsible for overseeing implementation of the Research Plan. Three months before the end of each of Research Year 1 and Research Year 2, and six months before the end of each of Research Year 3 and Research Year 4, VERTEX and SCHERING will review and update the Research Plan as may be necessary to reflect past developments and changed expectations for the future, and will agree on a detailed research plan for the following twelve months which will not be inconsistent with the five year plan referenced in (i) above, as modified in accordance herewith. The Chemistry Subplan as a component of the Research Plan will be reviewed and, if necessary, revised on a quarterly basis (or more frequently, as the parties may agree) by the Research Committee. Amendments to the Research Plan, including the Chemistry Subplan, shall be effective only if agreed in writing by both parties in accordance with the provisions of this Agreement. VERTEX and SCHERING shall each allocate a sufficient number of qualified employees to the Research Program to carry out the tasks allocated to each party under the Research Plan. VERTEX will as a general rule allocate at any one time at least [\*\*\*] to the Research Program during Research Years 1 through 3.

- 2.6 Selection of New Compounds. VERTEX and SCHERING may each from time to time propose the synthesis and study of chemical entities which are not Base Compounds but which fall within the framework of the Chemistry Subplan, and the Research Committee will coordinate all such activities which may be undertaken by either party. Any chemical entity which is synthesized during the course of the Research Program or within [\*\*\*] after termination of the Research Program in accordance with the Chemistry Subplan will become a "New Compound" hereunder. Either party may also propose that the Chemistry Subplan be modified or amended and any such proposal shall be submitted to the Research Committee, with a copy delivered to the other party hereto. The Research Committee shall review the proposal as soon as practicable and decide whether to approve it or disapprove it. The decision of the Committee shall be provided immediately to both parties hereto. If and when a disease mechanism is identified by VERTEX and SCHERING as a desirable target for drugs which the parties wish to develop hereunder, any compounds discovered or designed hereunder which are active with respect to that target will also be deemed to be New Compounds hereunder.
- 2.7 Development Criteria. VERTEX and SCHERING have agreed upon initial criteria, based upon currently known scientific and commercial factors, to be applied in the identification of a Program Compound as a drug candidate suitable for development. A copy of those criteria is attached hereto as Schedule 2.7. The criteria shall be reviewed at the request of either Party at each formal Research Committee meeting hereafter, and at any other time upon the request of either VERTEX or SCHERING, and may be modified by agreement of the parties, as appropriate, to reflect material scientific or commercial developments. These criteria, as so modified from time to time, are referred to herein as the "Development Criteria." Disagreements between VERTEX and SCHERING with respect to a proposed change in the Development Criteria of the kind described in Section 2.4(b)(ii) above (but no other kind) shall be resolved as set forth in that Section.

#### 2.8 Exchange of Information.

- (a) VERTEX and SCHERING will meet informally on a regular basis to discuss the Research Program, and will freely share Technical Information useful in connection with the Research Program which is not subject to restrictions imposed by a Third Party on disclosure to or use by the other party. VERTEX and SCHERING each represents and covenants that it is not, as of the date hereof, subject to any such restrictions and that it will inform the other prior to entering any agreement with a Third Party which would impose any such restriction.
- (b) Neither VERTEX nor SCHERING shall use Technology disclosed by the other party (including information regarding assays but excluding information which is no longer subject to confidentiality restrictions under Section 4.1 by reason of the exceptions set forth in Section 4.2) for any purpose other than carrying out the Research Program or discharging its respective responsibilities under the License and Development Agreement.

(c) VERTEX and SCHERING will each provide the quarterly written reports to the Research Committee referenced in Section 2.4 (a)(ii) above. Each party will enable any representatives of the other party on the Research Committee, or other authorized representatives of such party, to review the ongoing research being conducted by the first party 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. The parties also shall institute periodic working meetings between scientists from VERTEX and SCHERING, to enhance the coordination and application of each party's resources and to provide an effective vehicle for sharing and exchanging research results. Representatives of VERTEX or SCHERING receiving confidential information from representatives of the other party and any representatives of one party who may by agreement participate in an exchange of scientists with the other party, or who may otherwise spend a significant period of time at the laboratories of the other party, shall sign appropriate agreements ensuring that information disclosed to them is held in confidence in accordance with the provisions of Article IV of this Agreement.

#### 2.9 [\*\*\*].

2.10 Redirection or Termination of Research Program. If at any time during the term of this Agreement, the Research Committee shall determine in good faith (i) that the Research Program or any portion thereof cannot be successfully completed or if so completed will not produce Program Compounds that are commercially viable, or (ii) that, in other material respects the Research Program will not conform to the parties= reasonable expectations when entering into this Agreement, the Research Committee may suggest revision, reorientation or termination of the Research Program to each party's own top management, and upon mutual consent VERTEX and SCHERING shall thereafter promptly modify their respective activities in connection with the Research Program, or terminate the Research Program, accordingly.

#### Article III

#### License Rights

- 3.1. License and Development Option. VERTEX hereby grants to SCHERING (i) a nonexclusive worldwide license and/or sublicense under VERTEX Technology to the extent necessary to permit SCHERING to carry out its rights and obligations set forth in this Agreement, and (ii) an option (the "Development Option") to license one or more Program Compounds and to develop, manufacture, have manufactured, market, use, sell and import for sale Bulk Drug Substance, Drug Product Candidates and Drug Products incorporating those Program Compounds in the Field in the Territory, upon the terms and conditions set forth in the License and Development Agreement. While the Development Option is in effect, VERTEX will not grant to any Third Party rights to VERTEX Technology which are inconsistent with the grant of the Development Option to SCHERING hereunder. VERTEX shall deliver to SCHERING all information which SCHERING may reasonably request with respect to Program Compounds at any time while the Development Option is in effect. SCHERING shall have the right to select such Program Compounds pursuant to Section 3.2 hereof in its complete discretion at any time following the Effective Date; provided, however, that the Development Option will expire and SCHERING shall no longer have the right to select any Program Compound upon the first to occur of:
  - (1) Early termination of the Research Program by SCHERING under Section 8.4(i) hereof;
  - (2) [\*\*\*] following early termination of the Research Program by SCHERING under Section 8.4(ii) hereof;
  - (3) [\*\*\*] following termination of the Research Program by SCHERING for Cause under Section 8.2 hereof,
  - (4) Termination of the Research Program by VERTEX for cause under Section 8.3 hereof; and
  - (5) [\*\*\*] following expiration of the term of the Research Program and the receipt by SCHERING of all information in the possession of VERTEX which SCHERING may reasonably require with respect to Program Compounds.
- 3.2 Exercise. The Development Option with respect to a Program Compound may be exercised by SCHERING by delivery to VERTEX, prior to expiration of the Development Option as set forth in Section 3.1 above, of written notice of exercise (an "Exercise Notice"), specifying the Program Compound as to which the Development Option is being exercised. The parties shall then promptly execute a license and development agreement substantially identical

- to the form of License and Development Agreement attached hereto as Exhibit A (the "License and Development Agreement"), unless the Development Option has previously been exercised with respect to another Program Compound, in which case the License and Development Agreement in effect with respect to that Program Compound will be amended to reflect the addition of another Program Compound for development. Development of each Program Compound as to which the Development Option is exercised shall proceed thereafter in accordance with the terms of the License and Development Agreement.
- 3.3 Recommendation of Development Candidates by VERTEX. VERTEX may propose to SCHERING that a particular Program Compound be developed under the terms of a License and Development Agreement as set forth in Section 3.2, and shall submit with any such proposal a preliminary development plan for review by the Research Committee, which shall attempt to agree on a recommendation to SCHERING and VERTEX whether the Program Compound meets the Development Criteria and should be developed. The Research Committee shall promptly notify SCHERING and VERTEX in writing of any recommendation to develop a Program Compound, and will include in that notice a detailed report fully describing the Program Compound and its qualification under the Development Criteria. Notwithstanding any such recommendation, SCHERING shall not be obligated in any case to exercise its Development Option but shall have complete discretion to determine whether to exercise its Development Option with respect to any Program Compound.
- 3.4 Refused Compound. Notwithstanding the provisions of Section 3.3 hereof, if within [\*\*\*] after receipt by SCHERING of (i) written notice from VERTEX recommending a Program Compound for development which meets the Development Criteria (in the good faith opinion of both parties, subject to determination by Third Party Referral if the parties shall disagree, and (ii) all available information which SCHERING may reasonably require (in a written notice delivered to VERTEX within [\*\*\*] after receipt of the initial notice from VERTEX with respect to the Program Compound), SCHERING has not exercised its Development Option with respect to such Program Compound (a "Refused Compound"); and if SCHERING is not, at the time VERTEX proposes that Program Compound for development, developing or marketing any other Program Compound or any Drug Product Candidate or Drug Product under the terms of a License and Development Agreement; then the Development Option shall expire only with respect to that Refused Compound (subject to the proviso set forth below) and VERTEX will thereafter be free to develop and commercialize the Refused Compound; provided that upon written notice delivered to VERTEX[\*\*\*], SCHERING shall have the further option (the "Buy-

back Option") to exercise the Development Option with respect to that Refused Compound in accordance with the following conditions, and undertake development pursuant to a License and Development Agreement as set forth in Section 3.2 hereof. VERTEX will give SCHERING at least [\*\*\*] prior written notice of each [\*\*\*] and will provide SCHERING with all available information reasonably necessary for SCHERING to make a decision with respect to the Refused Compound. If SCHERING elects to exercise the Development Option at the First Opportunity, SCHERING shall reimburse VERTEX for [\*\*\*]. If SCHERING elects to exercise the Development Option with respect to a Refused Compound at the Second Opportunity, it shall reimburse VERTEX for [\*\*\*] If SCHERING exercises the Development Option at either the First Opportunity or the Second Opportunity, it will at the time of exercise pay to VERTEX [\*\*\*].

3.5 Continued Development of VX-853. (a) Both parties recognize that VX-853 has already been administered to humans and that certain pharmacological and pharmacokinetic properties of VX-853 are already known. While the parties therefore acknowledge that an early goal of the Research Program is[\*\*\*], the parties also acknowledge that SCHERING may find it necessary or desirable to obtain additional data with respect to the characteristics of VX-853 before determining whether to exercise its Development Option with respect thereto. In order to accommodate these requirements while at the same time avoiding any significant delay in the development of VX-853, and notwithstanding any other provisions of this Article III,[\*\*\*]. VERTEX will review with the Research Committee on a regular basis the design of all tests and protocols for studies which VERTEX wishes to conduct and will provide SCHERING with all data resulting from any such tests and studies. In any case VERTEX will review all available data with SCHERING at a meeting

of the Research Committee to be held approximately 30 days after execution of this Agreement, and at each subsequent meeting of the Research Committee. The provisions of Section 3.3 and 3.4 shall apply to VX-853 in the same way as to other Program Compounds subject only to Sections 3.5(d) and 7.4(b)(i) below.

- (b) Nothing in this Section 3.5 shall be interpreted as giving VERTEX: (i) [\*\*\*] except under the provisions of Section 3.4 as modified by Subsection 3.5(d) below.
- (c) In the event SCHERING does exercise its Development Option with respect to VX-853  $[\ ^{***}]\,.$
- (d) [\*\*\*] and SCHERING chooses nonetheless not to exercise its Development Option, then VERTEX, may, based on its own judgment of the therapeutic potential of [\*\*\*] in which case the provisions of Section 3.4 above shall apply except :
- (i) Solely for purposes of this Section 3.5(d) the "First Opportunity" shall mean any time from the expiry of the notice period referred to in Section 3.4 and the satisfaction of all conditions of that section [\*\*\*] of the execution of this Agreement;
- (ii) Solely for purposes of this Section 3.5(d), the Second Opportunity shall mean any time from expiry of the First Opportunity until [\*\*\*] and
- (iii) If SCHERING elects to exercise its option at such Second Opportunity, SCHERING shall reimburse VERTEX for [\*\*\*]

(e) If VERTEX proceeds with the [\*\*\*] under the provisions of Section 3.5(d) above, and at a later time during the term of this Agreement additional data is generated to demonstrate that[\*\*\*], VERTEX shall provide all such data to SCHERING (unless the Second Opportunity has passed, and Schering has not exercised its Development Option with respect thereto). If VERTEX shall thereafter recommend VX-853 for development hereunder then SCHERING will have a further period of [\*\*\*] from the date of delivery of such recommendation to SCHERING within which to assess whether it wishes to exercise the Development Option with respect to VX-853 and, in the event that SCHERING does not exercise its Development Option during such [\*\*\*] day period, the provisions of Section 3.4 shall apply.

#### 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  $\ensuremath{\mathsf{VERTEX}}$ Know-How and SCHERING Know-How. Each party shall take any and all reasonable and 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, to authorized licensees and sublicensees, and to subcontractors in connection  $% \left( 1\right) =\left( 1\right) \left( 1\right)$ with the development, manufacture or sale of Bulk Drug Substance, Drug Product Candidates and Drug Products, to the extent necessary to enable such parties to perform their obligations hereunder or under the applicable license, sublicense or subcontract, as the case may be; provided, that such officers, employees, agents, licensees, 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 the 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 parties will agree upon the timing and content of any initial press releases or other public communications relating to this Agreement and the transactions contemplated herein. Except to the extent already disclosed in that initial press release or other public communication, no public announcement concerning the existence or the terms of this Agreement or concerning the transactions described herein shall be made, either directly or indirectly, by VERTEX or SCHERING, except as may be legally required by applicable laws, regulations, or judicial order, without first obtaining the approval of the other party and agreement upon the nature, text, and timing of such announcement, which approval and agreement shall not be unreasonably withheld. The party desiring to make any such public announcement shall provide the other party with a written copy of the proposed announcement in sufficient time prior to public release to allow such other party to comment upon such announcement, prior to public release.

Except as required by law, VERTEX shall not issue any press release or make any public announcement which includes the name "Schering" in reference to SCHERING or its Affiliates and which refers to the collaboration between VERTEX and SCHERING set forth in the Research Agreement and the License Agreement, without first providing SCHERING with 10 days written notice thereof and the opportunity to make any amendment to the manner in which the "Schering" name is used in such release or announcement as may be reasonably necessary to comply with SCHERING's now-existing contractual obligations with respect to use of the name "Schering." The foregoing prior notice requirement shall not apply to any release or announcement the content of which, as it refers to SCHERING, is substantially identical to the content of releases or announcements previously approved by SCHERING.

4.4 Survival. The provisions of this Article IV shall survive the termination of this Agreement, and shall extend for a period of [\*\*\*] years thereafter.

## Article V

## Indemnification

- 5.1 Environmental Indemnification. Notwithstanding any other indemnification obligation in this Agreement, and in addition to any rights the parties hereto may have under relevant federal, state, or local statutory and common laws, each Party (the "Indemnifying Party") shall indemnify and hold harmless the other party and its Affiliates, their directors, officers, employees, successors and assignes (the "Indemnified Party") from and against any and all claims, actions, investigation costs, response costs, losses, damages, and other costs and expenses (including reasonable attorney and consulting fees) incurred as a result of Environmental Matters (as defined below) except for any and all claims, actions, investigation costs, response costs, losses, damages, and other costs and expenses (including attorney and consulting fees) caused by the gross negligence or willful misconduct of the Indemnified Party, in which case the Indemnified Party who engaged in such gross negligence or willful misconduct shall indemnify and hold harmless the Indemnifying Party and its Affiliates, their directors, officers, employees, successors and assigns.
- 5.2 Environmental Matters. The term "Environmental Matters" shall mean:
- (a) The ownership or operation by the Indemnifying Party, or any entity which produces or manufactures Drug Product(s) or any raw material used therefor or provides services relating thereto under a subcontracting arrangement with such Indemnifying Party, of any site or facility in a manner that (i) is not in compliance with any Environmental Law; or (ii) is in violation of any Environmental Law.
- (b) Any action or inaction by the Indemnifying Party where (i) there has been a release of Hazardous Materials into the environment; or (ii) Hazardous Materials have been disposed of at a site as the term "disposed" is defined in applicable Environmental Laws.
- (c) Any failure by the Indemnifying Party to obtain or maintain all permits or provide all notices required by Environmental Laws for the lawful operation of any facility or site.
- (d) Any other actual or alleged act or omission by the Indemnifying Party relating to the generation, handling, treatment, storage, transportation, release, threatened release or omission of Hazardous Materials at any facility or site.

The term "Environmental Law" shall mean any federal, state or local law, ordinance, rule or regulation, order, decree, judgment, injunction, or other requirement relating to pollution or protection of the environment, including without limitation the Comprehensive Environmental Response, Compensation and Liability Act, 42 U.S.C. Section 9601, et seq.

("CERCLA"); the Resource Conservation and Recovery Act, 42 U.S.C. Section 6901, et seq. ("RCRA"); the Toxic Substances Control Act, 15 U.S.C. Section 26019 et seq.; the Clean Air Act, 42 U.S.C. Section 7401 et seq.; the Clean Water Act, 33 U.S.C. Section 1257 et seq.; and the Occupational Safety and Health Act, 29 U.S.C. Sections 641 et seq.

