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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K/A
(Amendment No. 1)

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the Fiscal Year Ended December 31, 2003

or

o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES 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 of incorporation)	**04-3039129** (I.R.S. Employer Identification No.)
130 Waverly Street **Cambridge, Massachusetts** (Address of principal executive offices)	**02139-4242** (Zip Code)

(617) 444-6100

(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Exchange Act: None

Securities registered pursuant to Section 12(g) of the Exchange Act:

Common Stock, $0.01 Par Value Per Share
(Title of class)

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 by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. [X]

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b-2 of the Act). Yes [X] No [ ]

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) based on the last reported sale price of the Common Stock on The Nasdaq Stock Market on June 30, 2003, was $826,746,640.

As of August 4, 2004, the registrant had 80,113,087 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive Proxy Statement for the 2004 Annual Meeting of Stockholders held on May 6, 2004 are incorporated by reference into Part III.

Explanatory Note

This Annual Report on Form 10-K/A (Amendment No. 1) (the "Amendment") amends Item 7 (Management's Discussion and Analysis of Financial Condition and Results of Operations) of our Annual Report on Form 10-K for the year ended December 31, 2003, which was filed with the Securities and Exchange Commission on March 15, 2004 (the "Original Filing"), to add certain disclosure relating to our research and development expenses and to add certain disclosure relating to the drug discovery process. No other aspects of the Original Filing have been amended or modified. Pursuant to the applicable rules of the Securities and Exchange Commission, Item 7, as amended, is set forth in this Amendment in its entirety. We have also included, as Exhibit 10.35 to this Amendment, a more complete copy of the First Revised and Restated Research and Early Development Agreement between Vertex and Novartis Pharma AG, dated February 3, 2004 (the "Novartis Agreement"). The Novartis Agreement was previously filed as Exhibit 10.35 to the Original Filing. The copy of the Novartis Agreement included as an exhibit to this Amendment includes certain text that we had not previously publicly disclosed. We have withdrawn our request to the Securities and Exchange Commission for confidential treatment of some, but not all, of the redacted text set forth in the copy of the Novartis Agreement filed as an Exhibit to the Original Filing. Item 15 has also been amended (and reproduced in its entirety) to reflect the Sarbanes-Oxley Act of 2002 Section 302 Certifications submitted with this Amendment as well as the partially unredacted copy of the Novartis Agreement.

This Amendment has no impact on any reported amount or disclosure, nor does it modify any guidance previously provided by us (including but not limited to disclosure and guidance set forth in our Quarterly Report on Form 10-Q for the period ended June 30, 2004, which was filed with the Securities and Exchange Commission on August 9, 2004).

This Amendment continues to speak as of the date of the Original Filing, and we have not updated the disclosures contained therein to reflect any events that occurred at a date subsequent to the filing of the Original Filing. Accordingly, this Amendment should be read in conjunction with the Original Filing and our subsequent filings with the Securities and Exchange Commission, including but not limited to our Quarterly Reports on Form 10-Q for the periods ended March 31, 2004 and June 30, 2004.

Forward-Looking Statements

Our disclosure in this Amendment contains some forward-looking statements. Forward-looking statements give our current expectations or forecasts of future events. You can identify these statements by the fact that they do not relate strictly to historical or current facts. Such statements may include words such as "anticipate," "estimate," "expect," "project," "intend," "plan," "believe" and other words and terms of similar meaning in connection with any discussion of future operating or financial performance. In particular, these statements include, among other things, statements relating to:

- our business strategy;
- our predicted development and commercial timelines;
- the selection, development and approval of our products;
- the establishment, development and maintenance of collaborative partnerships;
- our ability to identify and develop new potential products;
- our ability to achieve commercial acceptance of our products;
- our ability to scale up our manufacturing capabilities and facilities;
- our estimates regarding liabilities associated with our Kendall Square lease;
- the potential for the acquisition of new and complementary technologies, resources and products;
- our projected capital expenditures; and
- our liquidity.

Any or all of our forward-looking statements in this Amendment may turn out to be wrong. They can be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. Many factors mentioned in our discussion in this Amendment will be important in determining future results. Consequently, no forward-looking statement can be guaranteed. Actual future results may vary materially. A more detailed reference to our forward-looking statements can be found under "Forward-looking Statements" in Item 7 of this Amendment.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Overview

We are a biotechnology company in the business of discovering, developing, and marketing small molecule drugs for serious diseases including HIV infection, chronic hepatitis C virus infection, inflammatory and autoimmune disorders and cancer, independently and with collaborators. To date, we have discovered and advanced two products that have reached the market, Agenerase (amprenavir) and Lexiva (fosamprenavir calcium). Agenerase was approved and launched in the United States in early 1999, and Lexiva was approved and launched in the United States in late 2003. We earn a royalty on the sales of Agenerase and Lexiva and co-promote these products in collaboration with GlaxoSmithKline. Our drug candidate pipeline is principally focused on the development and commercialization of new treatments for viral and inflammatory diseases. We have built a drug discovery capability that integrates advanced biology, chemistry, biophysics, automation and information technologies, with a goal of making the drug discovery process more efficient and productive.

Drug Discovery and Development

Discovery and development of a single new pharmaceutical product is a lengthy and resource-intensive process which may take 10 to 15 years or more. During this process, potential drug candidates are subjected to rigorous evaluation, driven in part by stringent regulatory considerations, designed to generate information concerning toxicity profiles, efficacy, proper dosage levels and a variety of other characteristics which are important in determining whether a proposed drug candidate should be approved for marketing. Most chemical compounds which are investigated as potential drug candidates never progress into formal development, and most drug candidates which do advance into formal development never become commercial products.

We have a variety of drug candidates in clinical development and a broad-based drug discovery effort. Given the uncertainties of the research and development process, it is not possible to predict with confidence which, if any, of these efforts will result in a marketable pharmaceutical product. We constantly monitor the results of our discovery research and our nonclinical and clinical trials and regularly evaluate and re-evaluate our portfolio investments with the objective of balancing risk and potential return in view of new data and scientific, business and commercial insights. This process can result in relatively abrupt changes in focus and priority as new information comes to light and we gain new insights into ongoing programs.

Business Strategy

We have elected to diversify our research and development activities across a relatively broad array of investment opportunities, due in part to the high risks associated with the biotechnology and pharmaceutical business. We focus our efforts both on programs which we expect to control throughout the development and commercialization process, and programs which we expect will be conducted in the development and commercial phase principally by a collaborative partner. Since we have incurred losses from our inception and expect to incur losses for the forseeable future, our business strategy is dependent in large part on our continued ability to raise significant funding to finance our operations and meet our long term contractual commitments and obligations. In the past, we have secured funds principally through capital market transactions, strategic collaborative agreements, proceeds from the disposition of assets, investment income and the issuance of stock under our employee benefit programs. At December 31, 2003 we had $583 million of cash, cash equivalents and available for sale securities and $315 million of 5% Convertible Subordinated Notes due 2007 (the "2007 Notes"). During 2003 and early 2004 we took a number of steps to address our cash position and investment requirements in support of our existing business strategy.

Debt Exchange. On February 13, 2004, we exchanged approximately $153.1 million in aggregate principal amount of our 2007 Notes for approximately $153.1 million in aggregate principal amount of newly issued 5.75% Convertible Senior Subordinated Notes due 2011 (the "2011 Notes"). This transaction had an effect of significantly deferring the repayment date for almost half of our outstanding debt.

Sale of Business. In two independent transactions closed in March and December 2003, we sold the assets of our Discovery Tools and Services business for an aggregate of $101 million of cash and the assumption of certain liabilities, to Invitrogen Corporation ("Invitrogen") and to a company organized by Telegraph Hill Partners, respectively. As a result of the disposition of the Discovery Tools and Services business, we now operate in a single operating segment: Pharmaceuticals.

Novartis Restructuring. In January 2004, we amended our existing collaboration agreement with Novartis. We will continue to receive research funding through April 2006, consistent with the original agreement, and up to $35 million in pre-commercial payments for each preclinical drug candidate which we propose and Novartis accepts for preclinical development. We will no longer be responsible for the early development of drug candidates through proof-of-concept, as required under the original agreement, except that we may elect to develop VX-680 under the terms of the original agreement. We believe the restructured agreement remains financially attractive for us, and we are now free to devote our internal development resources to Vertex-controlled compounds in our areas of principal therapeutic interest.

Rebalancing of Research and Development

During 2003, we elected to focus our internal development and commercialization activity on two principal areas for the intermediate term: viral and inflammatory diseases. Our most advanced drug candidates in these areas are merimepodib (HCV), VX-950 (HCV) and VX-765 (inflammatory diseases). In preparation for advancing these and other Vertex-controlled drug candidates, we restructured our operations during the second half of the year to rebalance our relative investment in research, development and commercialization. This restructuring included a workforce reduction and a decision not to occupy our Kendall Square facility in Cambridge, Massachusetts. Of the terminated employees, 59% were from research, 30% were from sales, general and administrative functions primarily supporting research, and 11% were from development. Our investment in Company-sponsored research declined during 2003 approximately 22% from 2002 levels, while our investment in Company-sponsored development during 2003 increased over 2002 levels by approximately 57%. Collaborator-sponsored research increased approximately 14% while our Collaborator-sponsored development declined in 2003 by 44%. Overall we expect our total research and development investment in 2004 to be comparable to 2003, with any increases, if any, resulting principally from activities funded in whole or in part by new collaborators.

Collaborative Revenue

Collaborations have been and will continue to be an important component of our business strategy going forward.