- 5.3 Indemnification by VERTEX. VERTEX will indemnify and hold SCHERING and its Affiliates, and their employees, officers and directors harmless against any loss, damages, action, suit, claim, demand, liability, expense, bodily injury, death or property damage (a "Loss"), that may be brought, instituted or arise against or be incurred by such persons to the extent such Loss is based on or arises out of: (a) the development, manufacture, use, sale, storage or handling of a Program Compound, a Drug Product Candidate or a Drug Product by VERTEX or its Affiliates or their representatives, agents or subcontractors under this Agreement, or any actual or alleged violation of law resulting therefrom (with the exception of Losses based on infringement or misappropriation of intellectual property rights), or (b) the breach by VERTEX of any of its covenants, representations or warranties set forth in this Agreement; provided that the foregoing indemnification shall not apply to any Loss to the extent such Loss is caused by the negligent or willful misconduct of SCHERING or its Affiliates.
- 5.4 Indemnification by SCHERING. SCHERING will indemnify and hold VERTEX and its Affiliates, and their employees, officers and directors harmless against any Loss that may be brought, instituted or arise against or be incurred by such persons to the extent such Loss is based on or arises out of: (a) the development, manufacture, use, sale, storage or handling of a Program Compound, a Drug Product Candidate or a Drug Product by SCHERING or its Affiliates or their representatives, agents or subcontractors under this Agreement, or any actual or alleged violation of law resulting therefrom (with the exception of Losses based on infringement or misappropriation of intellectual property rights), or (b) the breach by SCHERING of any of its covenants, representations or warranties set forth in this Agreement; provided that the foregoing indemnification shall not apply to any Loss to the extent such Loss is caused by the negligent or willful misconduct of VERTEX or its Affiliates.
- 5.5 Claims Procedures. Each Party entitled to be indemnified by the other Party (an "Indemnified Party") pursuant to Sections 5.1, 5.3 or 5.4 hereof shall give notice to the other Party (an "Indemnifying Party") promptly after such Indemnified Party has actual knowledge of any threatened or asserted claim as to which indemnity may be sought, and shall permit the Indemnifying Party to assume the defense of any such claim or any litigation resulting therefrom; provided that counsel for the Indemnifying Party, who shall conduct the defense of such claim or any litigation resulting therefrom, shall be approved by the Indemnified Party (whose approval shall not unreasonably be withheld) and the Indemnified Party may participate in such defense at such party's expense (unless (i) the employment of counsel by such Indemnified Party has been

authorized by the Indemnifying Party, or (ii) the Indemnified Party shall have reasonably concluded that there may be a conflict of interest between the Indemnifying Party and the Indemnified Party in the defense of such action, in each of which cases the Indemnifying Party shall pay the reasonable fees and expenses of one law firm serving as counsel for the Indemnified Party, which law firm shall be subject to approval, not to be unreasonably withheld, by the Indemnifying Party); and provided further, that the failure of any Indemnified Party to give notice as provided herein shall not relieve the Indemnifying Party of its obligations under this Agreement to the extent that the failure to give notice did not result in harm to the Indemnifying Party. No Indemnifying Party, in the defense of any such claim or litigation, shall, except with the approval of each Indemnified Party which approval shall not be unreasonably withheld, consent to entry of any judgment or enter into any settlement which (i) would result in injunctive or other relief being imposed against the Indemnified Party or (ii) does not include as an unconditional term thereof the giving by the claimant or plaintiff to such Indemnified Party of a release from all liability in respect to such claim or litigation. Each Indemnified Party shall furnish such information regarding itself or the claim in question as an Indemnifying Party may reasonably request in writing and as shall be reasonably required in connection with the defense of such claim and litigation resulting therefrom.

- $5.6\,$  Compliance. The parties shall comply fully with all applicable laws and regulations in connection with their respective activities under this Agreement.
- 5.7 Insurance. Each party shall use all commercially reasonable efforts to maintain insurance, including product liability insurance, with respect to its obligations hereunder. Such insurance shall be in such amounts and subject to such deductibles as the parties may agree based upon standards prevailing in the industry at the time. Either party may satisfy its obligations under this Section through self-insurance to the same extent. At such time as Drug Product(s) is being manufactured by a party for commercial sale, each party shall name the other party as an additional insured on any such policies.

#### Article VI

## Publication

Publication. Each of SCHERING and VERTEX reserves the right to publish or publicly present the results (the "Results") of the Research Program, subject to the following terms and conditions. The party proposing to publish or publicly present the Results (the "publishing party") will submit a draft of any proposed manuscript or speech to the other party (the "non-publishing party") for comments at least thirty (30) days prior to submission for publication or oral presentation. The non-publishing party shall notify the publishing party in writing within

fifteen (15) days of receipt of such draft whether such draft contains (i) information of the non-publishing party which it considers to be confidential under the provisions of Article IV hereof, (ii) information that if published would have an adverse effect on a patent application which the non-publishing party intends to file, or (iii) information which the non-publishing party reasonably believes would be likely to have a material adverse impact on the development or commercialization of a Drug Product. In any such notification, the non-publishing party shall indicate with specificity its suggestions regarding the manner and degree to which the publishing party may disclose such information. In the case of item (ii) above, the non-publishing party may request a delay and the publishing party shall delay such publication, for a period not exceeding ninety (90) days, to permit the timely preparation and filing of a patent application or an application for a certificate of invention on the information involved. In the case of item (i) above, no party may publish confidential information of the other party without its consent in violation of Article IV of this Agreement. In the case of item (iii) above, if the publishing party shall disagree with the non-publishing party's assessment of the impact of the publication, then the issue shall be referred to the Research Committee for resolution. If the Research Committee is unable to reach agreement on the matter within thirty (30) days after such referral, the matter shall be referred by the Research Committee to the appropriate member of the SCHERING Vorstand and the Chief Executive Officer of VERTEX who shall attempt in good faith to reach a fair and equitable resolution of this disagreement. If the disagreement is not resolved in this manner within four (4) weeks of referral by the Research Committee as aforesaid, then the decision of the publishing party as to publication shall be final. Subject always to the provisions of Article IV hereof, the publishing party shall have the final authority to determine the scope and content of any publication, provided that such authority shall be exercised with reasonable regard for the interests of the non-publishing The parties agree that authorship of any publication will be determined based on the customary standards then being applied in the relevant scientific journal. The parties will use their best efforts to gain the right to review proposed publications relating to the subject matter of the Research Program by consultants or contractors.

## Article VII

## Patentable Inventions

- 7.1 Ownership. All inventions made and all Know-How generated by either party or its Affiliates in the Field after the date of this Agreement in connection with, or within six (6) months after termination or expiration of, the Research Program which fall within the scope of the Research Program will be disclosed to the other party promptly after the disclosing party recognizes the significance thereof, unless in the case of process developments the same shall have been developed as part of a collaboration with a Third Party, the terms of which prohibit disclosure to the other party. All inventions shall be owned by the party making the invention claimed, or if such invention is made jointly, shall be owned jointly, all as determined in accordance with United States laws of inventorship.
- 7.2 Preparation. VERTEX shall take responsibility for the preparation, filing, prosecution and maintenance of all VERTEX Patents, and any patents and patent applications claiming jointly owned inventions, and SCHERING shall take responsibility for the preparation, filing, prosecution and maintenance of all SCHERING Patents, in each case after consulting from time to time with the other party and the Research Committee with respect to such preparation, filing, prosecution and maintenance. The Research Committee shall review and discuss with the parties those countries in which patent applications are to be filed and prosecuted. The party initially responsible for preparation, filing, prosecution and maintenance of a particular Patent or patent application (the "Initial Responsible Party") shall give thirty (30) days advance notice (the "Discontinuance Election") to the other party of any decision to cease preparation, filing, prosecution and maintenance of that patent in any jurisdiction (a "Discontinued Patent"). In such case, the other party may elect at its sole discretion to continue preparation, filing and prosecution or maintenance of the Discontinued Patent at its sole expense. The party so continuing shall own any such patent application and patents maturing therefrom; and the Initial Responsible Party shall execute such documents and perform such acts as may be reasonably necessary for the other party to file or to continue prosecution or maintenance, including assigning ownership of such patents and inventions to such electing party. Discontinuance may be on a country-by-country basis or for a patent application or patent series in total. Each party will endeavor in good faith to coordinate its efforts with those of the other party to minimize or avoid interference with the other party's patent applications.
- 7.3 Costs. [\*\*\*] incurred in the preparation, prosecution and maintenance of SCHERING Patents, and [\*\*\*] incurred in the preparation, prosecution and maintenance of VERTEX Patents. [\*\*\*] of preparation, prosecution and maintenance of Joint Patents.

## 7.4 Inventions Outside the Field.

(a) Except as set forth in (b) and (c) below: (i) [\*\*\*]; and (ii) if either VERTEX or SCHERING during the course of the Research Program makes an invention (or a joint invention with the other party) which involves the use of a Program Compound which is being developed as a Drug Product Candidate or developed or marketed as a Drug Product, then [\*\*\*]. In the event that an invention which involves the use of a Program Compound is made prior to the exercise by SCHERING of the Development Option with respect to that Program Compound but before the Development Option with respect thereto has expired, neither party will apply that invention to the development Option with respect thereto.

## (b) Notwithstanding the foregoing:

(i) if SCHERING has not exercised its Development Option with respect to VX-853 within [\*\*\*], or having done so, thereafter fails to develop VX-853 in accordance with the terms of the License Agreement, then VERTEX upon 30 days written notice to SCHERING (the "Notice Period") may elect to develop VX-853 [\*\*\*] period referenced above may be extended, but not beyond [\*\*\*] in total, upon SCHERING's written request delivered to VERTEX within the Notice Period, but only if the following conditions are met:[\*\*\*]. If the parties are unable to agree whether the foregoing conditions have been met, the matter shall be submitted for determination by Third Party Referral under Section 10.2(b) hereof. If SCHERING has exercised its Development Option with respect to VX-853 and is diligently developing or marketing it under the License Agreement, then in lieu of an election as set forth above with respect to VX-853, [\*\*\*]

(ii) During the course of the Research Program, VERTEX may from time to time designate a Program Compound (other than a Program Compound owned by SCHERING) for development outside the Field; provided that a Program Compound may be so designated only [\*\*\*]. VERTEX may during the course of the Research Program designate a maximum of [\*\*\*] such Program Compounds which are subsequently added to the list of Excluded Compounds as set forth below. VERTEX will provide written notice to SCHERING with respect to any Program Compound which it proposes to designate for development outside this Agreement and to add to the list of Excluded Compounds hereunder. such event, VERTEX will also provide to SCHERING, contemporaneously, all material information in its possession and not previously delivered to SCHERING, concerning the utility of that Program Compound for use in the Field, along with an analysis of that Program Compound in comparison with the Development Criteria then-applicable under this Agreement. [\*\*\*] after receipt of the aforementioned notice by SCHERING, the Program Compound shall be deemed added to the list of Excluded Compounds and Schedule 1.2(b) shall be updated accordingly and, as so updated, shall be binding on the parties hereto, unless during the [\*\*\*] referenced above[\*\*\*]

If within [\*\*\*] after receipt by VERTEX of the aforementioned notice from SCHERING, SCHERING and VERTEX are unable to agree on the issues raised by SCHERING in its notice, as referenced above, then those issues shall be considered a Disputed Matter and resolved by Third Party Referral as set forth in Section 10.2(b) hereof. The Program Compound shall be added to the list of Excluded Compounds only upon determination under the provisions of Section 10.2(b) that it meets the conditions for designation set forth in the first sentence of this subsection 7.4(b)(ii). Notwithstanding the foregoing, any such Program Compound added to the list of Excluded Compounds in accordance with the provisions of this Section 7.4(b)(ii) shall be considered a Program Compound for purposes of Section 8.1(b) of this Agreement.

## (c) Notwithstanding the foregoing:

- (i) SCHERING shall not be required to obtain VERTEX's consent in order to develop a Program Compound during the course of the Research Program, and thereafter, for an indication outside the Field, [\*\*\*];
- (ii) During the course of the Research Program, SCHERING may from time to time designate a Program Compound (other than a Program Compound owned by VERTEX or by VERTEX jointly with SCHERING) for development outside the Field; provided that a Program Compound may be so designated only[\*\*\*]

SCHERING may during the course of the Research Program designate a maximum of [\*\*\*] such Program Compounds ("Designated Program Compounds"). SCHERING will provide written notice to VERTEX with respect to any Designated Program Compound and will provide to VERTEX, contemporaneously, all material information in its possession and not previously delivered to VERTEX, concerning the utility of that Designated Program Compound for use in the Field, along with an analysis of that Designated Program Compound in comparison with the Development Criteria then-applicable under this Agreement. [\*\*\*] after receipt of the aforementioned notice by VERTEX, SCHERING may develop the Designated Program Compound outside the Field without the further consent of VERTEX, unless during the [\*\*\*]referenced above[\*\*\*]. If within [\*\*\*] after receipt by SCHERING of the aforementioned notice from VERTEX, VERTEX and SCHERING are unable to agree on the issues raised by VERTEX in its notice, as referenced above, then those issues shall be considered a Disputed Matter and resolved by Third Party Referral as set forth in Section 10.2(b) hereof.

(d) Except as set forth in (a), (b) and (c) above, VERTEX and SCHERING shall each be free to exploit outside the Field any inventions which such party makes and any inventions which the parties make jointly in the course of the Research Program; provided, that VERTEX shall have the exclusive right to exploit any such inventions of SCHERING for[\*\*\*], upon negotiation of a mutually agreeable royalty arrangement with SCHERING, which the parties shall negotiate in good faith.

## Article VIII

## Term and Termination

- 8.1 Term. (a) This Agreement will extend until the termination (including any early termination hereunder) of the Research Program (including any extension thereof) and thereafter for six months after the termination of the Research Program, unless earlier terminated by either party hereto in accordance with this Agreement.
- (b) Subject to any early termination or extensions thereof in accordance with this Agreement, the Research Program shall expire at the end of its initial five-year term. If (i) the Research Program expires without early termination by SCHERING or if the Research Program is terminated early by mutual agreement of the parties, and (ii) SCHERING is then developing or commercializing a Program Compound in accordance with the terms of a License Agreement, then VERTEX may not, without SCHERING's prior written consent, develop or commercialize any Program Compound in the Field or grant any such right to a Third Party; provided, that the foregoing shall be inapplicable to the development and commercialization of a Refused Compound. If the Research Program is terminated early by SCHERING under Section 8.4(ii) hereof, and SCHERING is then developing or commercializing a Program Compound for particular indications in accordance with the terms of a License Agreement, then VERTEX may not, without SCHERING's prior written consent, develop or commercialize any Program Compound (other than a Refused Compound) in the Field for the same indications, or grant any such right to a Third Party.
- (c) If (i) the Research Program expires without early termination by SCHERING or if the Research Program is terminated early by mutual agreement of the parties, and (ii) SCHERING is not then developing or commercializing a Program Compound in accordance with the terms of a License Agreement, then VERTEX shall thereafter be free to develop and commercialize any Program Compound belonging to it; provided that VERTEX has disclosed to SCHERING prior to expiration of this Agreement all material information known to it about that Program Compound, and SCHERING has not exercised its Development Option with respect thereto before the last to occur of (x) termination of this Agreement pursuant to Section 8.1(a) above, or (y) six months after VERTEX has complied with the foregoing disclosure obligations.
- 8.2 Termination of the Research Program by SCHERING for Cause. Upon written notice to VERTEX, SCHERING may at its sole discretion unilaterally terminate the Research Program and this Agreement upon the occurrence of any of the following events:
- (a) VERTEX shall materially breach any of its material obligations under this Agreement, or the License Agreement and such material

breach shall not have been remedied or steps initiated to remedy the same to SCHERING's reasonable satisfaction, within sixty (60) days after SCHERING sends written notice of breach to VERTEX; or

(b) VERTEX shall cease to function as a going concern by suspending or discontinuing its business for any reason except for interruptions caused by Force Majeur, strike, labor dispute or any other events over which it has no control.

In the event of any valid termination under this Section 8.2, SCHERING shall not be required to make any payments under Section 2.3 hereof which are not due and payable prior to receipt by VERTEX of the notice of breach referenced under Section 8.2 (a) or receipt by VERTEX of the notice of termination pursuant to Section 8.2 (b), as the case may be. Notwithstanding the foregoing, any License Agreement then in effect shall continue in effect unless it is expressly terminated in accordance with its terms.

- 8.3 Termination of the Research Program by VERTEX for Cause. VERTEX may in its absolute discretion terminate this Agreement upon written notice to SCHERING upon the occurrence of any of the following events:
- (a) SCHERING shall materially breach any of its material obligations under this Agreement or the License Agreement and such material breach shall not have been remedied or steps initiated to remedy the same to VERTEX's reasonable satisfaction, within sixty (60) days after VERTEX sends written notice of breach to SCHERING; or
- (b) SCHERING 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.

Notwithstanding the foregoing, any License Agreement then in effect shall continue in effect unless it is expressly terminated in accordance with its terms.

8.4 Early Termination of Research Program by SCHERING. SCHERING may in its absolute discretion terminate its participation in the Research Program (i) at the end of the First Research Year upon three months' prior written notice to VERTEX, in which event SCHERING must nevertheless make all of the research payments required to be made under Section 2.3 hereof on account of the Second Research Year; or (ii) after a minimum of three (3) Research Years, upon six month's written notice (the "Notice Period") delivered to VERTEX at any time on or after six (6) months before the end of the Third Research Year. SCHERING will continue to make research support payments under the Research Program which fall due during the Notice Period. The Development Option shall terminate upon delivery of a termination notice under

Section 8.4(i) above or six months following delivery by SCHERING of a termination notice under Section 8.4(ii).

- 8.5 Effect of Termination. (a) Except where explicitly provided elsewhere herein, 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, expressly or from the context thereof, are intended to survive termination or expiration of this Agreement, including obligations of confidentiality under Article IV hereof and the representations and warranties under Article IX hereof.
- (b) Upon termination or expiration of this Agreement, VERTEX shall have [\*\*\*].
- 8.6 Termination for Bankruptcy. If at any time during the term of this Agreement, an Event of Bankruptcy (as defined below) relating to either Party (the "Bankrupt Party") occurs, the other Party (the "Other Party") shall have, in addition to all other legal and equitable rights and remedies available hereunder, the option to terminate this Agreement and the License Agreement, if any, upon 30 days' written notice to the Bankrupt Party. It is agreed and understood that if the Other Party does not elect to terminate this Agreement or the License Agreement, if any, in the event of an Event of Bankruptcy, except as may otherwise be agreed with the trustee or receiver appointed to manage the affairs of the Bankrupt Party, the Other Party shall continue to make all payments required of it under this Agreement as if the Event of

Bankruptcy had not occurred, and the Bankrupt party shall not have the right to terminate any license granted herein. As used above, the term "Event of Bankruptcy" shall mean (a) dissolution, termination of existence, liquidation or business failure of either Party, (b) the appointment of a custodian or receiver for either Party who has not been terminated or dismissed within 90 days, (c) the institution by either Party of any proceeding under national, federal or state bankruptcy, reorganization, receivership or other similar laws affecting the rights of creditors generally or the making by either Party of a composition or any assignment or trust mortgage for the benefit of creditors or under any national, federal or state bankruptcy, reorganization, receivership or other similar law affecting the rights of creditors generally, which proceeding is not dismissed within 90 days of filing.

## Article IX

## Representations and Warranties

- $9.1\,$  Representations and Warranties of VERTEX. VERTEX represents and warrants to SCHERING as follows:
- (a) Authorization. This Agreement has been duly executed and delivered by VERTEX and constitutes the valid and binding obligation of VERTEX, enforceable against VERTEX in accordance with its terms except as enforceability may be limited by bankruptcy, fraudulent conveyance, insolvency, reorganization, moratorium and other laws relating to or affecting creditors' rights generally and by general equitable principles. The execution, delivery and performance of this Agreement have been duly authorized by all necessary action on the part of VERTEX, its officers and directors.
- (b) No Third Party Rights. VERTEX owns or possesses adequate licenses or other rights to use all VERTEX Technology relating to the Field and to grant the licenses herein. The granting of the license to SCHERING hereunder does not violate any right known to VERTEX of any Third Party.
- (c) Third Party Patents. Except as disclosed in writing between the parties to this Agreement or their respective agents, VERTEX is not aware of any pending patent application that, if issued, would be infringed by the development, manufacture, use or sale of any Program Compound, Bulk Drug Substance, Drug Product Candidate or Drug Product pursuant to this Agreement.
- 9.2 Representations and Warranties of SCHERING. SCHERING represents and warrants to VERTEX as follows:

- (a) Authorization. This Agreement has been duly executed and delivered by SCHERING and constitutes the valid and binding obligation of SCHERING, enforceable against SCHERING in accordance with its terms except as enforceability may be limited by bankruptcy, fraudulent conveyance, insolvency, reorganization, moratorium and other laws relating to or affecting creditors' rights generally and by general equitable principles. The execution, delivery and performance of this Agreement have been duly authorized by all necessary action on the part of SCHERING, its officers and directors.
- (b) Third Party Rights. SCHERING owns or possesses adequate licenses or other rights to use all SCHERING Technology relating to the Field in accordance with the provisions of this Agreement.
- (c) Third Party Patents. Except as disclosed in writing between the parties to this Agreement or their respective agents, SCHERING is not aware of any pending patent application that, if issued, would be infringed by the development, manufacture, use or sale of any Program Compound, Bulk Drug Substance, Drug Product Candidate or Drug Product pursuant to this Agreement.

## Article X

## Dispute Resolution

- 10.1 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 with respect to contract disputes hereunder, and to accept and agree to venue in that State.
  - 10.2 Dispute Resolution Process.
- (a) General. Except as set forth in (b) below or as otherwise explicitly provided herein, in the event of any controversy or claim arising out of or relating to any provision of this Agreement or the collaborative effort contemplated hereby, the parties shall initially refer such dispute to the President of VERTEX and the member of the Vorstand of SCHERING responsible for research and development, who shall, as soon as practicable, attempt in good faith to resolve the controversy or claim. If such controversy or claim is not resolved within sixty (60) days of the first written request for dispute resolution under this Article X, either party shall be free to initiate proceedings in the courts of the Commonwealth of Massachusetts.
- (b) Third Party Referral. Any dispute or claim relating to the "Referral Matters" as defined below which the parties are unable to resolve pursuant to the other dispute resolution mechanisms provided in this Agreement (other than litigation) shall, upon the written

request of one party delivered to the other party, be submitted to and settled by a panel of Third Parties (a "Third Party Panel") appointed by VERTEX and SCHERING as provided below. The "Referral Matters" shall consist solely of disagreements concerning (i) whether it is appropriate to amend the definition of Development Criteria as referenced in Section 2.7 of this Agreement; (ii) the question whether a particular Program Compound recommended for development by VERTEX under Sections 3.3 and 3.4 of this Agreement meets the Development Criteria then in effect; (iii) the question whether a chemical entity identified pursuant to Section 1.23 hereof has a therapeutic or diagnostic mechanism similar to other Program Compounds, within the meaning of this Agreement; (iv) whether a Program Compound proposed by VERTEX for exclusion from this Agreement under Section 7.4(b)(ii) hereof or proposed by SCHERING for exclusion under Section 7.4(c)(ii) hereof [\*\*\*] and (v) whether the conditions specified in Section 7.4(b)(i) have been met. Within 15 days after delivery of the above-referenced written request, each party will appoint one person knowledgeable in the areas of pharmaceutical science, business and commercial aspects of drug development and sale, or the clinical development of pharmaceuticals, to hear and determine the dispute. The two persons so chosen will select another impartial Third Party and their majority decision will be final and conclusive upon the parties hereto. If either party fails to designate its appointee within the 15 day period referenced above, then the appointee who has been designated will serve as the sole member of the Third Party Panel and will be deemed to be the single, mutually approved party to resolve the dispute. Each party will bear its own costs in the Third Party Referral process, and the parties will split equally the costs of the Third Party Panel members. The Third Party Panel will, upon the request of either party, issue its final determination in writing.

## Article XI

## Miscellaneous Provisions

- 11.1 Official Language. English shall be the official language of this Agreement and the License Agreement, and all communications between the parties hereto shall be conducted in that language.
- 11.2 Waiver. No provision of this Agreement may be waived except in writing by both parties hereto. No failure or delay by either party hereto in exercising any right or remedy hereunder or under applicable law will operate as a waiver thereof, or a waiver of any right or remedy on any subsequent occasion.

- 11.3 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.
- 11.4 Severability. Should one or more provisions of this Agreement be or become invalid, then the parties hereto shall attempt to agree upon valid provisions in substitution for the invalid provisions, which in their economic effect come so close to the invalid provisions that it can be reasonably assumed that the parties would have accepted this Agreement with those new provisions. If the parties are unable to agree on such valid provisions, the invalidity of such one or more provisions of this Agreement shall nevertheless not affect the validity of the Agreement as a whole, unless the invalid provisions are of such essential importance for this Agreement that it may be reasonably presumed that the parties would not have entered into this Agreement without the invalid provisions.
- 11.5 Government Acts. In the event that any act, regulation, directive, or law of a country or its government, including its departments, agencies or courts, should make impossible or prohibit, restrain, modify or limit any material act or obligation of SCHERING 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, if good faith negotiations between the parties to make such modifications therein as may be necessary to fairly address the impact thereof, after a reasonable period of time are not successful in producing mutually acceptable modifications to this Agreement.
- 11.6 Government Approvals. Each party will obtain any government approval required 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.
- 11.7 Export Controls. This Agreement is made subject to any restrictions concerning the export of materials and 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, SCHERING will not export, directly or indirectly, any VERTEX Technical Information or any Licensed Products 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.

- 11.8 Assignment. This Agreement may not be assigned or otherwise transferred by either party without the prior written consent of the other party; provided, however, that either party may assign this Agreement, without the consent of the other party, (i) to any of its Affiliates, if the assigning party guarantees the full performance of its Affiliates' obligations hereunder, or (ii) in connection with the transfer or sale of all or substantially all of its assets or business or in the event of its merger or consolidation with another company. Any purported assignment in contravention of this Section 11.8 shall, at the option of the nonassigning party, be null and void and of no effect. No assignment shall release either party from responsibility for the performance of any accrued obligation of such party hereunder.
- 11.9 Affiliates. Each party may perform its obligations hereunder personally or through one or more Affiliates, although each party shall nonetheless be solely responsible for the performance of its Affiliates. Neither party shall permit any of its Affiliates to commit any act (including any act or omission) which such party is prohibited hereunder from committing directly.
- 11.10 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.
- 11.11 No Agency. Nothing herein contained shall be deemed to create an agency, joint venture, amalgamation, partnership or similar relationship between SCHERING and VERTEX. 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.
- 11.12 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 such other addresses as may be designated by one party to the other by notice pursuant hereto, 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 SCHERING, at:

SCHERING AG
Muellerstrasse 178
D-13342 Berlin
GERMANY
Attention: Prof. C. Braestrup
with a copy to legal department

with copies to

Schering Berlin Venture Corporation 110 East Hanover Avenue Cedar Knolls, NJ 07927 Attention: President

and

Cravath, Swaine & Moore Worldwide Plaza 825 Eighth Avenue New York, NY 10019-7475 Attention: James M. Edwards, Esq.

if to VERTEX, at:

Vertex Pharmaceuticals Incorporated 130 Waverly Street Cambridge, MA U.S.A. 02139-4211 Attention: Richard H. Aldrich, Senior Vice President and Chief Business Officer

with a copy to:

Warner & Stackpole LLP 75 State Street Boston, MA U.S.A. 02109 Attention: Kenneth S. Boger, Esq. Fax: (617) 951-9151

- 11.3 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.
- 11.4 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 such party may have with any other person or company. Each party has relied on that representation in entering into this Agreement.

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

# VERTEX PHARMACEUTICALS INCORPORATED

 $\label{eq:Schedule 1.2(a)} Schedule \ \textbf{1.2(a)}$  Base Compound Patent and Patent Application

Docket No.	Туре	Country	Serial No.	Filed	Status	Patent No.
[***]	[***]	[***]	[***]	[***]	[***]	[***]
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# Excluded Compounds

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# **SCHERING Patents**

## **VERTEX Patents**

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## Schedule 2.5

# Research Plan (including Chemistry Subplan)

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- B. [\*\*\*] 1. [\*\*\*] 2. [\*\*\*] 3. [\*\*\*]
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IV. [\*\*\*]

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- C. [\*\*\*]
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- E. [\*\*\*]
- F. [\*\*\*]

[\*\*\*]

- I. [\*\*\*].
  - A. B. C. D. E. F.

  - H. I. J. K. L.
- II. [\*\*\*].
  - - A. B. C. D. E.
- III. [\*\*\*].

  - A. [\*\*\*] B. [\*\*\*] C. [\*\*\*]

## Schedule 2.7

# Development Criteria

Parameter	Counter-Proposal				
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[***]	[***]				
[***] [***]	[***] [***]				
[***] [***]	[***] [***]				
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# Exhibit A

# Form of License and Development Agreement

11253-42:222586 v11

# License and Development Agreement

between

Vertex Pharmaceuticals Incorporated

and

Schering AG

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## License and Development Agreement

This Agreement is made and entered into as of \_\_\_\_\_\_, \_\_\_\_ ( the "Effective Date") between Vertex Pharmaceuticals Incorporated (hereinafter "VERTEX"), a Massachusetts corporation with principal offices at 130 Waverly Street, Cambridge, MA 02139-4242, and SCHERING AG (hereinafter "SCHERING"), a German corporation with principal offices at Muellerstrasse 178, D-13342 Berlin, GERMANY.

#### Introduction

WHEREAS, VERTEX and SCHERING are parties to a certain Research Agreement dated as of April \_\_\_\_\_, 1998 (the "Research Agreement") under which SCHERING and VERTEX are attempting to design and discover compounds for use in the treatment of conditions and diseases of the central nervous system and peripheral nervous system; and

WHEREAS, SCHERING has the option to develop and commercialize one or more such compounds under the terms of a license and development agreement between the parties as set forth in the Research Agreement; and

WHEREAS, SCHERING has exercised its option and has elected to develop and commercialize the Program Compounds designated on Schedule 1.13 hereto, in accordance with the terms of this License and Development Agreement; and

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

## Article I Definitions

1.1. "Affiliate" shall mean, with respect to any Person, any other Person which directly or indirectly, by itself or through one or more intermediaries, controls, or is controlled by, or is under direct or indirect common control with, such Person. The term "control" means the possession, direct or indirect, of the power to direct or cause the direction of the management

and policies of a Person, whether through the ownership of voting securities, by contract or otherwise. Control will be presumed if one Person owns, either of record or beneficially, 40% or more of the voting stock of any other Person.

- 1.2. "Bulk Commercial Supply Option" shall have the meaning ascribed to it in Section 4.2 hereof.
- 1.3. "Bulk Drug Substance" shall mean a Drug Product Candidate in bulk crystal, powder or other form suitable for incorporation in a Drug Product.
- 1.4. "Co-promote" shall mean the right of SCHERING and VERTEX, subject to applicable law, to market and Detail (as defined below) Drug Products in the Field through their respective sales forces and to otherwise engage in activities in accordance with the provisions of Section 5.3 or Section 5.4 hereof, as may be applicable. "Detail" as used above shall have the meaning assigned to it in Section 5.3 hereof.
- 1.5. "Core Development Activities" shall mean all activities regardless of where they are performed which are part of a Development Program for a Drug Product Candidate and which the Development Committee believes are reasonably necessary in order to obtain Regulatory Approval from the [\*\*\*]. Notwithstanding the foregoing, "Core Development Activities" shall not include studies required by the regulatory authority of a particular country with respect to a particular geographic or ethnic population, or a subset thereof, and not otherwise required by the FDA.
  - 1.6. "Core Development Costs" shall mean the total of all [\*\*\*]

- 1.8. "Development Plan" shall have the meaning ascribed to it in Section 3.3 hereof.
- 1.9. "Development Program" shall mean activities associated with development of a Drug Product Candidate and/or a Drug Product for sale, including but not limited to (a) selection of one or more Drug Product Candidates from among lead Program Compounds, and preparation for preclinical assessment thereof; (b) formulation of the Drug Product Candidate 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 Investigational New Drug application (or the applicable equivalent); (d) manufacture and formulation of Program Compounds and Drug Product Candidates for preclinical and clinical studies; (e) planning, implementation, evaluation and administration of human clinical trials; (f) manufacturing process development and scale-up for the manufacture of Bulk Drug Substance and Drug Product; (g) preparation and submission of applications for Regulatory Approval; and (h) post-market surveillance of approved drug indications, as required or agreed as part of a marketing approval by any governmental regulatory authority.
- 1.10. "Drug Product" shall mean a finished dosage form which is prepared from Bulk Drug Substance and is ready for administration to the ultimate consumer as a pharmaceutical.
- 1.11. "Drug Product Candidate" shall mean any Program Compound listed from time to time on Schedule 1.12 hereof, as to which SCHERING has exercised its Development Option under Article III of the Research Agreement and which has become the subject of this License Agreement in accordance with the provisions of Section 3.2 of the Research Agreement.
- 1.12. "Effective Date" shall mean the date specified in the first paragraph of this Agreement, which shall be the date upon which this Agreement is executed by the parties hereto following exercise of the Development Option by SCHERING.
- 1.13. "Field" shall mean the diagnosis, treatment or prevention in humans of conditions or diseases of the central nervous system and/or peripheral nervous system.
- 1.14. "First Commercial Sale" shall mean the first sale of a Drug Product by SCHERING or an Affiliate or sublicensee of SCHERING in a country in the Territory following Regulatory Approval of the Drug Product in that country or, if no such Regulatory Approval or similar marketing approval is required, the date upon which the Drug Product is first commercially launched in such country.