We currently have significant collaborations with Novartis, Aventis, GlaxoSmithKline, and Serono. In these collaborations, we have retained a share of downstream product revenue and may be entitled to significant pre-commercial milestone payments as drug candidates progress in development. We currently receive research funding from Novartis and Serono, and we currently have drug candidates in clinical development and commercialization under the collaborations with GlaxoSmithKline and Aventis and under a collaboration with Kissei. In 2003 we realized $69.1 million in royalties and collaborative revenue, all of which was earned under our pharmaceutical partnerships. This represented a significant decline from the 2002 level of $94.8 million and reflected the conclusion of funding from our collaborations with Lilly, Taisho and Schering AG and our lack of any new source of collaboration

revenue since 2000. Our collaborations with Novartis and GlaxoSmithKline accounted for 64% and 17%, respectively, of our total revenue in 2003.

A significant portion of our total research effort is being conducted under our collaboration with Novartis, which is scheduled to conclude, along with our research funding from Novartis, in April 2006. Under the terms of our agreement with Novartis, we will retain all rights to the intellectual property which we generate during that collaboration, except for rights licensed to Novartis in connection with the development and commercialization of specific preclinical drug candidates that Novartis accepts for development. Our access to these retained rights may help us initiate other collaborative opportunities in the kinase inhibitor field if our collaboration with Novartis is not extended beyond 2006. We will need to seek those opportunities or other financing alternatives in order to maintain our discovery effort at its existing level. It is not possible to predict at present whether any of those collaborations or other financing alternatives will be available in 2006 and beyond.

Based on the value that we believe we have built through research and development investments in certain of our drug discovery and development programs and our perception of the level of interest in certain of our programs among some potential collaborators, we believe that we could enter into additional collaborative agreements in 2004 which could be material to our business. Our business development priorities include new collaborations to support development and commercialization, in Europe and Japan, of our HCV clinical candidates and our oral cytokine inhibitor, VX-765. Our product development pipeline also includes drug candidates that are outside our core therapeutic areas of viral and inflammatory diseases, such as VX-702 (acute coronary syndromes), VX-944 (oncology) and VX-680 (oncology). In 2004 and future periods we expect to identify collaborative development and commercialization opportunities for these drug candidates in order to continue their clinical advancement, as we maintain focus on our Company-sponsored opportunities. We are also seeking collaborators for our ion channels and other discovery programs.

Lease Restructuring

For the twelve months ended December 31, 2003, we recorded restructuring and other related expenses of $91.8 million, of which $78.7 million relates to the potential restructuring of our Kendall Square lease. The restructuring accrual remaining at December 31, 2003 was $69.5 million. The liability at December 31, 2003 represents our best judgment of the assumptions and estimates most appropriate in measuring the outcome of the potential lease restructuring. Although it is possible that this liability will be paid in full over the next 24 months, the actual amount and timing of any payments will depend on the actual terms of any lease restructuring transaction(s). If we are successful in restructuring the lease, we could potentially be relieved of a future lease obligation of approximately $16 to $18 million per year and a contractual construction obligation which could be in excess of $30 million through 2006.

Financial Guidance

The key financial measures for which we have provided guidance in 2004 are as follows:

- Our full year loss is expected to be between $140 and $150 million, before any gains or charges, including additional charges relating to the potential lease restructuring and the convertible note debt exchange.

- Total revenue is expected to be in the range of $90 to $100 million in 2004. This is expected to be comprised of $60 to $65 million in committed funding and milestones from existing collaborative partners, and $15 to $18 million from HIV product royalties. In addition, we are currently in discussions with pharmaceutical companies regarding strategic research and product development agreements, and the successful conclusion of such discussions may result in additional revenue and cash flow in 2004.

- As we prioritize our investment toward proprietary drug candidates and realize the benefits from the operational restructuring in drug discovery during 2003, we anticipate that research and development expenses will be in the range of $190 to $205 million for the full year of 2004.

- We expect sales, general and administrative expenses to be between $38 and $43 million in 2004.

- We expect cash, cash equivalents and available for sale securities to be in excess of $350 million at the end of 2004.

The financial measures set forth above are forward looking and are subject to risks and uncertainties that could cause our actual results to vary materially, as referenced in the section below entitled "Forward-Looking Statements."

Contractual Commitments and Obligations

The first part of the following table sets forth commitments and obligations that have been recorded on our consolidated balance sheet as of December 31, 2003. Certain other obligations and commitments, while not required under accounting principles generally accepted in the United States ("GAAP") to be included in the consolidated balance sheets, may have a material impact on liquidity. We have presented these items, all of which have been entered into in the ordinary course of business, in the table below in order to present a more complete picture of our financial position and liquidity.

December 31, 2003	Less than 1 year	1 to 3 years	3 to 5 years	5 years or more	Total
			(in thousands)		
Commitments and Obligations Recorded on the Balance Sheet at December 31, 2003:					
Capital leases	$ 113	$ —	$ —	$ —	$ 113
Collaborator development loans	14,000	—	18,460	—	32,460
Convertible subordinated notes*	—	—	315,000	—	315,000
Off-Balance Sheet Commitments and Obligations at December 31, 2003:					
Operating leases	44,962	108,180	59,740	182,847	395,729
Purchase obligations	3,000	6,000	—	—	9,000
Research and development and other commitments	2,769	2,365	—	—	5,134
Total contractual obligations and commitments	$ 64,844	$ 116,545	$ 393,200	$ 182,847	$ 757,436

* See description below of our Note exchange, which closed on February 13, 2004, pursuant to which we have deferred approximately $153.1 million of principal repayment obligations from 2007 to 2011.

Commitments and Obligations Recorded on the Balance Sheet at December 31, 2003:

Capital leases relate to equipment leases that expire at various dates though June 2004.

The collaborator development loans in the table above represent indebtedness to Novartis in the amount of $32,460,000 that was advanced under a loan facility established pursuant to the original collaboration agreement with Novartis. Loans under the facility were intended to fund early clinical studies of kinase inhibitor compounds that we selected for early development. In February 2004, we amended the terms of the Novartis collaboration agreement. We will continue to be responsible for drug discovery and Novartis will continue to provide research funding through the balance of the research term ending in April 2006, as provided in the original agreement. However, Novartis will now

be responsible for all nonclinical and clinical development of drug candidates which it accepts for development, and consequently the loan facility providing funding for development activities by Vertex has been terminated. We may either continue development of VX-680 under the terms of the original agreement using loan proceeds we have received under the Novartis loan facility, or elect to develop and commercialize VX-680 independent of Novartis. If we elect to develop and commercialize VX-680 independent of Novartis, loan amounts with respect to that drug candidate which are unspent and uncommitted at the time of our election will be repayable immediately. Outstanding loans which funded amounts either spent or committed to be spent on development activities relating to a particular compound will be forgiven if that compound is selected by Novartis for development. If not, the related loan will be repayable without interest in May 2008. At December 31, 2003, approximately $14 million in development loans previously advanced to us were unspent and uncommitted. Please refer to Note P to our consolidated financial statements included in this Annual Report on Form 10-K.

At December 31, 2003 we had $315,000,000 in 2007 Notes. On February 13, 2004, we concluded an exchange of approximately $153.1 million in aggregate principal amount of 2007 Notes for approximately $153.1 million in aggregate principal amount of newly issued 2011 Notes. As a result of this transaction, the Company has outstanding $161.9 million in aggregate principal amount of 2007 Notes and $153.1 million in aggregate principal amount of 2011 Notes. Our annual interest payment obligation increased by $1.1 million to $16.9 million, reflecting the slightly higher coupon rate on the 2011 Notes.

Off-Balance Sheet Commitments and Obligations at December 31, 2003:

At December 31, 2003, our future minimum commitments and contractual obligations included facilities operating leases, a purchase obligation and contractual commitments related to our research and development programs. These items are not required to be recorded on our consolidated balance sheets under GAAP. They are disclosed in the table presented above and described more fully in the following paragraphs in order to provide a more complete picture of our financial position and liquidity at December 31, 2003.

Our Kendall Square lease term began January 1, 2003 and lease payments commenced in May 2003. We have an obligation, staged over a number of years, to build out the space into finished laboratory and office space. The lease will expire in 2018 with options to extend the lease for two consecutive terms of ten years each, ultimately expiring in 2038. In June 2003, we decided not to occupy the space under this lease and to attempt to restructure the lease. See Note E to our consolidated financial statements included in this Annual Report on Form 10-K. The Company's future minimum commitments under this lease including lease payments and a construction obligation are $29.2 million for less than 1 year, $68.4 million for 1 to 3 years, $38.7 million for 3 to 5 years and $176.2 million for 5 years or more and are included in the table above.

Commitments under research and development programs represent contractual commitments entered into for materials and services in the normal course of business.

The purchase obligations referred to above include an agreement to purchase a minimum of $3 million of certain specified products from Invitrogen annually for three years after the completion of the sale of certain assets of the Discovery Tools and Services business on March 28, 2003.

Liquidity and Capital Resources

We have incurred operating losses since our inception and have historically financed our operations principally through public stock offerings, private placements of our equity and debt securities, strategic collaborative agreements, which include research and development funding, milestones and royalties on the sales of products, proceeds from disposition of assets of our Discovery Tools and Services business, investment income and proceeds from the issuance of stock under our employee benefit programs.

At December 31, 2003 we had cash, cash equivalents and marketable securities of $583,164,000, which is a decrease of $51,820,000 from $634,984,000 at December 31, 2002. The decrease of $51,820,000 is primarily the result of cash used by operations of $167,623,000 offset by the net cash consideration received from the sale of the assets of the Discovery Tools and Services business of approximately $96,561,000. Additionally, expenditures for property and equipment were $17,351,000, cash receipts from the issuance of common stock under our employee benefit programs were approximately $11,959,000 and we drew down $27,460,000 under the Novartis loan facility in 2003, bringing the balance outstanding under the loan facility to $32,460,000 at December 31, 2003.

As part of our strategy to manage our long term operational cash needs, in early 2004 we exchanged approximately $153.1 million in aggregate principal amount of our 2007 Notes for approximately $153.1 million in aggregate principal amount of newly issued 2011 Notes. The 2011 Notes were issued through a private offering to qualified institutional buyers. The 2011 Notes are convertible, at the option of the holder, into common stock at a price equal to $14.94, subject to adjustment under certain circumstances. The 2007 Notes are convertible, at the option of the holder, into common stock at a price equal to $92.26.

The restructuring accrual remaining at December 31, 2003 of $69.5 million, relating to the potential Kendall Square lease restructuring, could possibly be paid in full over the next 24 months. However, the actual amount and timing of such payments will be dependent upon the ultimate terms of any lease restructuring. We review our estimates underlying the restructuring accrual on at least a quarterly basis, and the accrual could change with any future change in our estimates.

We expect to continue to invest significantly in our pipeline, particularly in clinical trials of merimepodib, VX-950 and VX-765, and in our ion channel and kinase discovery efforts. Consequently, we expect to incur losses on a quarterly and annual basis for the foreseeable future as we continue to develop and commercialize existing and future drug candidates. We also expect to incur substantial administrative expenditures in the future and expenses related to filing, prosecution, defense and enforcement of patent and other intellectual property rights. We expect our capital expenditures to remain at levels consistent with 2003, and we expect to complete 2004 with cash, cash equivalents and marketable securities in excess of $350 million.

Beyond 2004, the adequacy of our available funds to meet our future operating and capital requirements, including repayment of the 2007 Notes and the 2011 Notes, will depend on many factors, including the number, breadth and prospects of our discovery and development programs and the costs and timing of obtaining regulatory approvals for any of our product candidates. Collaborations have been and will continue to be an important component of our business strategy. We will continue to rely on cash receipts from our existing research and development collaborations, including research funding, development reimbursements and potential milestone payments, and from new collaborations we may enter, in order to help fund our research and development efforts.

From time to time during 2004, we may repurchase our existing 2007 Notes in privately negotiated transactions, or market purchases or otherwise, depending on market conditions. Any such repurchases may be material.

To the extent that our current cash and marketable securities, in addition to the above-mentioned sources, are not sufficient to fund our activities, it will be necessary to raise additional funds through public offerings or private placements of securities or other methods of financing. We will continue to manage our capital structure and consider financing opportunities to strengthen our long term liquidity profile. There can be no assurance that such financing will be available on acceptable terms, if at all.

Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations is based upon our consolidated financial statements prepared in accordance with generally accepted accounting principles in the United States of America. The preparation of these financial statements requires us to make

certain estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenue and expense during the reported periods. These items are constantly monitored and analyzed by management for changes in facts and circumstances, and material changes in these estimates could occur in the future. Changes in estimates are recorded in the period in which they become known. We base our estimates on historical experience and various other assumptions that we believe to be reasonable under the circumstances. Actual results may differ from our estimates if past experience or other assumptions do not turn out to be substantially accurate.

We believe that the application of the accounting policies for restructuring and other expenses, research and development expenses, and revenue recognition, all of which are important to our financial position and results of operations, require significant judgments and estimates on the part of management. Our accounting polices, including the ones discussed below, are more fully described in Note B to our consolidated financial statements included in this Annual Report on Form 10-K.

Restructuring and Other Expense

We record liabilities associated with restructuring activities based on estimates of fair value in the period the liabilities are incurred, in accordance with SFAS 146 "Accounting for Costs Associated with Exit or Disposal Activities" ("SFAS 146"). These estimates are reviewed and may be adjusted in subsequent periods. Adjustments are based, among other things, on management's assessment of changes in factors underlying the estimates, the impact of which is measured using the credit-adjusted risk-free rate applied in the initial period.

On June 10, 2003, we announced a plan to restructure our operations in preparation for increased investment in the clinical development and commercialization of our drug candidates. We designed the restructuring to rebalance our relative investment in research, development and commercialization, to better support our long-term objective of becoming an integrated drug company. The restructuring included a workforce reduction, write-offs of certain assets and a decision not to occupy the Kendall Square facility. We are actively trying to restructure the lease obligation.

As a result of the Company's restructuring plan and in accordance with SFAS 146, we recorded an initial estimate of the fair value of the estimated liability in the second quarter of 2003. We have reviewed our assumptions and estimates quarterly and updated the liability as changes in circumstances have required. For the twelve months ended December 31, 2003, we recorded restructuring and other related expenses of $91.8 million. The $91.8 million includes $78.7 million of potential lease restructuring expense (of which $34.9 million, $42.4 million and $1.4 million was recorded in the second, third and fourth quarters of 2003, respectively). In addition to the $78.7 million, other costs included in the $91.8 million charge include $6.0 million of lease operating expense incurred prior to the decision not to occupy the Kendall Square facility, $2.6 million for severance and related employee transition benefits and $4.5 million for a write-off of leasehold improvements and other assets.

The charge for the potential lease restructuring is the most significant component of the total restructuring charge and requires us to make significant judgments and assumptions. We use probability weighted discounted cash flows in order to calculate the amount of the liability associated with the potential lease restructuring. In accordance with SFAS 146, we used a credit-adjusted risk-free rate of approximately 10% in discounting our estimated cash flows. The probability weighted cash flows are based on management's assumptions and estimates regarding the possible outcomes of the potential lease restructuring. In estimating the liability we considered several possible outcomes of the potential lease restructuring, including a sublease of the entire space, a buy-out of our obligation, partial subleases by multiple parties, and other variations of these same outcomes. We also included in these potential outcomes the contractually required commitment for build-out of the leased space. We validate our estimates and assumptions through consultations with independent third parties having relevant expertise. We increased our estimated lease restructuring expense from the second quarter to the third quarter by $42.4 million, based on our judgment that a significant decline in the real estate

market in Cambridge, Massachusetts had occurred. We believe an increase in available laboratory and office space in Cambridge, Massachusetts and certain other factors led to a corresponding overall decline in real estate market fundamentals from the previous quarter. Accordingly, we revised our expectations of attainable sublease terms, assuming lower sublease rental rates and a delay in occupancy by potential subtenants.

It is possible that our estimates and assumptions will change in the future resulting in additional adjustments to the amount of the liability, and the effect of such adjustments could be material. For example, if sublease rental rates differ from our assumption by approximately 10% in either direction, our recorded liability will be negatively or positively adjusted by approximately $8 million. If the time to finalize the restructuring is delayed by six months from our estimated completion date, the impact could be as high as approximately $10 million in additional liability, or more if there is further delay. We will review our assumptions and judgments related to the potential lease restructuring on at least a quarterly basis, until the outcome is finalized, and make whatever modifications we believe are necessary, based on our best judgment, to reflect any changed circumstances.

Revenue Recognition

Our revenue recognition policies are in accordance with the SEC's Staff Accounting Bulletin No. 101 ("SAB 101"), "Revenue Recognition in Financial Statements," as amended by SEC Staff Accounting Bulletin No. 104, "Revenue Recognition," and for revenue arrangements entered into after June 30, 2003, Emerging Issues Task Force Issue No. 00-21, "Revenue Arrangements with Multiple Deliverables" ("EITF 00-21").

Our collaborative and other research and development revenue is generated primarily through collaborative research and development agreements with strategic partners. The terms of these agreements typically include non-refundable up-front license fees, funding of research and development efforts, payments based upon achievement of certain milestones and royalties on product sales.

We recognize revenue from non-refundable, up-front license fees and milestones, not specifically tied to a separate earnings process, ratably over the contracted or estimated period of performance. Changes in estimates could impact revenue in the period the estimate is changed. If our estimate of the period of performance shortens or lengthens, the amount of revenue we recognize from non-refundable, up-front license fees and milestones could increase or decrease in the period the change in estimate becomes known. Future related revenues would be adjusted accordingly. To date, changes to our estimates have not had a material impact on our financial position or results of operations. Research funding is recognized ratably over the period of effort, as earned. Milestones that are based on designated achievement points and that are considered at risk and substantive at the inception of the collaborative contract, are recognized as earned when the corresponding payment is considered reasonably assured. We evaluate whether milestones are at risk and substantive based on the contingent nature of the milestone, specifically reviewing factors such as the technological and commercial risk that must be overcome and the level of investment required.

Under EITF 00-21, in multiple element arrangements, license payments are recognized together with any up-front payment and the research and development funding as a single unit of accounting, unless the delivered technology has stand-alone value to the customer and we have objective and reliable evidence of fair value of the undelivered elements in the arrangement. License payments received during the course of a collaboration that do not meet the separation criteria above are recognized, when earned, in proportion to the period of time completed on the contract relative to the total contracted or estimated period of performance on the underlying research and development collaboration, with the remaining amount deferred and recognized ratably over the remaining period of performance. Payments received after performance obligations are complete are recognized when earned. We did not receive any license payments in 2003.

Royalty revenue is recognized based upon actual and estimated net sales of licensed products in licensed territories, as provided by our collaborative partner, and is recognized in the period the sales

occur. Differences between actual royalty revenues and estimated royalty revenues, which have not been historically significant, are reconciled and adjusted for in the quarter they become known.