- 1.15. "Foreign Filing" shall mean any application or regulatory filing to be filed hereunder with a foreign regulatory authority for approval to manufacture and sell Drug Product(s) outside the U.S. and any correspondence and/or approvals or licenses relating thereto.
- 1.16. "GLP" shall mean the current good Laboratory Practices regulations promulgated by the FDA, published at 21 CFR Part 58, as such regulations may be from time to time amended, and such equivalent foreign regulations or standards as may be applicable with respect to Bulk Drug Substance or Drug Product(s) manufactured or sold outside the United States.
- 1.17. "GMP" shall mean the Current Good Manufacturing practice regulations promulgated by the FDA, published at 21 CFR Part 210 et seq., as such regulations may be amended, and such equivalent foreign regulations or standards as may be applicable with respect to Bulk Drug Substance or Drug Product(s) manufactured or sold outside the United States.
- 1.18. "Hazardous Materials" includes, but is not limited to, any substance or material which is or contains a substance designated or defined as oil and/or a hazardous material, hazardous waste, hazardous substance, medical waste, infectious waste, chemicals known to cause cancer or reproductive toxicity, air pollutant, water pollutant, asbestos and polychlorinated biphenyls, as such substances are defined under any applicable federal, state or local statute, regulation, rule or ordinance.
- 1.19. "IND" means the investigational new drug application relating to a Drug Product Candidate(s) to be filed with the FDA pursuant to 21 CFR Part 312, including any amendments thereto. References herein to IND shall include, to the extent applicable, any comparable Foreign Filing(s) (such as a CTX in the European Union).
- 1.20. "Know-How" shall mean all data, technical information, know-how, experience, inventions, discoveries, trade secrets, compositions of matter and methods, whether currently existing or developed or obtained during the course of this Agreement and whether or not patentable or confidential, that are now owned, co-owned (other than with the other Party or its Affiliates) or licensed (with a right to disclose and sublicense) or hereafter acquired or licensed (with a right to disclose and sublicense) by a Party or its Affiliates, and that relate to the research, development, utilization, manufacture or use of any Drug Product Candidate or Drug Product, including but not limited to processes, techniques, methods, products, materials and compositions.
- 1.21. "Live Claim" shall mean a claim of any issued, unexpired United States or foreign patent which shall not have been withdrawn, canceled or disclaimed, nor held invalid or unenforceable by a court of competent jurisdiction in an unappealed or unappealable decision.

- 1.22. [\*\*\*].
- 1.23. "Major Markets" shall mean Japan and each country in North America and the European Union.
- 1.24. "Manufacturing Cost" shall have the meaning ascribed to it in Section 6.3 hereof.
- 1.25. "Net Sales" shall mean, with respect to a Drug Product, [\*\*\*]; provided that:
- 1.25.1. In the case of any sale or other disposal of a Drug Product between or among SCHERING and its Affiliates, sublicensees or marketing partners, for resale, Net Sales shall be calculated as above only on the value charged or invoiced on the first arms'-length sale thereafter to a Third Party;
- 1.25.2. In the case of any sale which is not invoiced or is delivered before invoice, Net Sales shall be calculated at the time of delivery or when the Drug Product is paid for, if paid for before delivery or invoice;
- 1.25.3. In the case of any other sale or other disposal for value, such as barter or counter-trade, of any Drug Product, or part thereof, other than in an arm's length transaction exclusively for money, Net Sales shall be calculated as above on the fair market price (if higher) in the country of sale or disposal;

- 1.25.4. In the event the Drug Product is sold as part of a combination product, the Net Sales of the Drug Product, for the purposes of determining royalty payments, shall be determined [\*\*\*]. In the event that such [\*\*\*] cannot be determined for both the Drug Product and the other product(s) in combination, Net Sales for purposes of determining royalty payments shall be mutually agreed by the parties based on relative value contributed by each component, and such agreement shall not be unreasonably withheld.
- 1.25.5. For the purpose of calculating the Net Sales of SCHERING and its Affiliates, sublicensees or marketing partners (collectively, the "Seller"), the parties recognize and acknowledge that [\*\*\*].
- 1.26. "Patents" shall mean all existing patents and patent applications and all patent applications hereafter filed, including any continuation, continuation-in-part, division, provisional or any substitute applications, any patent issued with respect to any such patent applications, any reissue, reexamination, renewal or extension (including any supplemental patent certificate) of any such patent, and any confirmation patent or registration patent or patent of addition based on any such patent, and all foreign counterparts of any of the foregoing and that are now owned, co-owned or licensed (with a right to disclose and sublicense) or hereafter acquired or licensed (with a right to disclose and sublicense) by a Party or its Affiliates.
- 1.27. "Person" shall mean any individual, corporation, partnership, association. joint-stock company, trust, unincorporated organization or government or political subdivision thereof.
- 1.28. "Phase I Clinical Trials" shall mean the initial clinical trials conducted in humans to establish the safety profile of a Drug Product candidate and to collect initial data on its pharmacokinetics and pharmacological effects.
- 1.29. "Phase II Clinical Trials" shall mean well-controlled human clinical trials conducted in a relatively small number of patients (usually no more than several hundred) to collect preliminary data regarding efficacy in the particular indication tested, as well as to obtain some indication of the dosage regimen required.

- 1.30. "Phase III Clinical Trials" shall mean large scale human clinical trials conducted in patients and intended to generate data concerning the safety and efficacy of a Drug Product Candidate in the particular indication tested sufficient to evaluate the overall benefit-risk relationship of the Drug Product Candidate, to provide an adequate basis for product labeling, and to support registration of the Drug Product Candidate with health regulatory authorities.
- 1.31. "Product Launch" shall mean, with respect to a particular Drug Product, the First Commercial Sale of that Drug Product.
  - 1.32. "Program Compound" shall mean a Base Compound or a New Compound.
- 1.33. "Regulatory Approval" shall mean all authorizations by the appropriate governmental entity or entities necessary for commercial sale of Drug Product (including exports) in each jurisdiction in which SCHERING elects to market the Drug Product including, without limitation and where applicable, approval of labeling, price, reimbursement and manufacturing. Ir the United States "Regulatory Approval" shall mean final approval of a new drug application pursuant to 21 CFR 314, permitting distribution of the applicable Drug Product in interstate commerce in the United States.
- 1.34. "Research Agreement" shall mean that certain Research Agreement between VERTEX and SCHERING dated as of August 24, 1998.
  - 1.35. "SCHERING Know-How" shall mean all Know-How of SCHERING.
- 1.36. "SCHERING Patents" shall mean any Patents owned by SCHERING or any of its Affiliates, or under which SCHERING or any of its Affiliates acquires rights (other than under this Agreement or the License Agreement, and unless those acquired rights may not be included under this Agreement by reason of restrictions imposed by a Third Party from which the rights were acquired), claiming (i) a compound discovered or identified during the course of the Research Program, or an improvement to the subject matter of a VERTEX Patent, which, if discovered or developed by VERTEX in the course of the Research Program, would be a Program Compound or otherwise the subject of a VERTEX Patent as defined in this Agreement; (ii) a method of using any such compound; or (iii) any processes (including manufacturing processes) discovered or developed by SCHERING or any of its Affiliates in the course of the Research Program or the Development Program which are or may be useful in the Field, and including any continuation, continuation-in-

part, or division of any such Patent. A list of SCHERING Patents will be appended hereto as Schedule 1.36 and updated periodically to reflect additions thereto during the course of the Research Program. SCHERING shall keep VERTEX currently informed in writing of all SCHERING Patents.

- 1.37. "SCHERING Technology" shall mean all SCHERING Patents and all SCHERING Know-How.
  - 1.38. "Territory" shall mean all the countries in the world.
- 1.39. "Third Party" shall mean any entity which is not a party or Affiliate of any party to this Agreement.
  - 1.40. "VERTEX Know-How" shall mean all Know-How of VERTEX.
- "VERTEX Patents" shall mean any Patents owned by VERTEX or any of its Affiliates or under which VERTEX or any of its Affiliates acquires rights (other than under this Agreement or the License Agreement, and unless those acquired rights may not be included under this Agreement by reason of restrictions imposed by a Third Party from which the rights were acquired), claiming (i) Base Compounds; (ii) a compound discovered or identified during the course of the Research Program, or an improvement to the subject matter of a SCHERING Patent which, if discovered or developed by VERTEX in the course of the Research Program, would be a Program Compound or otherwise the subject of a VERTEX Patent as defined in this Agreement; (iii) a method of using any such compound referenced in items (i) and (ii) above; or (iv) any processes (including manufacturing processes) discovered or developed by VERTEX or any of its Affiliates in the course of the Research Program or the Development Program, which are or may be useful in the Field, and including any continuation, continuation-in-part, or division of any such Patent. A list of VERTEX Patents will be appended hereto as Schedule 1.41 and updated periodically to reflect additions thereto during the course of the Research Program. VERTEX shall keep SCHERING currently informed in writing of all VERTEX patents.
- 1.42. "VERTEX Technology" shall mean all VERTEX Patents and all VERTEX Know-How.
- 1.43. The terms "North America," "Europe," the "Middle East," and "Africa" shall include those countries referenced on Schedule 1.43 hereto.

Capitalized terms used but not otherwise defined herein which are defined in the Research Agreement shall have the meaning ascribed to them therein.

## Article II License

# 2.1. Grant to SCHERING.

- (a) Subject to the other provisions of this Agreement and to the provisions of the last sentence of Section 7.4 of the Research Agreement with respect to any Program Compound covered thereby, VERTEX hereby grants to SCHERING an exclusive worldwide license and/or sublicense under VERTEX Technology to the extent useful to permit SCHERING to carry out its rights and obligations set forth in this Agreement and to develop, manufacture, have manufactured, market, use, sell and import for sale Bulk Drug Substance (to the extent provided in Article IV hereof), Drug Product Candidates and Drug Products in the Field in the Territory. Notwithstanding the foregoing grant, VERTEX shall have the right to use all VERTEX Technology to discharge its obligations and exercise its rights under this Agreement, including but not limited to its right to manufacture and supply Bulk Drug Substance under Article IV hereof and its rights under Article V hereof. VERTEX retains all rights to VERTEX Technology except to the extent explicitly granted to SCHERING hereunder.
- (b) SCHERING may sublicense its rights under the foregoing license to manufacture, market and sell Drug Products: [\*\*\*]; provided that before entering into any such sublicense, SCHERING will notify VERTEX of its intention to do so, identifying the proposed partner, will provide VERTEX with a reasonable opportunity to comment on the proposal and will consider in good faith any suggestion by VERTEX with respect to the choice of sublicensee, before concluding the sublicense. SCHERING shall guarantee and be responsible to VERTEX for the performance by the sublicensee under any such sublicensee and under any provisions of this Agreement for which the sublicensee is responsible pursuant to the terms of the sublicense. SCHERING shall not permit any subcontractors or sublicensees to use VERTEX Technology without provisions safeguarding confidentiality at least equivalent to those provided in this Agreement.

- 2.2. Grant to VERTEX. Subject to the other provisions of this Agreement, SCHERING hereby grants to VERTEX an exclusive, worldwide license and/or sublicense under SCHERING Technology to the extent useful to permit VERTEX to carry out its rights and obligations set forth in this Agreement and to develop, manufacture, have manufactured, market, use and sell Bulk Drug Substance, Drug Product Candidates and Drug Products in the Field in the Territory, to the extent provided for herein. Notwithstanding the foregoing grant, SCHERING shall have the right to use all SCHERING Technology to discharge its obligations and exercise its rights under this Agreement. VERTEX shall have the right to grant sublicenses of its manufacturing rights under the foregoing license on terms consistent with this Agreement. VERTEX shall guarantee and be responsible to SCHERING for the performance by the sublicensee under any such sublicense and under any provisions of this Agreement for which the sublicensee is responsible pursuant to the terms of the sublicense. VERTEX shall not engage any Third Party to manufacture Bulk Drug Substance without prior consultation and review with SCHERING; and provided further that VERTEX shall not engage any such Third Party which does not have a demonstrated ability to deliver high quality pharmaceutical products on a timely basis at volumes likely to be required by VERTEX and SCHERING. VERTEX will also refrain from engaging any Third Party manufacturer to which SCHERING has reasonable objection; provided that SCHERING notifies VERTEX of its objection, and the detailed basis therefor, within thirty (30) days of receipt of notice from VERTEX of its intention to employ the Third Party. VERTEX shall not permit any subcontractors or sublicensees to use SCHERING Technology without provisions safeguarding confidentiality equivalent to those provided in this Agreement. SCHERING retains all rights to SCHERING Technology except to the extent explicitly granted to VERTEX hereunder.
- 2.3. Information Transfer. Subject to the provisions of Section 4.5, each party shall deliver to the other all information in its possession (unless subject to restrictions pursuant to agreement with a Third Party) and requested by the other party relating to Program Compounds, Bulk Drug Substance, Drug Product Candidates and Drug Products, and methods of manufacturing the same, which is necessary or useful for exercise by such other party of the rights granted hereunder. The information to be delivered shall include copies of all Patents, copyrights, copyright registrations and applications therefor and all other manifestations of the intellectual property embodied in the Program Compounds, Bulk Drug Substance, Drug Product Candidates or Drug Products, whether in human or machine readable form.

## Article III Development

3.1. Commencement of Development Program. SCHERING and VERTEX shall promptly and diligently commence and pursue a Development Program with respect to each Program Compound as soon as practicable after exercise by SCHERING of its Development Option, as set forth in the Research Agreement, with respect to that Program Compound.

## 3.2. Development Committee.

- (a) Formation and Responsibilities. Upon the execution of this Agreement, VERTEX and SCHERING will establish a Development Committee made up of equal numbers of VERTEX and SCHERING personnel. The Development Committee will be responsible for the preparation and overall implementation of the Development Plan with respect to each Drug Product Candidate, and may act directly or through such sub-committees as it may deem appropriate to establish. If the Development Committee chooses to designate a Committee Chair, the Chair will be elected from among the members of the Committee by a majority vote of the Committee, and may be removed in the same manner. The Development Committee shall meet formally at least quarterly, or with such other frequency, and at such time and location, as may be established by the Committee, for the following purposes, among others:
  - (i) To prepare, review and, if necessary, revise the overall Development Plan as set forth in Section 3.3 below, to oversee and coordinate development activities and to review the conduct of development and manufacturing of Bulk Drug Substance, Drug Product Candidates and Drug Products;
  - (ii) To assign operational responsibility to VERTEX or SCHERING for the conduct of particular activities specified in the Development Plan;
  - (iii) To receive and review reports by VERTEX and SCHERING, which shall be prepared by each party and submitted to the other party and to the Development Committee on a quarterly basis within thirty (30) days after the end of the quarter, setting forth in reasonable detail, with supporting data, the results of work performed during the preceding calendar quarter under the Development Program by the

party submitting the report, including any planned or filed patent applications covering Bulk Drug Substance, Drug Product Candidates, Drug Products and methods of manufacturing either;

- (iv) To assist in coordinating scientific interactions and resolving issues between VERTEX and SCHERING during the course of the Development Program;
- (v) To discuss matters relating to patents, including but not limited to issues of inventorship and decisions relating to the filing, prosecution and maintenance of patents and patent applications.

Notwithstanding the foregoing, each party shall retain the rights, powers, and discretion expressly granted to it under this Agreement, and the Development Committee shall not be delegated or vested with any such rights, powers or discretion except as expressly provided in this Agreement. The Development Committee shall not have the power to amend or modify this Agreement, which may only be amended or modified as provided in Section 16.15 hereof.

# (b) Decision Making.

(i) The objective of the Development Committee shall be to reach agreement by consensus on all matters falling within its authority hereunder, within the scope of the Development Plan. However, if the Development Committee cannot reach consensus on any matter (a "Disputed Matter"): (a) except as otherwise set forth below, if the Disputed Matter relates to Core Development Activities, the parties shall attempt in good faith to resolve the disagreement through discussions among executive representatives from each Company, and if resolution of the Disputed Matter has not occurred within sixty (60) days after either party has notified the other in writing of the existence of the Disputed Matter, the Disputed Matter shall be referred for resolution to the President of VERTEX and the member of the Vorstand of SCHERING responsible for research and development, to resolve the Matter referred to them in a binding, nonappealable manner; and (b) if the Disputed Matter relates to development activities which are not Core Development Activities, a

- person designated by SCHERING, who may or may not be a member of the Development Committee, shall have final authority, after full consultation with VERTEX and discussion among executive representatives from each Company, to make all decisions hereunder regarding such Matter.
- (ii) Except as provided in (i) above, any substantial changes to the Development Plan must be agreed to in writing by both VERTEX and SCHERING. Any day-to-day nonsubstantial changes (the characterization of which changes as "nonsubstantial" shall be determined by at least two of the Development Committee members appointed by SCHERING and at least two of the Development Committee members appointed by VERTEX) to the Development Plan may be approved by a majority vote of the Development Committee.
- 3.3. Development Plan. (a) General. The Development Committee shall prepare and oversee the implementation of an overall development plan (the "Development Plan") for each Drug Product Candidate which shall describe fully the proposed preclinical studies, toxicology, clinical trials, regulatory plans, clinical trial and commercial material requirements and any other key elements of obtaining Regulatory Approval in each country where the Drug Product is to be marketed. The Development Plan will include, among other things, a plan (the "Core Development Plan") for the conduct of Core Development Activities, and will provide for the allocation of development tasks between VERTEX and SCHERING. Each party assigned a development task will, in a timely fashion, prepare a detailed plan for the accomplishment of that task and will submit that plan to the Development Committee for its review. Development tasks shall be advanced in parallel rather than serially where practicable and appropriate, if doing so would be likely to advance the ultimate date of product approval and launch and is otherwise commercially reasonable.
- (b) Process Development. VERTEX will be responsible for the development of processes for manufacture of Bulk Drug Substance ("Bulk Process Development"), and for the preparation and implementation of a plan to accomplish that task. SCHERING will be responsible for the development of processes for formulation and manufacture of Drug Products from Bulk Drug Substance ("Finished Process Development"), and for the preparation and implementation of a plan to accomplish that task. Each party will work with the Development Committee to coordinate its plans with those of the other party, with the objective of ensuring operationally effective and timely

integration of the two plans, as necessary to meet the overall schedule for process development and the supply of Bulk Drug Substance and Drug Product as set forth in the Development Plan.