Research and Development Costs

All research and development costs, including amounts funded by research and development collaborations, are expensed as incurred. Research and development expenses are comprised of costs incurred in performing research and development activities including salaries and benefits, facilities costs, overhead costs, clinical trial costs, contract services and other outside costs. Clinical trial, contract services and other outside costs require that we make estimates of the costs incurred in a given accounting period and record accruals at period end as the third party service periods and billing terms do not always coincide with our period end. We base our estimates on our knowledge of the research and development programs, services performed for the period, past history for related activities and the expected duration of the third party service contract where applicable.

Results of Operations

The following discussion of revenues and expenses is based only on the results of our continuing operations. We sold the assets of the Discovery Tools and Services business in two independent transactions in March and December 2003. In accordance with SFAS No. 144, "Accounting for the Impairment of Long-Lived Assets" ("SFAS No. 144"), the results of operations associated with the assets sold have been reclassified on the consolidated financial statements under the heading "discontinued operations" for all periods presented. The reclassification of the amounts to discontinued operations have been prepared using estimates and assumptions we have deemed appropriate based upon the information currently available. Prior to 2002, the Discovery Tools and Services business was not separately managed operationally or financially and therefore, we have estimated certain operating expenses, based on certain assumptions, including relative costs of the business being sold compared to historical site costs. Amounts reclassified to discontinued operations are not necessarily indicative of the results that would have been achieved had the Discovery Tools and Services business operated on a stand-alone basis during the periods presented.

As a result of the disposition of these assets, we now operate in a single operating segment: Pharmaceuticals.

Year Ended December 31, 2003 Compared with Year Ended December 31, 2002

Our net loss for 2003 was $196,767,000 or $2.56 per basic and diluted common share, compared to a net loss for 2002 of $108,621,000 or $1.43 per basic and diluted common share. Our loss in 2003 includes restructuring and other expense of $91,824,000 and income from discontinued operations of $69,646,000. Included in the income from discontinued operations is a gain from the sale of assets of $70,339,000. Included in our net loss for 2002 was income from discontinued operations of $28,337,000.

In addition to restructuring and other expense, offset by income from discontinued operations, our net loss for 2003 as compared with our net loss for 2002 increased primarily as a result of decreased revenue and interest income.

Total revenues decreased to $69,141,000 in 2003 compared to $94,770,000 in 2002. In 2003, revenue was comprised of $9,002,000 in royalties and $60,139,000 in collaborative and other research and development revenue, as compared with $10,054,000 in royalties and $84,716,000 in collaborative research and development revenue in 2002.

Royalties consist primarily of Agenerase royalty revenue. Agenerase royalty revenue is based on actual and estimated worldwide net sales of Agenerase. We began earning royalties on sales of Lexiva in the United States in November 2003. We expect to receive marketing approval for Lexiva in the European Union in 2004. We pay a royalty to a third party on sales of Agenerase and Lexiva.

Collaborative and other research and development revenue decreased $24,577,000 or 29% in 2003 as compared with 2002. The decrease in collaborative and other research and development revenue is due to the conclusion of certain of our collaborative research and development arrangements, mainly in late 2002, partially offset by additional revenue recognized under our Novartis collaboration and a milestone payment received from GlaxoSmithKline in connection with FDA approval of Lexiva. The table presented below is a summary of significant revenue arrangements for the year ended 2003 as compared with the year ended 2002.

	Year Ended December 31,	
	2003	2002
	(In thousands)	
Collaborative and other research and development revenue:		
Summary of significant collaborative revenue arrangements:		
Novartis	$ 44,502	$ 41,894
Serono	5,280	5,280
GlaxoSmithKline	2,500	1,500
Eli Lilly	—	12,054
Schering	—	5,000
Kissei	267	4,574
Taisho	—	4,187
Other	7,590	10,227
Total collaborative and other research and development revenue	$ 60,139	$ 84,716

We have not entered into any significant collaborative research and development agreements since 2000. Additionally as shown in the table above, research funding under our partnerships with Eli Lilly, Schering and Taisho concluded in 2002.

We expect that collaborative and other research and development revenues will continue to be a significant source of our total revenues and we believe we could enter into additional collaborative agreements in 2004 which could be material to our business.

Research and development expenses remained relatively consistent at $199,636,000 in 2003 compared to $198,338,000 in 2002.

Research and development expenses consist primarily of salary and benefits, laboratory supplies, contractual services and infrastructure costs, including facilities costs and depreciation. Set forth below

is a summary that reconciles our total research and development expenses for the years ended December 31, 2003 and 2002 into these major categories (in thousands):

	Year Ended December 31,			
	2003	2002	$ Change	% Change
Research Expenses:				
Salary and benefits	$ 38,140	$ 35,724	$ 2,416	6.8%
Laboratory supplies and other direct expenses	20,025	20,046	(21)	—
Contractual services	6,390	14,718	(8,328)	(56.6)%
Infrastructure costs	48,880	49,918	(1,038)	(2.1)%
Total research expenses	$ 113,435	$ 120,406		
Development Expenses:				
Salary and benefits	$ 19,796	$ 16,300	$ 3,496	21.4%
Laboratory supplies and other direct expenses	5,307	6,976	(1,669)	(23.9)%
Contractual services	42,594	39,697	2,897	7.3%
Infrastructure costs	18,504	14,959	3,545	23.7%
Total development expenses	$ 86,201	$ 77,932		
Total Research and Development Expenses:				
Salary and benefits	$ 57,936	$ 52,024	$ 5,912	11.4%
Laboratory supplies and other direct expenses	25,332	27,022	(1,690)	(6.3)%
Contractual services	48,984	54,415	(5,431)	(10.0)%
Infrastructure costs	67,384	64,877	2,507	3.9%
Total research and development expenses	$ 199,636	$ 198,338		

(a) In order to show comparative information, certain research costs in 2002 have been allocated among the categories of expense, based on certain estimates and assumptions. These estimates and assumptions include allocations based upon ratios of actual expenses in comparative periods.

(b) Aurora Biosciences Corporation, which we acquired in July 2001, did not track research and development expenses in a manner consistent with Vertex and, as a result, we are unable to provide this reconciliation for 2001.

Our investment in research has decreased due to the operational restructuring in June 2003 while our investment in development has increased as a result of our proprietary drug candidates entering and advancing through clinical development. In 2003 our clinical trials focused on multiple drug candidates. The results of these trials enabled us to focus our clinical pipeline on two core therapeutic areas—viral and inflammatory diseases. Our lead drug candidates in these areas are merimepodib (HCV), VX-950 (HCV) and VX-765 (inflammatory diseases). In 2003 our development investment also focused on drug candidates with potential therapeutic indications outside our current core therapeutic areas, such as VX-702 (acute coronary syndromes), VX-148 (autoimmune diseases), VX-944 (oncology) and VX-680 (oncology). In 2004 and future periods we will seek to identify licensing opportunities for these drug candidates in order to continue their clinical development. We continue to focus our main drug discovery efforts on the protein kinase and ion channel gene families as well as other targeted areas.

Our collaborative partners have agreed to fund portions of our research and development programs related to specified drug candidates. Our research and development expenses for 2003, 2002 and 2001 were as follows:

	2003			2002			2001		
	Research	Development	Total	Research	Development	Total	Research	Development	Total
Collaborator-Sponsored	$ 62,162	$ 19,935	$ 82,097	$ 54,509	$ 35,675	$ 90,184	$ 49,490	$ 20,262	$ 69,752
Company-Sponsored	51,273	66,266	117,539	65,897	42,257	108,154	43,427	28,809	72,236
Total	$ 113,435	$ 86,201	$ 199,636	$ 120,406	$ 77,932	$ 198,338	$ 92,917	$ 49,071	$ 141,988

Our product pipeline is principally focused on viral diseases, inflammatory and autoimmune diseases, and cancer.

Therapeutic Area and Product Candidate	Clinical Indications	Development Phase	Company With Marketing Rights (Region)
Antivirals			
Agenerase™(amprenavir)	HIV infection	Mktd	GlaxoSmithKline (Worldwide)*
Lexiva™(fosamprenavir calcium)**	HIV infection	Mktd/MAA filed	GlaxoSmithKline (Worldwide)*
VX-385	HIV infection	Phase I	GlaxoSmithKline (Worldwide)*
Merimepodib (VX-497)	Chronic hepatitis C	Phase II	Vertex (Worldwide)
VX-950	Chronic hepatitis C	Preclin	Vertex (Worldwide)
Inflammation and Autoimmune Disease			
VX-765	Inflammatory/autoimmune diseases	Phase I	Vertex (Worldwide)
VX-702	Acute coronary syndromes; inflammatory diseases	Phase II	Kissei (Japan); Vertex (R.O.W.)
Pralnacasan (VX-740)	Rheumatoid arthritis (RA); osteoarthritis (OA); other inflammatory/autoimmune diseases	Phase II	Aventis (Worldwide)*
Cancer			
VX-680	Oncology	Preclin	Novartis (Worldwide)†
VX-944	Oncology	Phase I	Vertex (Worldwide)

* Vertex has co-promotion rights in the U.S. and the E.U. Kissei has marketing rights to amprenavir (Prozei™) in Japan.

** GlaxoSmithKline is seeking marketing approval in the E.U. under the name "Telzir™".

† Vertex may elect by June 30, 2004 to continue the development of VX-680 under the original terms of the Novartis agreement, in which event Novartis will hold an option on worldwide commercial rights.

To date we have incurred in excess of $1 billion in research and development costs associated with drug discovery and development. We expect research and development expenses in 2004 to remain comparable with 2003. However, our anticipated 2004 research and development expenses could vary materially, depending on the occurrence and timing of clinical trials. We anticipate that research and development expenses will increase in future periods as we add personnel and capabilities to support the advancement of our lead drug candidates. However, we do not expect that our research expenses will increase significantly unless we obtain a significant amount of funding from new collaborations.