- 3.4. Development Costs. (a) Development costs shall consist of Core Development Costs incurred by VERTEX and SCHERING in accordance with the Core Development Plan, and all other costs ("Supplemental Development Costs") associated with conduct of the Development Plan in the Territory. SCHERING will bear [\*\*\*] of the Supplemental Development Costs and [\*\*\*] of the Core Development Costs, and VERTEX will bear [\*\*\*] of the Core Development Costs. Not later than sixty (60) days after the end of each calendar year, SCHERING and VERTEX will each submit to the other a summary of the Core Development Costs incurred by the submitting party during the calendar year just ended, and to the extent that either party has incurred Core Development Costs during such calendar year greater than its pro rata share, the other party will reimburse such party as necessary to restore the agreed [\*\*\*] proportion; or the parties may, by agreement, provide that the party obligated to provide reimbursement may instead bear a disproportionate share of Core Development Costs (either in cash or in kind) during the next succeeding year to the extent necessary to restore the agreed proportion.
- (b) Each party, upon the written request and at the expense of the other party, and in any event not more frequently than once in or in respect of any calendar year, shall permit an independent public accountant of national prominence selected by the other party to have access during normal business hours to those records of such party as may be reasonably necessary to verify the accuracy of the cost reports submitted by such party pursuant to this Section 3.4(b) in respect of any calendar year ending not more than thirty-six (36) months prior to the date of the aforementioned written request.
- 3.5. Regulatory Approvals. The parties shall use their respective commercially reasonable efforts to file for and obtain all necessary Regulatory Approvals within a reasonable time period. Unless otherwise required by law in the relevant jurisdiction, SCHERING shall have the sole right to obtain Regulatory Approvals, which shall be held by and in the name of SCHERING, and SCHERING shall own all submissions in connection therewith, provided that VERTEX shall have an irrevocable right of reference thereto, and provided further, that any Regulatory Approvals with respect to [\*\*\*] in the United States shall be held by and in the name of VERTEX until Product Launch of [\*\*\*], whereupon they will be transferred to SCHERING or at its direction to an Affiliate of SCHERING, and SCHERING shall have an irrevocable right of reference thereto for purposes of this Agreement. All formulary or marketing approvals shall also be obtained by and in the name of SCHERING or, with respect to [\*\*\*] in the United States, by and in the name of VERTEX, until Product Launch of [\*\*\*], whereupon they will be transferred to SCHERING or at

its direction to an Affiliate of SCHERING. In the Territory, other than in the United States with respect to [\*\*\*], SCHERING will be the principal interface with and will otherwise handle all interactions with regulatory agencies concerning any Drug Product including, to the extent legally possible, being the sole contact with such agencies, subject to the rights of VERTEX under Section 3.6 hereof; and provided that VERTEX shall have the right to be represented at all meetings between representatives of the FDA and SCHERING, and between representatives of the EMEA and SCHERING, and shall be provided by SCHERING with prompt access to all exchanges of correspondence with the FDA and the EMEA. VERTEX at the request of SCHERING will supply representatives to meet with regulatory agencies, if necessary in view of the tasks assigned to VERTEX, to obtain or maintain Regulatory Approval of any Drug Product. Notwithstanding the foregoing, if [\*\*\*] becomes a Drug Product Candidate, Regulatory Approvals shall continue to be obtained in the United States in the name of VERTEX, although SCHERING shall have an irrevocable right of reference thereto, and VERTEX will continue to act as the principal interface with the U.S. Food and Drug Administration with respect to [\*\*: until Product Launch, at which time VERTEX shall assign all Regulatory Approvals to SCHERING or at its direction to an Affiliate of SCHERING.

3.6. Step-In Rights. If either party (the "First Party") fails unreasonably, other than as a result of Force Majeure or a failure of the other party to discharge its obligations hereunder, to carry out the tasks allocated to it under the Development Plan in accordance with the time lines agreed therein, then the other party may, after ninety (90) days prior written notice to the First Party, undertake that particular task ("Work") and complete it at its own expense if the First Party has not at such time begun to carry out such Work in a manner reasonably likely to cure its default. Such party shall be entitled to reasonable cooperation and assistance from the First Party to accommodate its efforts, including assignment to such party of sponsorship of regulatory filings if necessary to permit the exercise by such party of its rights under this Section 3.6. If any such Work is of good quality, conforms with the requirements of the Development Plan, and is used in any part by the First Party to advance development of Bulk Drug Substance, a Drug Product Candidate or a Drug Product, the out-of-pocket cost of that Work will be reimbursed to the party incurring the cost as promptly as practicable.

# Article IV Manufacture and Supply

4.1. Supply of Bulk Drug Substance for Development Purposes. VERTEX will supply Bulk Drug Substance to SCHERING, at a price equal to [\*\*\*] as necessary to meet

SCHERING's reasonable requirements for conduct of the Development Program, including its requirements for pre-clinical studies, formulation process development and human clinical trials.

4.2. VERTEX Bulk Drug Substance Commercial Supply Option. VERTEX shall have the option (the "Bulk Commercial Supply Option") to manufacture or have manufactured subject to Section 2.2 and to supply SCHERING with its entire requirements of Bulk Drug Substance for Drug Product sales in territories (the "Supply Option Territories") other than North America, Europe, the Middle East and Africa. The Bulk Commercial Supply Option with respect to a particular Drug Product will be exercisable upon written notice delivered by VERTEX to SCHERING no later than ninety (90) days after receipt by VERTEX of written notice from SCHERING announcing that Phase II Clinical Trials with respect to such Drug Product have commenced and making specific mention of the Bulk Commercial Supply Option. If VERTEX exercises the Bulk Commercial Supply Option, SCHERING, its Affiliates, sublicensees and marketing partners shall purchase all of their respective requirements of Bulk Drug Substance from VERTEX for manufacture of Drug Product for sale in the Supply Option Territories.

In the event that VERTEX does not exercise the Bulk Commercial Supply Option with respect to a Drug Product in the Supply Option Territory, or is for any reason unable to provide material in sufficient quantities and of sufficient quality necessary to reasonably meet the objectives set forth in the Development Plan for the Supply Option Territory, SCHERING may undertake production using its own manufacturing resources or Third Party manufacturers pursuant to the license granted in Section 2.1(a) of this Agreement, and shall have access to all information generated by VERTEX relating to the supply of Bulk Drug Substance. In such event SCHERING shall pay to VERTEX a royalty of [\*\*\*] of Net Sales of that Drug Product in the Supply Option Territories.

4.3. SCHERING Bulk Drug Substance Commercial Supply Right; Manufacture of Drug Product. SCHERING shall have the right to manufacture or have manufactured Bulk Drug Substance to meet its requirements for Drug Product sales in Europe, the Middle East and Africa, and, subject to VERTEX's rights under Section 4.2, in the Supply Option Territories. In the event that VERTEX has exercised its Bulk Commercial Supply Option with respect to Bulk Drug Substance for a particular Drug Product, SCHERING will give due consideration to VERTEX as a potential Third Party manufacturer if SCHERING chooses to manufacture Bulk Drug Substance for Europe, the Middle East or Africa through a Third Party manufacturer and will provide VERTEX with an opportunity to negotiate a mutually agreeable manufacturing agreement before entering into any

such agreement with a Third Party. SCHERING shall formulate and manufacture or have manufactured and packaged from Bulk Drug Substance all requirements for Drug Products in the Territory.

- 4.4. Commercial Supply in North America. VERTEX shall manufacture or have manufactured all Bulk Drug Substance necessary to meet SCHERING's requirements for Drug Product sales in North America.
- 4.5. Manufacturing Technology. Each party shall provide to the other, free of charge, for use in the manufacture of Bulk Drug Substance, Drug Product Candidates and Drug Products hereunder, any manufacturing technology developed by it in connection with the Research Program or the Development Program, and any improvements made by it to any such technology. Other manufacturing technology which belongs to one party and which is useful in the manufacture of Bulk Drug Substance, Drug Product Candidates or Drug Products shall be made available to the manufacturing party for that purpose, subject to negotiation of a reasonable royalty or other compensation arrangement. If either party (a "Contracting Party") engages an Affiliate or a Third Party in the course of the Development Program to provide assistance to the Contracting Party in the development of processes useful for the manufacture of Bulk Drug Substance, Drug Product Candidates or Drug Products, the Contracting Party will ensure that any processes belonging to that Affiliate or Third Party and made available to the Contracting Party will also be made available to the other party on the same terms offered to the Contracting Party.
- 4.6. Bulk Drug Substance Supply Terms. All Bulk Drug Substance manufactured by VERTEX for SCHERING hereunder shall be supplied to SCHERING pursuant to the terms of a supply agreement to be negotiated by the parties based on the term sheet attached as Schedule 4.6 to this Agreement.
- 4.7. Coordination of Manufacturing Processes. The parties intend to coordinate the development of each Drug Product so that each form of Drug Product marketed or sold by SCHERING or VERTEX will be produced using substantially identical processes on a worldwide basis. The parties shall, as part of the supply agreement referenced in Section 4.6 above, agree upon procedures for adoption of process changes and other changes to manufacturing methods to ensure that manufacturing processes remain substantially identical for as long as the Drug Product is sold.

## Article V Commercialization

- 5.1. Marketing and Promotion. SCHERING shall have [\*\*\*] rights to market, sell and distribute all Drug Products in the Territory, including the right to sublicense marketing rights as set forth in Section 2.1(b) hereof, subject to the [\*\*\*] rights of VERTEX set forth in this Article V.
- 5.2. Global Marketing Plan. As soon as practicable but in any case no later than the date of first submission of an application for regulatory approval of a Drug Product in a Major Market, SCHERING in consultation with VERTEX will prepare and provide to VERTEX for its review and comment a marketing plan, budgets and other customary planning and marketing aids with respect to launch of the Drug Product in each Major Market (the "Global Marketing Plan"). The Global Marketing Plan will be consistent with the North America Marketing Plan prepared in accordance with the provisions of Section 5.3 below. SCHERING, in consultation with VERTEX, will periodically update the Global Marketing Plan to reflect materially changed circumstances as they occur, and will circulate the updated plan to VERTEX. SCHERING will provide VERTEX with the opportunity to be represented on any committee which it may establish to oversee the marketing effort under the Global Marketing Plan with respect to each Drug Product and in any event shall provide VERTEX with reasonable opportunities to comment on the creation of marketing strategies and plans, will meet periodically with VERTEX to review marketing matters, and will share with VERTEX on a regular basis materials and information (such as, to the extent available, market research, including market growth and trend data, reports, sales force deployment data and information concerning competition and competitors) generated by or at the direction of SCHERING or its Affiliates and sublicensees which is relevant to the marketing of Drug Products.

# 5.3. Marketing in North American

VERTEX and SCHERING will Co-Promote Drug Products in North America under the terms of a Co-Promotion Agreement (the "Co-Promotion Agreement") which shall be negotiated between the parties in good faith within thirty (30) days following the commencement of Phase III Clinical Trials for the first Drug Product. The Co-Promotion Agreement will incorporate, among other things, all of the principles set forth below.

(a) Profit-sharing. VERTEX and SCHERING will share equally in Operating Profits and Operating Losses from sales of Drug Products in North America. "Operating Profits" or "Operating Losses" shall mean [\*\*\*].

- (b) Marketing Committee. Commercialization and marketing of Drug Products in North America shall take place under the general coordination and direction of a Marketing Committee which shall be established not later than thirty days (30) following the commencement of Phase III Clinical Trials with respect to a Drug Product and which shall be composed of an equal number of VERTEX and SCHERING personnel. The Marketing Committee shall participate in the preparation and review of a detailed plan for the commercial launch and subsequent marketing and sale of Drug Products in North America (the "North American Marketing Plan").
- (c) Roles and Responsibilities of the Parties. The North American Marketing Plan will provide each party the opportunity to perform [\*\*\*]. In allocating tasks between VERTEX and SCHERING, the Marketing Committee will attempt to assign roles to each party which are reasonable in relation to that party's capabilities and consistent with relevant marketing requirements. As used in this agreement, [\*\*\*] according to generally recognized standards in the pharmaceutical industry.

At its discretion, VERTEX may elect to make a contribution to the marketing of Drug Products in North America [\*\*\*].

(d) Decisions of the Marketing Committee. Where Vertex elects [\*\*\*], except as to (a) those matters addressed in Section 5.3(i) below, which shall be decided under the procedures specified below for "Strategic Issues."

Where VERTEX elects [\*\*\*], the parties expect and intend that all decisions of the Marketing Committee shall be reached by consensus and will be agreeable to both parties. If consensus cannot be reached after discussion of any item within a regular meeting of the Marketing Committee [\*\*\*].

The parties acknowledge that with specific reference to the launch of Drug Products in North America certain decisions of the Marketing Committee are of key strategic importance to both SCHERING and VERTEX ("Strategic Issues") and that the collective and independent interests of both VERTEX and SCHERING must be protected. The following items have been identified as "Strategic Issues":

1. [\*\*\*].

- 2. [\*\*\*].
- 3. [\*\*\*].
- 4. [\*\*\*].

In the event that the Marketing Committee is unable to reach consensus on any of the above mentioned Strategic Issues, then the disagreement shall be referred for decision to the appropriate member of the SCHERING Vorstand and the Chief Executive Officer of VERTEX who shall in good faith reach a fair and equitable resolution of the disagreement within twelve weeks of referral of the dispute.

- (e) Operational Issues. Except for those matters which are the responsibility of the Marketing Committee or as otherwise provided in this Agreement, each party will be free to make its own decisions concerning the Detailing of Drug Products by its sales force in North America. It is further understood by both parties that operational or tactical responsibilities allocated to either VERTEX or SCHERING by the Marketing Committee and in accordance with the overall Marketing Plan are not subject to the authority of the Marketing Committee. The role of the Marketing Committee in this respect shall be one of coordination, such that the individual efforts of each party may be maximized and that overlap may be kept to a minimum.
- (f) Sublicensing. Either party may sublicense its Co-Promotion rights and obligations in North America without the consent of the other party; provided, however, that neither party shall grant any such sublicense without prior consultation with the other party, and provided, that neither party shall sublicense its Co-Promotion rights in North America to a third party if the other party can demonstrate on a concrete, objective basis that the proposed sublicensee is unsuitable to Co-Promote Drug Products in North America.

- (g) Supply of Bulk Drug Substance and Drug Product. VERTEX shall supply Bulk Drug Substance to SCHERING for manufacture into Drug Product for sale in North America, and SCHERING shall manufacture Drug Product from Bulk Drug Substance supplied by VERTEX, for compensation equal [\*\*\*].
- (h) Marketing Expense. VERTEX and SCHERING shall each be responsible for [\*\*\*] under the North American Marketing Plan. [\*\*\*]. As part of the Co-Promotion Agreement to be negotiated between the Parties pursuant to Section 5.3 above, the Parties will negotiate in good faith how Direct Marketing Costs will be allocated where the Drug Product is Detailed together with another product or products.
- (i) Pricing Variations, Third Party Promotion Support and Conflict of Interest. The Marketing Committee will coordinate and direct marketing of a Drug Product after its initial launch in accordance with the provisions of Section 5.3 (d) above. In the event that either party proposes pricing variations which may be reasonably forecast to result in a decline, when compared with actual experience in the prior year, of more than [\*\*\*] in the average net selling price for a Drug Product across all distribution channels (including managed care) for the year in which the reduction applies, and if the other party disagrees with the proposed pricing variations, then the disagreement shall be referred for decision to the appropriate member of the SCHERING Vorstand and the Chief Executive Officer of VERTEX who shall attempt in good faith to reach a fair and equitable resolution of the disagreement. If the parties are unable to resolve the disagreement within four (4) weeks of referral of the dispute, then [\*\*\*]. The foregoing method for resolving disagreements will also be applicable to any disagreements concerning (x) a proposal by either party to enter into a promotion support arrangement with a third party with respect to a Drug Product; or (y) any other matter as to which action is being proposed hereunder by one party which is demonstrably

and materially detrimental to the interests of the other party hereto but which is materially beneficial to the separate interests of the proposing party.

- (j) Revision of Profit-sharing Formula. [\*\*\*].
- (k) Product Recall If either party is of the opinion that a Drug Product being commercially marketed hereunder should be recalled as a result of bona fide concerns regarding its safety, then the Drug Product shall be recalled and the parties will cooperate to achieve that end.
- (1) Booking of Sales. All customer orders for Drug Products in North America will be [\*\*\*]
- (m) Training. Each party will be responsible for the cost of training its own sales force. The parties will consult on training programs to ensure a consistent, focused promotional strategy for each Drug Product.
- (n) Advertising. Neither party shall engage in any advertising or use any label, package, literature or other written material in connection with a Drug Product in North America unless the specific form and content is approved by the Marketing Committee.
- 5.4. European Co-promotion Rights. As set forth in Section 3.4 of the Research Agreement, if SCHERING exercises the Buy-back option with respect to a Refused Compound at the Second Opportunity, SCHERING shall grant VERTEX European Co-promotion Rights in the marketing of any Drug Product Candidates or Drug Products incorporating the Refused Compound. The nature and scope of those rights shall be determined in detail by negotiation between the parties at the time the European Co-Promotion Rights become applicable, and will involve a co-promotion

role for VERTEX that is reasonable in relation to its capabilities and consistent with relevant market requirements, but in any event shall approximate in substance the terms set forth in Section 5.3 with respect to North American Co-Promotion.