We estimate that it takes 10 to 15 years (the industry average is 12 years) to discover, develop and bring to market a new pharmaceutical product in the U.S. as outlined below:

Phase:	Objective:	Estimated Duration:
Discovery	Lead identification and target validation	2 to 4 years
Pre-Clinical	Initial toxicology for preliminary identification of risks for humans; gather early pharmacokinetic data	1 to 2 years
Phase I	Evaluate safety in humans; study how the drug works, metabolizes and interacts with other drugs	1 to 2 years
Phase II	Establish effectiveness of the drug and its optimal dosage; continue safety evaluation	2 to 4 years
Phase III	Confirm efficacy, dosage regime and safety profile of the drug	2 to 4 years
FDA approval	Approval by the FDA to sell and market the drug under approved labeling	6 months to 2 years

Animal and other nonclinical studies are typically conducted during each phase of human clinical studies.

The successful development of our products is highly uncertain and subject to a number of risk factors. The duration of clinical trials may vary substantially according to the type, complexity and novelty of the pharmaceutical product. The FDA and comparable agencies in foreign countries impose substantial requirements on the introduction of therapeutic pharmaceutical products through lengthy and detailed laboratory and clinical testing procedures, sampling activities and other costly and time-consuming procedures. Data obtained from preclinical, nonclinical and clinical activities at any step in the testing process may be adverse and lead to discontinuation of development. Data obtained from these activities also are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The duration and cost of discovery, preclinical, nonclinical and clinical activities may vary significantly over the life of a project and are difficult to predict. Therefore, we are unable to generate accurate and meaningful estimates of the ultimate costs and anticipated completion dates of our pharmaceutical research and development and commercialization efforts. The most significant costs associated with drug discovery and development are those costs associated with Phase II and Phase III clinical trials. Given the uncertainties related to development, we are currently unable to reliably estimate when, if ever, our drug candidates will generate revenue and cash flows. We do not expect to receive net cash inflows from any major discovery and development products until a drug candidate becomes a profitable commercial product.

Sales, general and administrative expenses decreased $1,974,000, or 5%, to $39,082,000 in 2003 from $41,056,000 in 2002, due primarily to a reduction in personnel resulting from our consolidation of certain general and administration functions to our corporate office location in Cambridge, Massachusetts, and from our restructuring in the second quarter of 2003.

Restructuring and other expense for the twelve months ended December 31, 2003 was $91.8 million. The activity related to restructuring and other expense for the twelve months ended December 31, 2003, is presented below (in thousands):

	Charge for the Twelve Months Ended December 31, 2003	Cash Payments in 2003	Non-cash Write-off in 2003	Accrual as of December 31, 2003
Lease restructuring expense and other operating lease expense	$ 84,726	$ 15,200	$ —	$ 69,526
Employee severance, benefits and related costs	2,616	2,616	—	—
Leasehold improvements and asset impairments	4,482	—	4,482	—
Total	$ 91,824	$ 17,816	$ 4,482	$ 69,526

In accordance with SFAS 146, we review on a quarterly basis the estimates and assumptions underlying our determination of the anticipated liability associated with the potential lease restructuring and adjust the liability as changes in circumstances require. It is possible that those estimates and assumptions could change in the future resulting in incremental expense or, alternatively, in reversal of expense, and the effect of any such adjustments could be material.

Interest income decreased approximately $13,310,000 to $15,412,000 in 2003 from $28,722,000 in 2002. The decrease is mainly the result of both a lower level of invested funds and lower portfolio yields due to a reduced interest rate environment.

Income from discontinued operations increased $69,646,000 in 2003 from $28,337,000 in 2002, due to our sale of the assets of our Discovery Tools and Services business in 2003. Included in the income from discontinued operations in 2003 is a gain on the sale of those assets of $70,339,000.

Year Ended December 31, 2002 Compared with Year Ended December 31, 2001

Our net loss for 2002 was $108,621,000 or $1.43 per basic and diluted common share compared to a net loss of $66,233,000 or $0.89 per basic and diluted common share for 2001. The net loss for 2002 includes income from discontinued operations of $28,337,000. The net loss for 2001 includes income from discontinued operations of $22,148,000, a charge of $25,901,000 representing a cumulative change in accounting principle related to revenue recognition and a gain of $17,749,000 representing a cumulative change in accounting related to derivative instruments.

Total revenues increased to $94,770,000 in 2002 compared to $85,297,000 in 2001. In 2002, revenue was comprised of $10,054,000 in royalties and $84,716,000 in collaborative and other research and development revenue, as compared with $10,783,000 in royalties and $74,514,000 in collaborative and other research and development revenue in 2001.

Collaborative and other research and development revenue increased $10,202,000 or 14% in 2002 as compared with 2001. The table presented below is a summary of significant revenue arrangements for the year ended 2002 as compared with the year ended 2001. As illustrated in the table below the overall increase in collaborative and other research and development revenue in 2002 is due to an increase in revenue recorded in connection with certan collaborations, such as Novartis and Eli Lilly, offset by a decrease in revenue earned under our arrangements with Kissei and Taisho. In 2002 we recognized an increased amount of revenue under our Novartis collaboration as a result of increased effort allocated to our kinase research program. In the fourth quarter of 2002, our research and development agreement with Lilly was restructured; the original contractual research term was to conclude in June 2003. In connection with the restructuring of the agreement and termination of the research term, we recognized approximately $1,637,000 in revenue that had been previously deferred. This deferred revenue related to the development milestone paid in December 2001 and the up-front payment received in June 1997 at the commencement of the collaboration. Additionally, in the fourth quarter of 2002 we received and recognized a milestone payment of $1,500,000 from GlaxoSmithKline in connection with the submission of a new drug application for market approval of Lexiva in the U.S.

We have not entered into any significant collaborative research and development agreements since 2000. Funding under our partnerships with Lilly, Schering and Taisho concluded in 2002.

	Year Ended December 31,	
	2002	2001
	(In thousands)	
Collaborative and other research and development revenue:		
Summary of significant collaborative revenue arrangements:		
Novartis	$ 41,894	$ 36,723
Serono	5,280	4,802
GlaxoSmithKline	1,500	—
Eli Lilly	12,054	6,686
Schering	5,000	5,000
Kissei	4,574	7,405
Taisho	4,187	5,583
Other	10,227	8,315
Total collaborative and other research and development revenue	$ 84,716	$ 74,514

Research and development expenses increased to $198,338,000 in 2002 from $141,988,000 in 2001, primarily due to investment in advancing our clinical pipeline and broadening our research efforts. Our clinical investment was directed primarily toward advancing our second generation p38 MAP kinase inhibitor (VX-702), our IMPDH inhibitors (VX-148 and merimepodib), our HCV protease inhibitor (VX-950) and ICE inhibitor (VX-765). Development investment increased from $49,071,000 in 2001 to $77,932,000 in 2002. Investment in research increased from $92,917,000 in 2001 to $120,406,000 in 2002, resulting principally from the expansion of our multi-target gene family research programs, including our kinase program and ion channel program. As a result of our continued expansion, personnel and facilities expenses also increased.

Sales, general and administrative expenses increased $9,200,000, or 29%, to $41,056,000 in 2002 from $31,856,000 in 2001. The increase is primarily attributable to increased personnel and professional expenses. Included in the increase in personnel and professional expenses is an increase in expenses relating to the addition of certain key executives, certain process consulting costs and legal and patent expenses related to continued protection of our intellectual property, including expenses associated with contesting a suit filed by Oregon Health Sciences University.

Merger related costs of $22,960,000 in 2001 consisted of investment banking, legal and accounting fees associated with the acquisition of Aurora Biosciences Corporation completed on July 18, 2001.

Interest income decreased approximately $16,411,000 to $28,722,000 in 2002 from $45,133,000 in 2001. The decrease is a result of both a lower level of invested funds, and lower portfolio yields due to a reduced interest rate environment.

Interest expense decreased to approximately $17,684,000 in 2002 from $19,318,000 in 2001. The decrease is a result of the reduction in principal amount of the 2007 Notes. In October 2001, we repurchased $30,000,0000 in principal amount of our 2007 Notes and recorded a gain of $10,340,000 on the retirement of the notes in the fourth quarter of 2001.

In April 2002, the Financial Accounting Standards Board ("FASB") issued Statement of Financial Accounting Standard ("SFAS") 145, "Recission of FASB Statements No. 4, 44 and 64, Amendment of FASB Statement No. 13, and Technical Corrections." FAS 145 recinds FAS 4 and FAS 64, which addressed the accounting for gains and losses from extinguishment of debt. Under FAS 145 the gain on retirement of convertible subordinated notes is considered an ordinary item. The gain on retirement of convertible subordinated notes was originally classified in 2001 as an extraordinary item but has been reclassified as part of loss from continuing operations. At December 31, 2002 and 2001, $315,000,000 of the 2007 Notes was outstanding.

Using the equity method of accounting, we recorded $662,000 as our share of loss in Altus Biologics Inc. (Altus), for the year ended December 31, 2001. The loss is included in other expense on the Statement of Operations. Effective September 28, 2001, coincident with a financial restructuring of Altus, we changed our method of accounting for Altus from the equity method to the cost method. See Note I to our consolidated financial statements included in this Annual Report on Form 10-K.

In the third quarter of 2001, in connection with our overall review of accounting policies concurrent with our merger with Aurora, we elected to change our revenue recognition policy for collaborative and other research and development revenues from the Emerging Issues Task Force No. 91-6 ("EITF 91-6") method to the Substantive Milestone Method, adopted retroactive to January 1, 2001. We believe this method is preferable because it is reflective of the Company's on-going business operations and is more consistent with industry practices following the implementation of SAB 101 throughout the biotechnology industry in 2000.

Pursuant to the 2001 change, we recorded a one-time, non-cash charge of $25,901,000, representing a cumulative change in accounting principle for periods prior to 2001. The amount of revenue recognized in 2003, 2002 and 2001 which was included in the one-time, non-cash charge was $2,809,000, $6,979,000 and $7,748,000, respectively. Additionally, $3,684,000, $3,628,000 and $1,053,000 will be recognized as revenue in 2004, 2005 and thereafter, respectively, which amounts were included in the January 2001 charge to income.

Effective July 1, 2001, we adopted Derivative Implementation Group Issue No. A17, "Contracts that Provide for Net Share Settlement" (DIG A17). Pursuant to the adoption of DIG A17, we recorded a $17,749,000 cumulative effect of a change in accounting principle to reflect the value of warrants held in Altus. This amount is included in investments in the December 31, 2001 balance sheet. As of September 30, 2001, the warrants no longer qualified as derivatives under DIG A17 due to changes in the terms of the warrants coincident with a financial restructuring of Altus.

Forward-looking Statements

This reports contains forward-looking statements about our business, including our expectation that (i) we are positioned to commercialize multiple products in the coming years that we expect will generate increased revenues; (ii) our losses will continue; (iii) research and development expenses will continue to increase, but research expenses will not increase without new funding from collaborations; (iv) we will enter into additional strategic collaborations for the development of our drug candidates which are outside our focus areas of viral and inflammatory diseases; (v) our financial results for 2004 will be as set forth in this Annual Report on Form 10-K; (vi) we will continue to collaborate with existing and new partners to develop and market Vertex-discovered products for selected major therapeutic areas; (vii) we and our partners will begin clinical trials on a number of our development stage drug candidates during 2004; (viii) Lexiva will be approved and launched in the E.U. in 2004; (ix) we will initiate expanded clinical trials of merimepodib in 2004, and believe we may be able to file an NDA for merimepodib as early as 2007; (x) development of pralnacasan will be delayed by at least 12-24 months, if the adverse toxicology finding is satisfactorily addressed; (xi) our Phase II clinical trial of VX-702 will be complete in 2004; (xii) our research programs will produce additional development candidates, including numerous kinase inhibitors, in the next several years; and (xiii) our liability to restructure the Kendall Square lease will be as we have estimated and we may pay the full amount in the next 24 months. While management makes its best efforts to be accurate in making forward-looking statements, such statements are subject to risks and uncertainties that could cause our actual results to vary materially. These risks and uncertainties include, among other things, our inability to further identify, develop and achieve commercial success for new products and technologies, the possibility of delays in the research and development necessary to select drug development candidates, the possibility of delays in the commencement or completion of clinical trials, the risk that clinical activities planned for 2004 may not commence as scheduled, the risk that clinical trials may not result in marketable products, the risk that we may be unable to successfully finance and secure regulatory approval of and market our drug candidates, including Lexiva, our dependence upon existing and new pharmaceutical

and biotechnology collaborations, the levels and timing of payments under our collaborative agreements, uncertainties about our ability to obtain new corporate collaborations on satisfactory terms, if at all, the development of competing systems, our ability to protect our proprietary technologies, patent-infringement claims, risks of new, changing and competitive technologies, the risk that there may be changing and new regulations in the U.S. and internationally and uncertainty about our ability to restructure our obligation under the Kendall Square facility lease. Please see the "Risk Factors" appearing elsewhere in this report for more details regarding these and other risks. We disclaim any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

Recent Accounting Pronouncements

In May 2003, the Financial Accounting Standards Board ("FASB") issued Statement of Financial Accounting Standards No. 150 ("SFAS 150"), Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity. SFAS 150 establishes standards for how an issuer classifies and measures certain financial instruments with characteristics of both liabilities and equity. The adoption of SFAS 150 in the third quarter of 2003 did not have a material impact on our results of operations or financial position.

In April 2003, the FASB issued Statement of Financial Accounting Standards No. 149 ("SFAS 149"), Amendment of Statement 133 on Derivative Instruments and Hedging Activities. SFAS 149 amends and clarifies financial accounting and reporting for derivative instruments and for hedging activities under Statement of Financial Accounting Standards No. 133, *Accounting for Derivative Instruments and Hedging Activities* (SFAS 133). The adoption of SFAS 149 in the third quarter of 2003 did not have a material impact on our results of operations or financial position.

In November 2002, the FASB issued Interpretation No. 45, "Guarantor's Accounting and Disclosure Requirements for Guarantees, Including Indirect Guarantees of Indebtedness of Others" ("FIN 45"). FIN 45 elaborates on the disclosures the Company must make about obligations under certain guarantees that the company has issued. It also requires the Company to recognize, at the inception of a guarantee, a liability for the fair value of the obligations undertaken in issuing the guarantee. The initial recognition and initial measurement provisions are to be applied only to guarantees issued or modified after December 31, 2002. The adoption of FIN 45 did not have a material impact on our results of operations or financial position. We have provided additional disclosure with respect to guarantees in Note U to the Consolidated Financial Statements.

In January 2003, the FASB issued FASB Interpretation No. 46 ("FIN 46"), "Consolidation of Variable Interest Entities, an Interpretation of ARB No. 51" and in December 2003 issued a revised FIN 46 ("FIN 46R") which addresses the period of adoption of FIN 46 for entities created before January 31, 2003. FIN 46 provides a new consolidation model which determines control and consolidation based on potential variability in gains and losses. The provisions of FIN 46 are effective for enterprises with variable interest entities created after January 31, 2003. We must adopt the provisions of FIN 46 in the first quarter of 2004 and do not expect the adoption to have a material impact on our financial position or results of operations.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES, AND REPORTS ON FORM 8-K

(a)(1) Financial Statements. The Financial Statements required to be filed by Item 8 of this Annual Report on Form 10-K (as filed with the Original Filing) are as follows:

(a)(2) Financial Statement Schedules. Financial Statement Schedules have been omitted because they are either not applicable or the required information is included in the consolidated financial statements or notes thereto.

(a)(3) Exhibits.

Exhibit Number	Exhibit Description
2.1	Agreement and Plan of Merger dated as of April 29, 2001, by and among Vertex, Aurora and Ahab Acquisition Sub Inc. (filed as Exhibit 2 to Vertex's Current Report on Form 8-K dated April 29, 2001 [File No. 000-19319] and incorporated herein by reference).
2.2	Asset Purchase Agreement among Vertex, PanVera LLC and Invitrogen Corporation dated February 4, 2003 (filed as Exhibit 2.2 to Vertex's 2002 Annual Report on Form 10-K [file No. 000-19319] and incorporated herein by reference).
3.1	Restated Articles of Organization filed with The Commonwealth of Massachusetts on July 31, 1991 (filed as Exhibit 3.1 to Vertex's 1997 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
3.2	Articles of Amendment filed with The Commonwealth of Massachusetts on June 4, 1997 (filed as Exhibit 3.2 to Vertex's 1997 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
3.3	Certificate of Vote of Directors Establishing a Series of a Class of Stock, as filed with the Secretary of The Commonwealth of Massachusetts on July 31, 1991 (filed as Exhibit 3.3 to Vertex's 1997 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
3.4	Articles of Amendment filed with The Commonwealth of Massachusetts on May 21, 2001 (filed as Exhibit 3.4 to Vertex's registration statement on Form S-4 [Registration Number 333-61480] and incorporated herein by reference.)
3.5	By-laws of Vertex as amended and restated as of March 12, 2001 (filed as Exhibit 3.4 to Vertex's 2000 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
4.1	Specimen stock certificate (filed as Exhibit 4.1 to Vertex's Registration Statement on Form S-1 [Registration No. 33-40966] or amendments thereto and incorporated herein by reference).

4.2	Stockholder Rights Plan (filed as Exhibit 4.2 to Vertex's Registration Statement on Form S-1 [Registration No. 33-40966] or amendments thereto and incorporated herein by reference).
4.3	First Amendment to Rights Agreement dated as of February 21, 1997 (filed as Exhibit 4.3 to Vertex's 1996 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
4.4	Indenture dated as of September 19, 2000 between Vertex and State Street Bank and Trust Company (filed as Exhibit 4.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 2000 [File No. 000-19319] and incorporated herein by reference).
4.5	Supplemental Indenture dated as of December 12, 2000 between Vertex and State Street Bank and Trust Company (filed as Exhibit 4.2 to Pre-Effective Amendment No. 1 to the Form S-3 filed by Vertex [Registration No. 333-49844] and incorporated herein by reference).
4.6	Second Amendment to Rights Agreement dated as of June 30, 2001 (filed as Exhibit 4.4 to Vertex's Quarterly Report on Form 10-Q for the quarter ended June 30, 2001 [File No. 000-19319] and incorporated herein by reference).
4.7	Indenture dated February 13, 2004 between Vertex and U.S. Bank National Association (filed as Exhibit 4.1 to Vertex's Current Report on Form 8-K dated February 23, 2004 [File No. 000-19319] and incorporated herein by reference).
10.1	1991 Stock Option Plan, as amended and restated as of September 14, 1999 (filed as Exhibit 10.1 to Vertex 1999 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*
10.2	1994 Stock and Option Plan, as amended and restated as of September 14, 1999 (filed as Exhibit 10.1 to Vertex 1999 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*
10.3	1996 Stock and Option Plan, Amended and Restated as of July 17, 2002 (filed as Exhibit 10.3 to Vertex's 2002 Annual Report on Form 10-K [file No. 000-19319] and incorporated herein by reference).*
10.4	Non-Competition and Stock Repurchase Agreement between Vertex and Joshua Boger, dated April 20, 1989 (filed as Exhibit 10.2 to Vertex's Registration Statement on Form S-1 [Registration No. 33-40966] or amendments thereto and incorporated herein by reference).*
10.5	Form of Employee Stock Purchase Agreement (filed as Exhibit 10.3 to Vertex's Registration Statement on Form S-1 [Registration No. 33-40966] or amendments thereto and incorporated herein by reference).*
10.6	Form of Employee Non-Disclosure and Inventions Agreement (filed as Exhibit 10.4 to Vertex's Registration Statement on Form S-1 [Registration No. 33-40966] or amendments thereto and incorporated herein by reference).
10.7	Form of Executive Employment Agreement executed by Joshua S. Boger and Vicki L. Sato (filed as Exhibit 10.6 to Vertex's 1994 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*
10.8	Form of Amendment to Employment Agreement executed by Joshua S. Boger and Vicki L. Sato (filed as Exhibit 10.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended June 30, 1995 [File No. 000-19319] and incorporated herein by reference).*
10.9	Executive Employment Agreement between Vertex and Iain P.M. Buchanan (filed as Exhibit 10.9 to Vertex's 2001 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*