- 5.5. Marketing in Japan. SCHERING has the rights to sublicense in Japan set forth in Section 2.1(b) hereof. The parties shall endeavor to ensure that the launch of a Drug Product in Japan shall not be delayed due in whole or in part to a lack of commercially adequate marketing capacity in that country. No later than the date of first submission of an application for Regulatory Approval of a Drug Product in Japan, the parties will develop a mutually acceptable sales and marketing plan covering the periods ending both one year and two years after projected Drug Product launch which will include reasonable forecasts for sales of the Drug Product. Such forecasts will be updated by agreement of the parties six months before the date of projected launch of the Drug Product, taking into account all information then available, and the forecasts for the second year will be updated six months after the date of first commercial sale. If SCHERING and its Affiliates and permitted sublicensees cannot reasonably demonstrate adequate marketing capacity in view of these forecasts, SCHERING will obtain a marketing partner in Japan, reasonably acceptable to VERTEX, which can undertake the marketing effort together with SCHERING. If SCHERING (including its Affiliates and permitted sublicensees) and/or its marketing partner, fail to reach [\*\*\*] (otherwise than for reasons beyond its reasonable control), and such failure is attributable to a failure by SCHERING, its Affiliates and permitted sublicensees to use commercially reasonable skill and efforts to exploit the full commercial potential of the Drug Product in Japan, then VERTEX may elect upon written notice to SCHERING to convert SCHERING's exclusive rights with respect to such Drug Product in Japan to semi-exclusive rights (meaning that, in addition to SCHERING, its Affiliates and permitted sublicensees and any then-existing marketing partner, VERTEX or an Affiliate of VERTEX may itself market and sell such Drug Product in Japan, or may license those rights to another Third Party, subject to the payment to SCHERING of a [\*\*\*] royalty provided that VERTEX will not license its rights in Japan to any Third Party on financial terms more favorable as a whole than those provided to SCHERING in Japan). In the event that SCHERING appoints a marketing partner in Japan, SCHERING shall have the right to supply Drug Product to that marketing partner at such prices as SCHERING shall determine, subject always to its royalty obligations to VERTEX based on Net Sales of Drug Product by SCHERING and its Affiliates, sub-licensees and marketing partners.
- $5.6.\ Further\ Co-Promotion\ Proposals.\ VERTEX\ may\ provide\ SCHERING\ at\ any\ time\ with\ a\ proposal\ for\ co-promotion\ of\ Drug\ Products\ in\ any\ market\ or\ territory\ in\ the\ world$

other than North America, and SCHERING will give due consideration to any such proposal but will otherwise be under no obligation with respect thereto.

5.7. Co-labeling. All labels, packaging and package inserts, sales literature, and product advertising relative to Drug Products shall bear the names of both SCHERING and VERTEX in a prominent position or to the extent permitted by law in a particular jurisdiction. SCHERING will cooperate with any reasonable request of VERTEX directed toward facilitating approval by a regulatory authority for co-labeling consistent with this Section 5.6.

## 5.8. Due Diligence.

- (a) SCHERING shall use diligent and commercially reasonable efforts consistent with the requirements of the Development Program and sound and reasonable business practices and judgment to effect introduction of Drug Products into Major Markets as soon as reasonably practicable, devoting the same degree of attention and diligence to such efforts that it devotes to such activities for other products of comparable market potential (without reference to any competing products in SCHERING's product portfolio). Following the First Commercial Sale of a Drug Product and until the expiration of this Agreement, SCHERING shall endeavor to keep Drug Products reasonably available to the public in each of the Major Markets. SCHERING shall promptly notify VERTEX if it shall determine that the marketing and sale of a Drug Product in any country is not commercially reasonable. In determining whether SCHERING is in compliance with the foregoing provisions, there shall be taken into account the normal course of assertive drug development programs in the pharmaceutical industry conducted with sound and reasonable business practices and judgment.
- (b) VERTEX shall have the right to terminate this Agreement upon ninety (90) days written notice to SCHERING if SCHERING shall be in default of any of its material obligations under subsection (a) above; unless SCHERING can demonstrate during such 90-day period that it has initiated and will continue actions which are reasonably likely to cure the default within a reasonable period of time. VERTEX shall also have the right to terminate SCHERING's license hereunder in any country at any time upon ninety (90) days written notice to SCHERING in each case, if within [\*\*\*] from the date of Regulatory Approval for the initial sale of a Drug Product in such country, SCHERING has not put the Drug Product into commercial use in such country, or following the First Commercial Sale in such country, is not keeping the Drug Product reasonably available to the public therein, unless SCHERING is using commercially reasonable efforts directed toward placing the Drug Product into commercial use in such country or keeping the Drug Product reasonably available to the public, respectively, as aforesaid, or unless SCHERING and VERTEX have agreed in writing, acting reasonably and in good faith, not to introduce that Drug Product into commercial use in such

country. If commercial conditions applicable to a country are such that SCHERING cannot reasonably be expected to generate a reasonable rate of return on Net Sales of a Drug Product in that country, then SCHERING's commercial rights hereunder in that country shall revert to VERTEX. During any applicable ninety (90)-day notice period referenced above, the parties shall make a good faith effort to resolve the issues complained of to their mutual satisfaction. Notwithstanding the foregoing, the rights of termination granted to VERTEX in this subsection (b) shall not apply if and so long as VERTEX is in material default of any of its material obligations under this Agreement.

# Article VI Payments

6.1. Development Payments by SCHERING. SCHERING will make the following payments to VERTEX upon the achievement of any of the following milestones with respect to [\*\*\*] Program Compound, Drug Product Candidate or Drug Product, upon the further terms and conditions set forth below.

[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]

Payments for the achievement of each of the milestones referenced above, including any payment made on account of the achievement of any milestone with respect to [\*\*\*], shall be required no more than [\*\*\*] times, no matter how many Program Compounds, Drug Product Candidates or Drug Products achieve such milestones. In addition, payments beyond the first payment made on account of any milestone shall be required only on account of the achievement of that milestone by a Program Compound, Drug Product Candidate or Drug Product [\*\*\*];

provided, further that no milestone shall be payable more than [\*\*\*]with respect to Program Compounds, Drug Product Candidates or Drug Products being developed for indications principally involving the peripheral nervous system, or for Program Compounds, Drug Product Candidates or Drug Products being developed for indications principally involving the central nervous system.

Payment shall be made on or before the fifteenth day following the occurrence of an event giving rise to a payment obligation hereunder. 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 SCHERING. Any payment which falls due on a date which is a Saturday, Sunday or a legal holiday in the Commonwealth of Massachusetts may be made on the next succeeding day which is not a Saturday, Sunday or a legal holiday in the Commonwealth.

- $6.2. \; \text{Supply Price for Bulk Drug Substance in the Supply Option Territories.}$
- 6.2.1. VERTEX Exercises Bulk Commercial Supply Option. If VERTEX exercises the Bulk Commercial Supply Option set forth in Section 4.2, the supply price for a unit of Bulk Drug Substance supplied by VERTEX for the manufacture of a Drug Product sold in the Supply Option Territories shall be determined as a fraction (the "Applicable Percentage," as determined below) of the Net Sales price of Drug Product sold in the Supply Option Territories containing an equivalent unit of Bulk Drug Substance.

The Applicable Percentage shall equal for any year the fraction obtained by dividing X by Y: where

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

- 6.2.2. Payment of Supply Price under Section 6.2.1 hereof. The purchase price for each unit of Bulk Drug Substance supplied to SCHERING by VERTEX under Section 6.2.1 hereof shall initially be calculated during any year based on a forecast of Net Sales of Drug Products per unit of Bulk Drug Substance for that year, and a forecast of the Applicable Percentage for that year, which shall be provided by SCHERING 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 Drug Substance will be recalculated accordingly, based on any material changes in the forecast. As part of the Supply Agreement to be negotiated under Section 4.6 above, SCHERING and VERTEX will agree upon a reasonable rate of yield in the manufacture of Drug Product from Bulk Drug Substance, and SCHERING will compensate VERTEX for any otherwise uncompensated loss above the agreed rate at the Manufacturing Cost thereof. Payments due to VERTEX based upon that forecasted price shall be made within thirty days of receipt from VERTEX of an invoice for Bulk Drug Substance purchased by SCHERING under the terms of the Supply Agreement, and annual adjustments shall be made within such time periods and applying such procedures as the parties may agree to reflect the actual worldwide Net Sales and Applicable Percentage for that year, and the actual manufacturing loss during that year. Any net adjustments shall be remitted forthwith to the party to whom the adjustment is due, with interest at the rate set forth in Section 6.6(e) of this Agreement.
- 6.2.3. VERTEX Does Not Exercise Bulk Commercial Supply Option. If VERTEX elects not to supply Bulk Drug Substance under Section 4.2 hereof for the manufacture of a Drug Product sold in the Supply Option Territories, SCHERING shall pay to VERTEX a royalty of [\*\*\*] of Net Sales of that Drug Product in the Supply Option Territories in lieu of the amount set forth in Section 6.2.1 hereof.

- 6.3. Supply Price for Bulk Drug Substance and Drug Product in North America. The supply price for a unit of Bulk Drug Substance supplied by VERTEX to SCHERING for the manufacture of a Drug Product sold in North America shall equal [\*\*\*].
- 6.4. Royalties. SCHERING shall pay to VERTEX a royalty on Net Sales of Drug Products in Europe, the Middle East and Africa of [\*\*\*]
- 6.5. Reduction in Payments. (a) If, at the end of the [\*\*\*] following First Commercial Sale of a Drug Product in a particular country, that Drug Product is not the subject of a Live Claim in that country held by either VERTEX or SCHERING: (i) the Applicable Percentage under Section 6.2 or the royalty percentage under Section 6.4, as may be applicable to the subject country, shall thereafter be reduced by [\*\*\*]; (ii) if SCHERING can demonstrate that a competitive product has been commercially launched by a Third Party in that country, and that the competitive product is of a type the sale of which would infringe a VERTEX Patent if made in any country in which there is a Live Claim covering the Drug Product, then the payment reductions provided in Subsection 6.5(b) below will become effective, notwithstanding the provisions of Section 6.5(a)(i), with respect to Net Sales of that Drug Product in that country; and (iii) prior to the expiration of the time period provided in Section 6.5(a)(i), if a previously issued Live Claim covering a Drug Product in that country shall thereafter expire, and there shall be no other Live Claims in that country covering that Drug Product, and if at the time of expiration there was no Live Claim covering that Drug Product in any Major Market, then the payment reductions provided in Subsection 6.5(b) shall become effective, with respect to Net Sales of that Drug Product in that country, notwithstanding the provisions of Section 6.5(a)(i).

(b) If, at the end of the [\*\*\*] following First Commercial Sale of a Drug Product in a particular country, that Drug Product is not the subject of a Live Claim in that country held by either VERTEX or SCHERING, then (except as provided in Section 14.1 hereof), as may be applicable: (i) the percentage of Net Sales as set forth in Section 6.2 of this Agreement relating to the supply of Bulk Drug Substance for the manufacture of Drug Products sold in that country shall be reduced by [\*\*\*]; or (ii) the royalty rate on Net Sales of that Drug Product in such country shall be reduced to [\*\*\*].

# 6.6. Sales Reports.

(a) During the term of this Agreement and after the first commercial sale of a Drug Product, SCHERING shall furnish or cause to be furnished to VERTEX on a quarterly basis a written report or reports covering each calendar quarter (each such calendar quarter being sometimes referred to herein as a "reporting period") showing (i) the Net Sales of each Drug Product in each country in the world during the reporting period by SCHERING and each Affiliate, sublicensee and marketing partner; (ii) the royalties, payable in United States Dollars ("Dollars"), which shall have accrued under Section 6.4 hereof in respect of such sales and the basis of calculating those royalties; (iii) amounts due under Section 6.2 hereof on account of the purchase of Bulk Drug Substance, and the basis for calculating those amounts due (including unit sales data); (iv) withholding taxes, if any, required by law to be deducted in respect of any such sales; (v) the exchange rates used in converting into Dollars, from the currencies in which sales were made, any payments due which are based on Net Sales; (vi) dispositions of Drug Products other than pursuant to sale for cash. With respect to sales of Drug Products invoiced in Dollars, the Net Sales amounts and the amounts due to VERTEX hereunder shall be expressed in Dollars. With respect to sales of Drug Products invoiced in a currency other than Dollars, the Net Sales and amounts due to VERTEX hereunder shall be expressed in the domestic currency of the party making the sale, together with the Dollar equivalent of the amount payable to VERTEX, calculated using SCHERING's then-current standard exchange rate methodology for the translation of foreign currency sales into U.S. dollars. In each report the methodology will be disclosed, will be identical to that employed by SCHERING, generally, in its external financial reporting, as reviewed and approved by its independent auditors and will be in conformity with SCHERING's usual and customary general accounting principles consistently applied. If any sublicensee or marketing partner makes any sales invoiced in a currency other than its domestic currency, the Net Sales shall be converted to its domestic currency in accordance with the sublicensee's normal accounting principles. SCHERING shall furnish to VERTEX appropriate evidence of payment of any tax or other amount required by applicable laws or regulations to be

deducted from any royalty payment, including any tax or withholding levied by a foreign taxing authority in respect of the payment or accrual of any royalty. Reports shall be due on the ninetieth (90th) day following the close of each reporting period, although SCHERING shall also provide VERTEX with a "flash" report of Net Sales, only, reasonably promptly after SCHERING closes its books with respect to the quarterly reporting period. SCHERING shall keep accurate records in sufficient detail to enable the amounts due hereunder to be determined and to be verified by VERTEX. SCHERING shall be responsible for all payments that are due to VERTEX but have not been paid by SCHERING's sublicensees or marketing partners.

- (b) Amounts shown to have accrued by each sales report provided for under Section 6.6(a) of this Agreement shall be due and payable on the date such sales report is due.
- (c) All payments shall be made in Dollars. If at any time legal restrictions prevent the prompt remittance of any payments with respect to any country of the Territory where Drug Product Candidates or Drug Products are sold, SCHERING or its sublicensees or marketing partners shall have the right and option to make such payments by depositing the amount thereof in local currency to VERTEX's account in a bank or depository in such country.
- (d) Upon the written request of VERTEX, at VERTEX's expense and not more than once in or in respect of any calendar year, SCHERING shall permit an independent public accountant of national prominence selected by VERTEX, to have access during normal business hours to those records of SCHERING as may be reasonably necessary to verify the accuracy of the sales reports furnished by SCHERING pursuant to this Section 6.6, in respect of any calendar year ending not more than thirty-six (36) months prior to the date of such notice. SCHERING shall include in each sublicense or marketing agreement entered into by it pursuant to this Agreement a provision requiring the sublicensee or marketing partner to keep and maintain adequate records of sales made pursuant to such sublicense or marketing agreement and to grant access to such records by the aforementioned independent public accountant for the reasons specified in this Section 6.6. Upon the expiration of thirty-six (36) months following the end of any calendar year, the calculation of amounts payable with respect to such fiscal year shall be binding and conclusive upon VERTEX, and SCHERING and its sublicensees and marketing partners shall be released from any liability or accountability with respect to payments for such year. The report prepared by such independent public accountant, a copy of which shall be sent or otherwise provided to SCHERING by such independent public accountant at the same time it is sent or otherwise provided to VERTEX, shall contain the conclusions of such independent public accountant regarding the audit and will specify that the amounts paid to VERTEX pursuant thereto were correct or, if incorrect, the amount of any underpayment or overpayment. If such independent public accountant's report shows any

underpayment, SCHERING shall remit or shall cause its sublicensees or marketing partners to remit to VERTEX within thirty (30) days after SCHERING's receipt of such report, (i) the amount of such underpayment and (ii) if such underpayment exceeds five percent (5%) of the total amount owed for the calendar year then being audited, the reasonable and necessary fees and expenses of such independent public accountant performing the audit, subject to reasonable substantiation thereof. Any overpayments shall be fully creditable against amounts payable in subsequent payment periods. Any disagreement of the parties with respect to the findings of the public accountant shall be subject to the dispute resolution mechanism set forth in Section 13.2 hereof. VERTEX agrees that all information subject to review under this Section 6.5 or under any sublicensee or marketing agreement is confidential and that VERTEX shall retain and cause its accountant to retain all such information in confidence.

- (e) In case of any delay in payment by SCHERING to VERTEX not occasioned by Force Majeure, interest at the rate of [\*\*\*] per month, assessed from the thirty-first day after the due date of the payment, shall be due from SCHERING without any special notice.
- 6.7. Withholding Tax. If during the term of this Agreement, withholding tax should be required by law to be deducted from any payments required to be made by SCHERING to VERTEX hereunder, the parties will agree upon an equitable division of liability for any sum which is withheld and for which VERTEX is not compensated or reimbursed by way of usable tax credits or otherwise. In that connection VERTEX at SCHERING's request shall sign a usual and customary exemption application and in addition shall apply for a tax refund at the request of SCHERING from any tax authority to which SCHERING has paid withholding tax on account of any payments made by SCHERING to VERTEX hereunder.