10.10 Agreement dated December 21, 2000 between Vertex and Richard H. Aldrich (filed as Exhibit 10.10 to Vertex's 2000 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*

10.11 Lease dated March 3, 1995, between Fort Washington Realty Trust and Vertex, relating to the premises at 130 Waverly Street, Cambridge, MA (filed as Exhibit 10.15 to Vertex's 1994 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).

10.12 First Amendment to Lease dated December 29, 1995 between Fort Washington Realty Trust and Vertex (filed as Exhibit 10.15 to Vertex's 1995 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).

10.13 Second Amendment to Lease and Option Agreement dated June 12, 1997 between Fort Washington Realty Trust and Vertex (filed as Exhibit 10.17 to Vertex 1999 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).

10.14 Third, Fourth and Fifth Amendments to Lease between Fort Washington Realty Trust and Vertex (with certain confidential information deleted) (filed as Exhibit 10.14 to Vertex's 2001 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).

10.15 Lease by and between Trustees of Fort Washington Realty Trust, Landlord, and Vertex, executed September 17, 1999 (filed, with certain confidential information deleted, as Exhibit 10.27 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 1999 [File No. 000-19319], and incorporated herein by reference).

10.16 Lease by and between Kendall Square, LLC, Landlord, and Vertex, executed January 18, 2001 (filed, with certain confidential information deleted, as Exhibit 10.16 to Vertex's 2000 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).

10.17 Agreement for Lease of Premises at 88 Milton Park, Abingdon, Oxfordshire between Milton Park Limited and Vertex Pharmaceuticals (Europe) Limited and Vertex Pharmaceuticals Incorporated (filed as Exhibit 10.18 to Vertex 1999 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).

10.18 Research and Development Agreement dated April 13, 1993 between Vertex and Kissei Pharmaceutical Co., Ltd. (filed, with certain confidential information redacted, as Exhibit 10.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended March 31, 1993 [File No. 000-19319] and incorporated herein by reference).†

10.19 Research Agreement and License Agreement, both dated December 16, 1993, between Vertex and Burroughs Wellcome Co. (filed, with certain confidential information redacted, as Exhibit 10.16 to Vertex's 1993 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).†

10.20 Research and Development Agreement between Vertex and Eli Lilly and Company effective June 11, 1997 (filed, with certain confidential information redacted, as Exhibit 10.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended June 30, 1997 [File No. 000-19319] and incorporated herein by reference).†

10.21 Research and Development Agreement between Vertex and Kissei Pharmaceutical Co. Ltd. effective September 10, 1997 (filed, with certain confidential information redacted, as Exhibit 10.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 1997 [File No. 000-19319] and incorporated herein by reference).†

10.22 Research Agreement between Vertex and Schering AG dated as of August 24, 1998 (filed, with certain confidential information redacted, as Exhibit 10.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 1998 [File No. 000-19319] and incorporated herein by reference).†

10.23	License, Development and Commercialization Agreement between Vertex and Hoechst Marion Roussel Deutschland GmbH dated September 1, 1999 (filed, with certain confidential information redacted, as Exhibit 10.27 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 1999 [File No. 000-19319], and incorporated herein by reference).†
10.24	Collaboration and Option Agreement between Vertex and Taisho Pharmaceutical Co., Ltd. dated November 30, 1999 (filed, with certain confidential information redacted, as Exhibit 10.27 to Vertex's 1999 Form 10-K [File No. 000-19319] and incorporated herein by reference).†
10.25	Research and Early Development Agreement between Vertex and Novartis Pharma AG dated May 8, 2000 (filed, with certain confidential information redacted, as Exhibit 10.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended March 31, 2000 [File No. 000-19319] and incorporated herein by reference).†
10.26	Research Agreement between Vertex and Laboratoires Serono S.A. dated December 11, 2000 (filed, with certain confidential information redacted, as Exhibit 10.26 to Vertex's 2000 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).†
10.27	Letter Agreement between Aurora and Stuart J. Collinson (filed as Exhibit 10.26 to Vertex's registration statement on Form S-4 [Registration No. 333-61480] and incorporated herein by reference).*
10.28	Executive Employment Agreement between Vertex and Kenneth S. Boger (filed as Exhibit 10.28 to Vertex's 2001 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*
10.29	Executive Employment Agreement between Vertex and Ian F. Smith (filed as Exhibit 10.29 to Vertex's 2001 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*
10.30	Letter Agreement between Vertex and N. Anthony Coles, M.D. (filed as Exhibit 10.30 to Vertex's 2001 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*
10.31	Form of Non-Competition Agreement between Vertex and Invitrogen Corporation dated March 28, 2003 (filed as Exhibit 10.31 to Vertex's 2002 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).
10.32	Form of letter agreement with John J. Alam, Senior Vice President of Drug Evaluation and Approval; Lynne H. Brum, Vice President of Corporate Communications and Financial Planning; Pamela Fritz, Vice President, Human Resources; Peter Mueller, Chief Scientific Officer and Senior Vice President, Drug Discovery and Innovation; Mark Murcko, Vice President and Chief Technology Officer; Steven Schmidt, Vice President, Information Systems; John A. Thomson, Vice President, Research; and Jeffrey D. Wilson, Vice President, Pharmaceutical Operations, covering special rights upon a change of control transaction (filed as Exhibit 10.32 to Vertex's 2002 Annual Report on Form 10-K [File No. 000-19319] and incorporated herein by reference).*
10.33	Dealer Manager Agreement dated February 10, 2004 between Vertex and UBS Securities LLC, (filed as Exhibit 10.1 to Vertex's Current Report on Form 8-K dated February 23, 2004 [File No. 000-19319] and incorporated herein by reference.
10.34	Resale Registration Rights Agreement dated as of February 13, 2004 between Vertex and UBS Securities LLC (filed as Exhibit 10.2 to Vertex's Current Report on Form 8-K dated February 23, 2004 [File No. 000-19319] and incorporated herein by reference).
10.35	First Revised and Restated Research and Early Development Agreement between Vertex and Novartis Pharma AG dated February 3, 2004 (filed, with certain confidential information redacted, as Exhibit 10.35 to the Original Filing [File No. 000-19319] and incorporated herein by reference).†

18.1	Letter from PricewaterhouseCoopers LLP dated November 14, 2001 re: Change in Accounting Principle (filed as Exhibit 18.1 to Vertex's Quarterly Report on Form 10-Q for the quarter ended September 30, 2001 [File No. 000-19319] and incorporated herein by reference).
21	Subsidiaries of Vertex (filed as Exhibit 21 to the Original Filing [File No. 000-19319] and incorporated herein by reference).
23.1	Consent of Independent Accountants, PricewaterhouseCoopers LLP (filed as Exhibit 23.1 to the Original Filing [File No. 000-19319] and incorporated herein by reference)
31.1	Certification of the Chief Executive Officer under Section 302 of the Sarbanes-Oxley Act of 2002 (filed herewith).
31.2	Certification of the Chief Financial Officer under Section 302 of the Sarbanes-Oxley Act of 2002 (filed herewith).
32.1	Certification of the Chief Executive Officer and the Chief Financial Officer under Section 906 of the Sarbanes-Oxley Act of 2002 (filed as Exhibit 32.1 to the Original Filing [File No. 000-19319] and incorporated herein by reference).

* Compensatory plan or agreement applicable to management and employees.

† Confidential portions of these documents have been filed separately with the Commission pursuant to a request for confidential treatment.

(b) Reports on Form 8-K.

On November 10, 2003, we furnished a report on Form 8-K-Item 9-Regulation FD Disclosure Item 12-Disclosure of Results of Operations and Financial Condition, reporting that the Company had issued two press releases, one regarding the development status of certain of its drug candidates and the second reporting that the Company had issued a press release to report the Company's financial results for the quarter ended September 30, 2003.

On December 5, 2003, we filed a report on Form 8-K-Item 5-Other Events, reporting that Joshua S. Boger, the Company's Chairman and CEO, entered into a plan with Goldman, Sachs & Co., pursuant to which Goldman will undertake to sell, subject to a limit order, an aggregate of 370,000 shares of the Company's stock issuable upon exercise of options held by Dr. Boger.

On December 5, 2003, we furnished a report on Form 8-K-Item 9-Regulation FD Disclosure, reporting that the Company had issued a press release on December 4, 2003 to announce the sale of certain instrumentation assets of Vertex's subsidiary Aurora Instruments LLC to Aurora Discovery, Inc., and updating our 2003 full-year financial guidance.