# Article VII

## Intellectual Property

#### 7.1. Information Sharing.

(a) Preclinical and Clinical Data. Each party will provide the other as promptly as possible with any and all preclinical and clinical data generated by it as part of the development of Bulk Drug Substance, Drug Product Candidates and Drug Products. The party receiving such information shall be free to use it solely for the purpose of developing, marketing and selling Drug Products and may cross-reference such information where appropriate in any application filed for regulatory approval.

(b) Improvements and Inventions

Each party shall keep the other fully advised of:

- (i) any improvements relating to Bulk Drug Substance, Drug Product Candidates or Drug Products made by such party or its Affiliates or sublicensees during the term of the Research Program;
- (ii) any other inventions, improvements, and Know-How relating to Bulk Drug Substance, Drug Product Candidates or Drug Products made jointly with the other party or its Affiliates during the term of the Research Program ("Joint Inventions").

# 7.2. Patentable Inventions and Know-How.

- 7.2.1. Ownership. Any inventions made and all Know-How generated by either party or its Affiliates during the term of this Agreement relating to the manufacture or use of Bulk Drug Substance, a Drug Product Candidate or a Drug Product will be disclosed to the other party promptly after the disclosing party recognizes the significance thereof unless in the case of process developments the same shall have been developed as part of a collaboration with a Third Party, the terms of which prohibit disclosure to the other party. All patents and technology shall be owned by the party making the invention claimed or contained therein or, if such invention is made jointly, shall be owned jointly, all as determined in accordance with U.S. laws of inventorship.
- Patent Prosecution. VERTEX shall be responsible for the preparation, filing, prosecution and maintenance of all patents and patent applications included in VERTEX Patents and all patents and patent applications included in Patents claiming inventions jointly owned with SCHERING. SCHERING shall be responsible for the preparation, filing, prosecution and maintenance of all patents and patent applications included in SCHERING Patents. In each case the responsible party shall consult from time to time with the other party and the Development Committee with respect thereto. The parties hereby agree that to the extent legally possible the responsible party shall, at a minimum, prepare file, prosecute and maintain patent coverage as described in this section in the countries listed in Schedule 7.2.2, subject to the next succeeding sentence. The party initially responsible for preparation, filing, prosecution and maintenance of a particular Patent (the "Initial Responsible Party") shall give thirty (30) days advance notice (the "Discontinuance Election") to the other party of any decision to cease preparation, filing, prosecution and maintenance of that Patent in any jurisdiction (a "Discontinued Patent"). In such case, the other party may elect at its sole discretion to continue preparation, filing and prosecution or maintenance of the Discontinued Patent at its sole expense. The party so continuing shall own any such Patent; and the Initial Responsible Party shall execute such documents and perform such

acts as may be reasonably necessary for the other party to file or to continue prosecution or maintenance, including assigning ownership of such Patent to such electing party. Discontinuance may be on a country-by-country basis or for a patent application or patent series in total.

Each party will consult the other party with respect to its choice of patent counsel and will keep that party continuously informed of all matters relating to the preparation, filing, prosecution and maintenance of Patents covered by this Agreement. Each party shall endeavor in good faith to coordinate its efforts with those of the other party to minimize or avoid interference with the prosecution of the other party's patent applications. To the extent practicable, each party shall provide the Development Committee with a copy of any patent application which first discloses any specific technology, prior to filing the first of such applications in any jurisdiction, for review and comment by the Committee or its designees.

7.2.3. Costs. Costs incurred in the preparation, prosecution and maintenance of Patents shall be borne by each party as set forth in Section 7.3 of the Research Agreement.

# 7.3. Infringement Claims by Third Parties.

If the manufacture, use or sale of Bulk Drug Substance and/or Drug Product results in a claim against a party hereto for patent infringement or for inducing or contributing to patent infringement ("Infringement Claim"), the party first having notice of an Infringement Claim shall promptly notify the other in writing. The notice shall set forth the facts of the Infringement Claim in reasonable detail.

In the event that the sale of a Drug Product in any country necessarily involves working within the scope of a Third Party's patent, which would otherwise be infringed by the practice of a VERTEX Patent in connection with sales or manufacture of the Drug Product in that country, then VERTEX will use reasonable efforts to obtain required license under the Third Party's patents with a right to sublicense to SCHERING, under terms reasonably acceptable to both VERTEX and SCHERING, and VERTEX and SCHERING will each bear [\*\*\*] of any financial obligation payable under such license; provided that VERTEX shall not be required to accept any license which carries a financial obligation which is materially in excess of the range of financial obligations customarily associated with comparable non-exclusive licenses; and provided further, that VERTEX shall not be required to accept any license obligation with respect to the sale of a Drug Product in a particular country if its financial obligations under that license, when aggregated with any other financial obligations with respect to Net Sales of the Drug Product in such country, is greater than [\*\*\*] in such country. If the terms of a required license under a Third Party patent do not meet the foregoing requirements and VERTEX therefore elects not to assume its share of any financial

obligation, SCHERING may nonetheless elect to obtain the license, to continue sales of Drug Product in such country and to pay, itself, any amounts due under such license. If SCHERING elects to pay such amounts under the circumstances stated, payments by SCHERING to VERTEX hereunder on account of Net Sales in such country shall be subject to the reduced payment rate specified in Section 6.5(a)(i) hereof.

If the required license is either unavailable or its terms are unacceptable both to VERTEX and to SCHERING, then SCHERING may elect in its sole discretion to discontinue sales of the Drug Product in such country or to undertake the defense of a patent infringement action or the prosecution of a declaratory judgment action with respect to the Third Party patents. The parties shall share [\*\*\*] all out-of-pocket costs and expenses incurred in conducting the defense of such Infringement Claims or the prosecution of such declaratory judgment actions, including the investigation and settlement thereof. Provided that SCHERING is conducting the defense of the Infringement Claim or the prosecution of such declaratory judgment actions, VERTEX shall bear its own costs. The costs and expenses of all suits brought by a party under this Section 7.3 shall be reimbursed to such party and then to the other party, if it participates in such suit, pro rata, out of any damages or other monetary awards recovered therein in favor of VERTEX or SCHERING. Any remaining compensatory damages shall be split between VERTEX and SCHERING as if they were Net Sales of SCHERING pursuant to the terms of this Agreement. Any remaining exemplary or punitive damages shall then be split equally between VERTEX and SCHERING. No settlement or consent judgment or other voluntary final disposition of a suit under this Section 7.3 may be entered into without the joint consent of VERTEX and SCHERING (which consent shall not be unreasonably withheld).

- 7.4. Infringement Claims Against Third Parties.
- 7.4.1. VERTEX and SCHERING each agree to take reasonable actions to protect their respective patents and technology from infringement and from unauthorized possession or use.
- 7.4.2. If any VERTEX Patents or SCHERING Patents are infringed or VERTEX Know-How or SCHERING Know-How is misappropriated, as the case may be, by a Third Party, the party to this Agreement first having knowledge of such infringement or misappropriation, or knowledge of a reasonable probability of such infringement or misappropriation, shall promptly notify the other in writing. The notice shall set forth the facts of such infringement or misappropriation in reasonable detail. The owner of the patent or technology, or VERTEX, in the case of joint ownership between the parties hereto, shall have the primary right, but not the obligation, to institute, prosecute, and control with its own counsel any action or proceeding with

respect to infringement or misappropriation of such patent or technology and the other party shall have the right, at its own expense, to be represented in such action by its own counsel. If the party having the primary right or responsibility to institute, prosecute, and control such action or prosecution fails to do so within a period of one hundred twenty (120) days after receiving notice of the infringement, the other party shall have the right to bring and control any such action by counsel of its own choice, and the other shall have the right, at its own expense, to be represented in any such action by counsel of its own choice. If one party brings any such action or proceeding, the second party may be joined as a party plaintiff and, in case of joining, the second party agrees to give the first party reasonable assistance and authority to file and to prosecute such suit. The costs and expenses of all suits brought by a party under this Section 7.4.2 shall be reimbursed to such party and then to the other party, if it participates in such suit, pro rata, out of any damages or other monetary awards recovered therein in favor of VERTEX or SCHERING. Any remaining compensatory damages shall be split between VERTEX and SCHERING as if they were Net Sales of SCHERING pursuant to the terms of this Agreement. Any remaining exemplary or punitive damages shall then be split equally between VERTEX and SCHERING. No settlement or consent judgment or other voluntary final disposition of a suit under this Section 7.4 may be entered into without the joint consent of VERTEX and SCHERING (which consent shall not be unreasonably withheld).

- 7.5. Notice of Certification. VERTEX and SCHERING each shall immediately give notice to the other of any certification filed under the U.S. "Drug Price Competition and Patent Term Restoration Act of 1984" claiming that a Licensed Patent is invalid or that any infringement will not arise from the manufacture, use or sale of any product by a third party. If VERTEX decides not to bring infringement proceedings against the entity making such a certification, VERTEX shall give notice to SCHERING of its decision not to bring suit within twenty-one (21) days after receipt of notice of such certification. SCHERING may then, but is not required to, bring suit against the party that filed the certification. Any suit by SCHERING or VERTEX shall either be in the name of SCHERING or in the name of VERTEX, or jointly by SCHERING and VERTEX, as may be required by law. For this purpose, the party not bringing suit shall execute such legal papers necessary for the prosecution of such suit as may be reasonably requested by the party bringing suit.
- 7.6. Patent Term Extensions. The parties shall cooperate in good faith with each other in gaining patent term extension wherever applicable to VERTEX Patents and SCHERING Patents covering Drug Product Candidates or Drug Products. SCHERING and VERTEX shall mutually determine which patents shall be extended. All filings for such extension shall be made by the party who owns the patent, provided, however, that in the event that the party who owns the patent elects not to file for an extension, such party shall (i) inform the other party of its intention not to file and (ii) grant the other party the right to file for such extension.

#### Article VIII

#### Reporting

#### 8.1. Exchange of Information.

- (a) General. VERTEX and SCHERING will promptly and freely share technical information useful in connection with the development of Bulk Drug Substance, Drug Product Candidates or Drug Products in the Field, including VERTEX Know-How and SCHERING Know-How. Each party will permit the other to review the ongoing activities which it is conducting under the Development Program and to discuss that information with its officers, all at such reasonable times and as often as may be reasonably requested.
- (b) Notice of Pharmaceutical Side-Effects. The parties shall, during the term of this Agreement, keep each other promptly and fully informed of all of their pharmacological, toxicological and clinical trials, investigations and findings relating to the Bulk Drug Substance, Drug Product Candidates or Drug Products. Each of the parties will notify appropriate authorities in accordance with applicable law, and the other party, promptly after receipt of information with respect to any serious adverse reaction, as defined by the World Health Organization, directly or indirectly attributable to the use or application of Bulk Drug Substance, a Drug Product Candidate or a Drug Product. In such a case, the parties shall meet as soon as possible to define, according to the local regulations in the concerned country, appropriate procedures and actions to address such difficulty. Each party also shall forward to the other party on a regular basis information on adverse reactions and any material difficulty associated with the clinical use, studies, investigations, tests and prescriptions of Drug Product Candidates and Drug Products. The parties will inform each other without delay of any other governmental action which may affect the situation of Bulk Drug Substance, Drug Product Candidates or Drug Products and to furnish each other copies of any relevant documents relating thereto.

# Article IX Representations and Warranties of VERTEX

9.1. Authorization. This Agreement has been duly executed and delivered by VERTEX and constitutes the valid and binding obligation of VERTEX, enforceable against VERTEX in accordance with its terms except as enforceability may be limited by bankruptcy, fraudulent conveyance, insolvency, reorganization, moratorium and other laws relating to or affecting creditors' rights generally and by general equitable principles. The execution, delivery and

performance of this Agreement have been duly authorized by all necessary action on the part of VERTEX, its officers and directors.

- 9.2. No Third Party Rights. Except as previously disclosed in writing to SCHERING, (a) VERTEX owns or possesses adequate licenses or other rights to use all VERTEX Technology, and to grant the licenses herein; and (b) the granting of the licenses to SCHERING hereunder does not violate any right known to VERTEX of any Third Party.
- 9.3. No Third Party Patents. Except as disclosed in writing by VERTEX to SCHERING or its agents, to VERTEX's knowledge and based on its current understanding of the Drug Product Candidate(s) and its use, the development, manufacture, use or sale of any Bulk Drug Substance, Drug Product Candidates or Drug Products pursuant to this Agreement will not infringe or conflict with any Third Party right or patent, and VERTEX is not aware of any pending patent application that, if issued, would be infringed by the development, manufacture, use or sale of any Bulk Drug Substance, Drug Product Candidates or Drug Products pursuant to this Agreement.
- 9.4. Maintenance of Patents and Licenses. Subject to the provisions of Section 7.2.2 with respect to Discontinued Patents, VERTEX will take all reasonable steps to obtain any consent required for and to maintain in effect, including by means of extension, any license, sublicense, patent or patent application applicable to the Field for which it has granted rights to SCHERING hereunder.

# Article X Representations and Warranties of SCHERING

SCHERING represents and warrants to VERTEX as follows:

10.1. Authorization. This Agreement has been duly executed and delivered by SCHERING and constitutes the valid and binding obligation of SCHERING, enforceable against SCHERING in accordance with its terms, except as enforceability may be limited by bankruptcy, fraudulent conveyance, insolvency, reorganization, moratorium and other laws relating to creditors' rights generally and by general equitable principles. The execution, delivery and performance of this Agreement have been duly authorized by all necessary action on the part of SCHERING, its officers and directors.

- 10.2. No Third Party Rights. Except as previously disclosed in writing to VERTEX, (a) SCHERING owns or possesses adequate licenses or other rights to use all SCHERING Technology, and to grant the licenses herein; and (b) the granting of the licenses to VERTEX hereunder does not violate any right known to SCHERING of any Third Party.
- 10.3. No Third Party Patents. Except as disclosed in writing by SCHERING to VERTEX or its agents, to SCHERING's knowledge and based on its current understanding of the Drug Product Candidate(s) and its use, the manufacture, use or sale of any Bulk Drug Substance, Drug Product Candidates or Drug Products pursuant to this Agreement will not infringe or conflict with any Third Party right or patent, and SCHERING is not aware of any pending patent application that, if issued, would be infringed by the development, manufacture, use or sale of any Bulk Drug Substance, Drug Product Candidates or Drug Products pursuant to this Agreement.
- 10.4. Maintenance of Patents and Licenses. Subject to the provisions of Section 7.2.2 with respect to Discontinued Patents, SCHERING will take all reasonable steps to obtain any consent required for and to maintain in effect, including by means of extension, any license, sublicense, patent or patent application applicable to the Field for which it has granted rights to VERTEX hereunder.

#### Article XI

#### Confidentiality

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 Know-How and SCHERING Know-How. 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, to authorized licensees and sublicensees, and to subcontractors in connection with the development or manufacture of Bulk Drug Substance, Drug Product Candidates or Drug Products, to the extent necessary to enable such parties to perform their obligations hereunder or under the applicable license, sublicense or subcontract, as the case may be; provided, that such officers, employees, agents, licensees, 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.

- 11.2. Exceptions. Notwithstanding the foregoing, the provisions of Section 11 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 the 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 or regulations, 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.
- of any initial press release or other public communications relating to this Agreement and the transactions contemplated herein. Except to the extent already disclosed in that initial press release or other public communication, no public announcement concerning the existence or the terms of this Agreement or concerning the transactions described herein shall be made, either directly or indirectly, by VERTEX or SCHERING, except as may be legally required by applicable laws, regulations, or judicial order, without first obtaining the approval of the other party and agreement upon the nature, text, and timing of such announcement, which approval and agreement shall not be unreasonably withheld. The party desiring to make any such public announcement shall provide the other party with a written copy of the proposed announcement in sufficient time prior to public release to allow such other party to comment upon such announcement, prior to public release.
- 11.4. Survival. The provisions of this Article VIII shall survive the termination of this Agreement and shall extend for a period of five (5) years thereafter.

# Article XII Publication

Each of SCHERING and VERTEX shall have the right to publish or publicly present the results (the "Results") of the Development Program and their respective rights and obligations in this regard shall be governed by the provisions of Article VI of the Research Agreement.

#### Article XIII Dispute Resolution

- 13.1. 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.
- 13.2. Dispute Resolution. Except as otherwise explicitly provided herein or in the Research Agreement, 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 initially refer such dispute to the President of VERTEX and the member of the Vorstand of SCHERING responsible for the subject matter of the dispute, who shall, as soon as practicable, attempt in good faith to resolve the controversy or claims. If such controversy or claim is not resolved within sixty (60) days of the first written request for dispute resolution under this Article XIII, either party shall be free to initiate proceedings in the courts of the Commonwealth of Massachusetts.

# Article XIV Term and Termination

14.1. Term. The term of this Agreement shall extend until the later of: (a) the last to expire of the VERTEX Patents; or (b) if there is no Live Claim under a VERTEX Patent, [\*\*\*] from the most recent date of First Commercial Sale of a Drug Product; provided that SCHERING shall have an option exercisable by delivery of notice to VERTEX not less than one year prior to the expiration of the last to expire of the VERTEX Patents or such [\*\*\*] period, respectively, to extend the term of this Agreement and its license to the VERTEX Know-How hereunder, for an additional term of [\*\*\*], in which event the provisions of Section 6.5(b) relating to the reduction in amounts payable to VERTEX shall be inapplicable until the expiration of such extended term.

- 14.2. Termination For Cause. 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 (i) 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; or (ii) upon termination by such party of the Research Agreement for cause in accordance with Section 8.3 or 8.4 of the Research Agreement.
- 14.3. Termination by SCHERING. SCHERING may terminate this Agreement at any time with respect to one or more Drug Product Candidates or Drug Products, upon six (6) months' prior written notice to VERTEX if the results of clinical studies, in SCHERING's sole judgment, do not warrant further development.
- Termination for Bankruptcy. If at any time during the term of this Agreement, an Event of Bankruptcy (as defined below) relating to either party (the "Bankrupt Party") occurs, the other party (the "Other Party") shall have, in addition to all other legal and equitable rights and remedies available hereunder, the option to terminate this Agreement upon 30 days' written notice to the Bankrupt Party. It is agreed and understood that if the Other Party does not elect to terminate this Agreement in the event of an Event of Bankruptcy, except as may otherwise be agreed with the trustee or receiver appointed to manage the affairs of the Bankrupt Party, the Other Party shall continue to make all payments required of it under this Agreement as if the Event of Bankruptcy had not occurred, and the Bankrupt Party shall not have the right to terminate any license granted herein. As used above, the term "Event of Bankruptcy" shall mean (a) dissolution, termination of existence, liquidation or business failure of either party; (b) the appointment of a custodian or receiver for either party who has not been terminated or dismissed within 90 days; (c) the institution by either party of any proceeding under national, federal or state bankruptcy, reorganization, receivership or other similar laws affecting the rights of creditors generally or the making by either party of a composition or any assignment or trust mortgage for the benefit of creditors or under any national, federal or state bankruptcy, reorganization, receivership or other similar law affecting the rights of creditors generally, which proceeding is not dismissed within 90 days of filing.
- 14.5. 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 and any supply price payments, 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 XV

#### Indemnification

- 15.1. Environmental Indemnification. Notwithstanding any other indemnification obligation in this Agreement, and in addition to any rights the parties hereto may have under relevant federal, state, or local statutory and common laws, each party (the "Indemnifying Party") shall indemnify and hold harmless the other party and its Affiliates, their directors, officers, employees, successors and assigns (the "Indemnified Party") from and against any and all claims, actions, investigation costs, response costs, losses, damages, and other costs and expenses (including reasonable attorney and consulting fees) incurred thereby as a result of Environmental Matters (as defined below) except for any and all claims, actions, investigation costs, response costs, losses, damages, and other costs and expenses (including attorney and consulting fees) caused by the gross negligence or willful misconduct of the Indemnified Party, in which case the Indemnified Party who engaged in such gross negligence or willful misconduct shall indemnify and hold harmless the Indemnifying Party and its Affiliates, their directors, officers, employees, successors and assigns.
- (a) The ownership or operation by the Indemnifying Party, or any entity which produces or manufactures Bulk Drug Substance, Drug Product Candidate(s) or Drug Product(s) or any raw material used therefor or provides services relating thereto under a subcontracting arrangement with such Indemnifying Party, of any site or facility in a manner that (i) is not in compliance with any Environmental Law; or (ii) is in violation of any Environmental Law.
- (b) Any action or inaction by the Indemnifying Party where (i) there has been a release of Hazardous Materials into the environment; or (ii) Hazardous Materials have been disposed of at a site as the term "disposed" is defined in applicable Environmental Laws.
- (c) Any failure by the Indemnifying Party to obtain or maintain all permits or provide all notices required by Environmental Laws for the lawful operation of any facility or site.
- (d) Any other actual or alleged act or omission by the Indemnifying Party relating to the generation, handling, treatment storage, transportation, release, threatened release or omission of Hazardous Materials at any facility or site.

The term "Environmental Law" shall mean any federal, state or local law, ordinance, rule or regulation, order, decree, judgment, injunction, or other requirement relating to

pollution or protection of the environment, including without limitation the Comprehensive Environmental Response, Compensation and Liability Act, 42 U.S.C. Section 9601, et seq. ("CERCLA"); the Resource Conservation and Recovery Act, 42 U.S.C. Section 6901, et seq. ("RCRA"); the Toxic Substances Control Act, 15 U.S.C. Section 26019 et seq.; the Clean Air Act, 42 U.S.C. Section 7401 et seq.; the Clean Water Act, 33 U.S.C. Section 1257 et seq.; and the Occupational Safety and Health Act, 29 U.S.C. Sections 641 et seq.

- 15.3. Indemnification by VERTEX. VERTEX will indemnify and hold SCHERING and its Affiliates, and their employees, officers and directors harmless against any loss, damages, action, suit, claim, demand, liability, expense, bodily injury, death or property damage (a "Loss"), that may be brought, instituted or arise against or be incurred by such persons to the extent such Loss is based on or arises out of: (a) the development, manufacture, use, sale, storage or handling of a Program Compound, a Drug Product Candidate or a Drug Product by VERTEX or its Affiliates or their representatives, agents or subcontractors under this Agreement, or any actual or alleged violation of law resulting therefrom (with the exception of Losses based on infringement or misappropriation of intellectual property rights); or (b) the breach by VERTEX of any of its covenants, representations or warranties set forth in this Agreement; provided that the foregoing indemnification shall not apply to any Loss to the extent such Loss is caused by the negligent or willful misconduct of SCHERING or its Affiliates.
- 15.4. Indemnification by SCHERING. SCHERING will indemnify and hold VERTEX, and its Affiliates, and their employees, officers and directors harmless against any Loss that may be brought, instituted or arise against or be incurred by such persons to the extent such Loss is based on or arises out of: (a) the development, manufacture, use, sale, storage or handling of Bulk Drug Substance, a Drug Product Candidate or a Drug Product by SCHERING or its Affiliates or their representatives, agents or subcontractors under this Agreement, or any actual or alleged violation of law resulting therefrom (with the exception of Losses based on infringement or misappropriation of intellectual property rights); or (b) the breach by SCHERING of any of its covenants, representations or warranties set forth in this Agreement; provided that the foregoing indemnification shall not apply to any Loss to the extent such Loss is caused by the negligent or willful misconduct of VERTEX or its Affiliates.
- 15.5. Claims Procedures. Each Party entitled to be indemnified by the other Party (an "Indemnified Party") pursuant to Section 15.3 or 15.4 hereof shall give notice to the other Party (an "Indemnifying Party") promptly after such Indemnified Party has actual knowledge of any threatened or asserted claim as to which indemnity may be sought, and shall permit the Indemnifying

Party to assume the defense of any such claim or any litigation resulting therefrom; provided that counsel for the Indemnifying Party, who shall conduct the defense of such claim or any litigation resulting therefrom, shall be approved by the Indemnified Party (whose approval shall not unreasonably be withheld) and the Indemnified Party may participate in such defense at such party's expense (unless (i) the employment of counsel by such Indemnified Party has been authorized by the Indemnifying Party; or (ii) the Indemnified Party shall have reasonably concluded that there may be a conflict of interest between the Indemnifying Party and the Indemnified Party in the defense of such action, in each of which cases the Indemnifying Party shall pay the reasonable fees and expenses of one law firm serving as counsel for the Indemnified Party, which law firm shall be subject to approval, not to be unreasonably withheld, by the Indemnifying Party); and provided further, that the failure of any Indemnified Party to give notice as provided herein shall not relieve the Indemnifying Party of its obligations under this Agreement to the extent that the failure to give notice did not result in harm to the Indemnifying Party. No Indemnifying Party, in the defense of any such claim or litigation, shall, except with the approval of each Indemnified Party which approval shall not be unreasonably withheld, consent to entry of any judgment or enter into any settlement which (i) would result in injunctive or other relief being imposed against the Indemnified Party; or (ii) does not include as an unconditional term thereof the giving by the claimant or plaintiff to such Indemnified Party of a release from all liability in respect to such claim or litigation. Each Indemnified Party shall furnish such information regarding itself or the claim in question as an Indemnifying Party may reasonably request in writing and shall be reasonably required in connection with the defense of such claim and litigation resulting therefrom.

- 15.6. Compliance. The parties shall comply fully with all applicable laws and regulations in connection with their respective activities under this Agreement.
- 15.7. Insurance. Each party shall use all commercially reasonable efforts to maintain insurance, including product liability insurance, with respect to its obligations hereunder. Such insurance shall be in such amounts and subject to such deductibles as the parties may agree based upon standards prevailing in the industry at the time. Either party may satisfy its obligations under this Section through self-insurance to the same extent. At such time as Drug Product(s) is being manufactured by a party for commercial sale, each party shall name the other party as an additional insured on any such policies.

#### Article XVI

#### Miscellaneous Provisions

- 16.1. Waiver. No provision of the Agreement may be waived except in writing by both parties hereto. No failure or delay by either party hereto in exercising any right or remedy hereunder or under applicable law will operate as a waiver thereof, or a waiver of a particular right or waiver of any right or remedy on any subsequent occasion.
- 16.2. Force Majeure. Neither party shall be held liable or responsible to the other party nor be deemed to have defaulted under or breached this Agreement for failure or delay in fulfilling or performing any term of this Agreement, other than an obligation to make a payment, when such failure or delay is caused by or results from fire, floods, embargoes, government regulations, prohibitions or interventions, war, acts of war (whether war be declared or not), insurrections, riots, civil commotions, strikes, lockouts, acts of God, or any other cause beyond the reasonable control of the affected party.
- 16.3. Registration of License. SCHERING may, at its expense, register the license granted under this Agreement in any country where the use, sale or manufacture of a Drug Product in such country would be covered by a Live Claim. Upon request by SCHERING, VERTEX agrees promptly to execute any "short form" licenses submitted to it by SCHERING in order to effect the foregoing registration in such country, but such licenses shall in no way alter or affect the obligations of the parties hereunder.
- 16.4. Severability. It is the intention of the parties to comply with all applicable laws domestic or foreign in connection with the performance of its obligations hereunder. 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, and the Agreement shall be deemed modified to the extent necessary to render the surviving provisions enforceable to the fullest extent permitted by law.
- 16.5. Government Acts. In the event that any act, regulation, directive, or law of a government, including its departments, agencies or courts, should make impossible or prohibit, restrain, modify or limit any material act or obligation of SCHERING 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, if good faith negotiations between the parties to make such modifications to this Agreement as may be necessary to fairly address the impact thereof, after

a reasonable period of time are not successful in producing mutually acceptable modifications to this Agreement.

- 16.6. Government Approvals. SCHERING will use reasonable efforts to obtain any government approval required 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.
- 16.7. Assignment. This Agreement may not be assigned or otherwise transferred by either party without the prior written consent of the other party; provided, however, that either party may assign this Agreement, without the consent of the other party, (i) to any of its Affiliates, if the assigning party guarantees the full performance of its Affiliates' obligations hereunder, or (ii) in connection with the transfer or sale of all or substantially all of its assets or business or in the event of its merger or consolidation with another company. Any purported assignment in contravention of this Section shall, at the option of the nonassigning party, be null and void and of no effect. No assignment shall release either party from responsibility for the performance of any accrued obligation of such party hereunder.
- 16.8. Affiliates. Each party may perform its obligations hereunder personally or through one or more Affiliates, although each party shall nonetheless be solely responsible for the performance of its Affiliates. Neither party shall permit any of its Affiliates to commit any act (including any act of omission) which such party is prohibited hereunder from committing directly.
- 16.9. 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.
- 16.10. No Agency. Nothing herein contained shall be deemed to create an agency, joint venture, amalgamation, partnership or similar relationship between SCHERING and VERTEX. Notwithstanding any of the provisions of this Agreement, neither party 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 undertaken or incurred by one party in connection with or relating to the development, manufacture or sale of Bulk Drug Substance, Drug Product Candidates or Drug Products shall be undertaken, incurred or paid exclusively by that party, and not as an agent or representative of the other party.
- 16.11. 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 designated by one party to the other by notice pursuant hereto, 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 letter given by the close of business on or before the next following business day:

#### if to SCHERING, at:

SCHERING AG
Muellerstrasse 178
D-13342 Berlin
GERMANY
Attention: Prof. C. Braestrup
with a copy to legal department

#### with copies to:

Schering Berlin Venture Corporation 110 East Hanover Avenue Cedar Knolls, NJ 07927 Attention: President

and

Cravath, Swaine & Moore Worldwide Plaza 825 Eighth Avenue New York, NY 10019-7475 Attention: James M. Edwards, Esq.

#### if to VERTEX, at:

Vertex Pharmaceutical Incorporated 130 Waverly Street Cambridge, MA U.S.A. 02139-4211 Attention: Richard H. Aldrich, Senior Vice President and Chief Business Officer

with a copy to:

Warner & Stackpole LLP 75 State Street Boston, MA U.S.A. 02109 Attention: Kenneth S. Boger, Esq. Fax: (617) 951-9151

- 16.12. 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.
- 16.13. 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 such party may have with any other person or company. Each party has relied on that representation in entering into this Agreement.

#### 16.14. Competition.

- (a) Neither VERTEX nor SCHERING will pursue development of a Drug Product for an indication outside the Field without first obtaining written agreement thereto from the other party.
- (b) During the term of the Research Program, and thereafter so long as SCHERING is developing or commercializing any Drug Product under this Agreement, VERTEX will not, other than under Section 3.4 of the Research Agreement relating to Refused Compounds, develop a Program Compound, a Drug Product Candidate or a Drug Product for an indication in the Field without first obtaining written agreement thereto from SCHERING.
- (c) During the term of the Research Program, and thereafter so long as SCHERING is developing or commercializing any Drug Product hereunder, VERTEX will not develop an Excluded Compound, including any Program Compound added to the list of Excluded Compounds pursuant to Section 7.4(b) of the Research Agreement, for an indication in the Field, without first obtaining written agreement thereto by SCHERING.

# 16.15. Entire Agreement.

This Agreement, including the Schedules appended hereto, contains the entire understanding of the parties relating to the matters referred to herein, except as matters referenced herein are also addressed in the Research Agreement, and may only be amended by a written document, duly executed on behalf of the respective parties.

VERTEX PHARMACEUTICALS INCORPORATED

By:/s/ 	Richard H. Aldrich
Title:	Senior Vice President and Chief Business Off
SCHERIN	G AG
By:/s/ 	
Title:	MEMBER OF EXECUTIVE BOARD OF DIRECTORS
By:/s/	
Titlo: ∐	EAD OF PRE-CLINICAL DRUG RESEARCH

# Schedule 1.12 List of Drug Product Candidates

To be supplied

## SCHERING Patents

As per Schedule 1.34 of the Research Agreement

# **VERTEX** Patents

As per Schedule 1.41 of the Research Agreement

## Region Definitions

"North America" shall mean

Canada

United States of America

"Europe" shall mean

Albania

Andorra

Austria

Belgium

Britain

Bulgaria

Cyprus

Czech Republic

Denmark

Finland

France

Germany

Greece

Hungary

Iceland

Ireland

Italy

Liechtenstein

Luxembourg

Malta

Monaco

Netherlands

Norway

Poland

Portugal

Romania

Slovak Republic

Spain

Sweden

Switzerland

Turkey

United Kingdom

Countries of the former USSR

Countries of former Yugoslavia

## Region Definitions (continued)

# "Middle East" shall mean:

Bahrain

Iran

Iraq

Israel

Jordan

Kuwait

Lebanon

Oman

Qatar

Saudi Arabia

Syria

United Arab Emirates

Yemen

## "Africa" shall mean

Algeria

Angola

Benin

Botswana

Burkina Faso

Burundi

Cameroon

Cape Verde

Central Africa

Chad

Comoro Islands

Congo

Djibouti

Egypt

Equatorial Guinea

Ethiopia

Gabon

Gambia

Ghana

Guinea Bissau

Guinea

Ivory Coast

Kenya

Lesotho

Liberia

## Region Definitions (continued)

Libya Madagascar Malawi Mali Mauritania

Mauritius Morocco

Mozambique Namibia

Niger Nigeria Rwanda

Sao Tome and Principe

Senegal Seychelles Sierra Leone Somalia South Africa

Sudan Swaziland

Tanzania Togo Tunisia

Uganda Zaire Zambia

Zimbabwe

# Terms of Supply

To be agreed

# Schedule 5.4 Terms of European Co-Promotion Rights

# Schedule 7.2.2

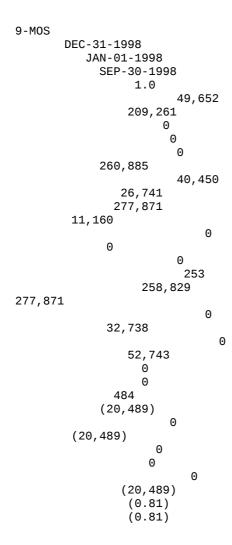
# Minimum Patent Filing Countries

[\*\*\*]

11253-42:222589 v12

THIS SCHEDULE CONTAINS SUMMARY FINANCIAL INFORMATION EXTRACTED FROM THE COMPANY'S QUARTERLY REPORT ON FORM 10-Q FOR THE NINE MONTHS ENDED SEPTEMBER 30, 1998 AND IS QUALIFIED IN ITS ENTIRETY BY REFERENCE TO SUCH FINANCIAL STATEMENTS.

1,000 U.S. DOLLARS



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, 1998 on our review of interim financial information of Vertex Pharmaceuticals Incorporated for the three month and nine month periods ended September 30, 1998 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, 33-12325, 333-27011 and 333-56179). 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.

PricewaterhouseCoopers LLP

Boston, Massachusetts November 13, 1998