On December 16, 2003, we filed a report on Form 8-K-Item 5-Other Events, reporting that on November 17, 2003, Iain P.M. Buchanan, the Company's Vice President of European Operations, entered into a plan with Lehman Brothers Inc., pursuant to which Lehman will undertake to sell, subject to a limit order, an aggregate of 50,000 shares of the Company's stock issuable upon exercise of options held by Mr. Buchanan.

On December 19, 2003, we filed a report on Form 8-K-Item 5-Other Events, reporting that Vicki L. Sato, the Company's President, entered into a plan with Goldman, Sachs & Co., pursuant to which Goldman will undertake to sell, subject to a limit order, an aggregate of 344,509 shares of the Company's stock issuable upon exercise of options held by Dr. Sato.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) 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

September 8, 2004 By: /s/ JOSHUA S. BOGER

Joshua S. Boger
Chief Executive Officer

QuickLinks

Exhibit 10.35

CONFIDENTIAL TREATMENT

FIRST REVISED AND RESTATED
RESEARCH AND EARLY DEVELOPMENT AGREEMENT

BETWEEN

VERTEX PHARMACEUTICALS INCORPORATED

AND

NOVARTIS PHARMA AG

[Certain redacted non-public information has been filed separately with the Securities and Exchange Commission.]

RESEARCH AND EARLY DEVELOPMENT AGREEMENT

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FIRST REVISED AND RESTATED

RESEARCH AND EARLY DEVELOPMENT AGREEMENT

First Revised and Restated Agreement made this 3rd day of February, 2004, (as so revised and restated, the "Research Agreement"), revising and restating that certain Research And Early Development Agreement dated May 8, 2000 (the "Original Agreement"), between VERTEX PHARMACEUTICALS INCORPORATED ("VERTEX"), a Massachusetts corporation with principal offices at 130 Waverly Street, Cambridge, MA 02139-4242, and NOVARTIS PHARMA AG ("NOVARTIS"), a Swiss corporation with principal offices at Lichtstrasse 35, CH-4056 Basel, Switzerland.

This Research Agreement is intended by the parties to replace and supercede the rights and obligations of the parties under the Original Agreement with respect to the subject matter thereof, except that the terms of the Original Agreement shall be deemed to govern the rights and obligations of the parties with respect to the Compounds known as VX-680 and VX-528, subject to the provisions of Section 4.8(b) of this Research Agreement.

INTRODUCTION

WHEREAS, VERTEX has undertaken a broad drug discovery program with the objective of designing novel, small-molecule compounds targeting the kinase protein super-family;

WHEREAS, NOVARTIS is also interested in developing and commercializing drugs targeting kinase proteins and has particular expertise in developing, registering, manufacturing, marketing and selling pharmaceuticals worldwide;

WHEREAS, both parties desire to revise and restate the Original Agreement to reflect agreed modifications to the original collaboration, which involve among other things a redirection of VERTEX's efforts from the delivery of compounds which have progressed through early clinical testing, to the delivery of Development Candidates, at an earlier stage in the development process, which target selected Kinases and meet certain pre-agreed Development Candidate Criteria; and

WHEREAS, NOVARTIS may elect to develop, market and sell any or all of those Compounds as drugs upon the terms set forth herein and in a License, Development and Commercialization Agreement identical in substance to Exhibit A hereto;

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

ARTICLE I
DEFINITIONS

For purposes of this Agreement, the terms defined in this Article 1 shall have the following meanings whether used in their singular or plural forms. Use of the singular shall include the plural and vice versa, unless the context requires otherwise:

CONFIDENTIAL TREATMENT REQUESTED

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, more than 50% of the voting stock of any other Person. For the avoidance of any doubt, the Novartis Institute for Functional Genomics, Inc. and The Friedrich Miescher Institute, as currently operated, are not Affiliates of NOVARTIS for the purposes of this Research Agreement.

1.1.1. "BACK-UP COMPOUND" shall mean, with reference to any particular Development Candidate or Drug Product Candidate, a Compound which (a) modulates the same Kinase as that Development Candidate or Drug Product Candidate; and [***].

1.2. "BULK DRUG SUBSTANCE" shall mean a Drug Product Candidate in bulk crystal, powder or other form suitable for incorporation in a Drug Product.

1.3. "COMPOUND" shall mean any chemical compound, including salts thereof, which affects a Kinase and which was or is synthesized and/or tested (including by screening) by or under the direction of VERTEX or its Affiliates during the term of the Research Program conducted under this Research Agreement, or was synthesized or tested by VERTEX or its Affiliates prior to the Effective Date in a program targeted toward Kinase modulation.

1.4. "CONTROLLED" shall mean the legal authority or right of a party hereto to grant a license or sublicense of intellectual property rights to another party hereto, or to otherwise disclose proprietary or trade secret information to such other party, without breaching the terms of any agreement with a Third Party, infringing upon the intellectual property rights of a Third Party, or misappropriating the proprietary or trade secret information of a Third Party.

1.5. (a) "Development Candidate" shall mean a Compound that meets the Development Candidate Criteria and which is either proposed by VERTEX, during the term of the Research Program [***], for formal pre-clinical development, or is selected by NOVARTIS on or before the Final Termination Date for formal pre-clinical development pursuant to the provisions of Section 4.1 hereof.

1.5. (b) "DEVELOPMENT CANDIDATE INFORMATION" will mean all material information known to VERTEX about a Development Candidate, including analytical results and raw data, which NOVARTIS reasonably needs in order to decide whether to exercise the Development Election with respect to the Development Candidate. The Development Candidate Information shall include any previously undisclosed information with respect to VERTEX Kinase Technology which is important to a scientific and commercial evaluation of the Development Candidate. Development Candidate Information will also include comparable information known to VERTEX concerning all Compounds which are Back-up Compounds, as defined herein, to the specific Development Candidate which is the subject of the Development Candidate Information. Pursuant to the provisions of Section 5.1 hereof, the Development Candidate Information shall also disclose [***]

1.5. (c) "DEVELOPMENT CANDIDATE CRITERIA" shall mean (a) the criteria set forth on Schedule 2.4.3 hereof and (b) such further, more specific criteria to be determined by the JRC as soon as possible after the start of each research project with respect to each particular Kinase target, each therapeutic application, special delivery forms, and the like, as set forth in Section 2.5.3 hereof.

CONFIDENTIAL TREATMENT REQUESTED

1.6. "DEVELOPMENT ELECTION" shall have the meaning set forth in Section 4.1 hereof.

1.7. "DEVELOPMENT PROGRAM" shall mean activities associated with development of a Drug Product Candidate as specified in the License Agreement.

1.8. [This section has been intentionally left blank.]

1.9. "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.

1.10. (a) "DRUG PRODUCT CANDIDATE" shall mean a Development Candidate which has been selected by NOVARTIS for development and commercialization under the License Agreement, pursuant to exercise of its Development Election under Section 4.1 hereof.

1.10. (b) "DRUG PRODUCT CANDIDATE BACKUP CANDIDATE" shall mean any Back-up Compound for which NOVARTIS has exercised its Development Election under Section 4.5 hereof.

1.11. [This section has been intentionally left blank.]

1.12. "EFFECTIVE DATE" shall mean the effective date of the Original Agreement as set forth on the first page hereof.

1.13. "EXCLUDED COMPOUNDS" shall mean any chemical compounds the therapeutic effect of which in humans is thought to be principally derived from an effect on one or more Excluded Kinases. "Excluded Compounds" shall also include the Compound known as [***]. An "analog" shall mean any compounds (or salts thereof) which are claimed in [***] which NOVARTIS can demonstrate by written record were synthesized by NOVARTIS before the Effective Date. "Excluded Compounds" shall also include any Compounds directed toward modulation of a

Kinase which has been added to the list of Excluded Kinases by the operation of Section 4.4 hereof; provided that in no event shall an Excluded Compound include a Drug Product Candidate.

1.14. "EXCLUDED KINASES" shall mean the human kinases specifically identified in Schedule 1.13 hereto. "Excluded Kinases" shall also include any Kinase hereafter added to the list of Excluded Kinases pursuant to the provisions of Section 4.4 hereof.

1.15. [This section has been intentionally left blank.]

1.16. "FIELD" shall mean the treatment or prevention of conditions or diseases in humans, principally by affecting a Kinase other than an Excluded Kinase.

1.17. "FINAL NOTICE PERIOD" shall have the meaning set forth in Section 4.1(d) hereof.

1.17.1. "FINAL REPORT" shall have the meaning set forth in Section 4.1(d) hereof.

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1.17.2. "FINAL REPORT PERIOD" shall have the meaning set forth in Section 4.1(d) hereof.

1.17.3. "FINAL TERMINATION DATE" shall have the meaning set forth in Section 4.1(d) hereof.

1.18. "FTE" shall mean the equivalent of the work of one VERTEX scientist or other project managerial professional, full time for one year, which equates to a total of forty-seven (47) weeks or one thousand eight hundred eighty (1880) hours per year of work, on or directly related to the Research Program. Work in the Research Program can include, but is not limited to, experimental laboratory work, project and research management, activities directed toward evaluation of the commercial potential of a possible Drug Candidate, recording and writing up results, reviewing literature and references, holding scientific discussions, attending appropriate seminars and symposia, and carrying out Joint Research Committee duties. FTE's shall include equivalent scientific work in the Research Program delegated to and carried out by contractors, under the general direction of VERTEX scientists; provided, that the nature and quantity (as a percentage of total program FTE's) of the delegated work shall not be such that the most substantial parts of the overall Research Program, in terms of projected value creation, have been delegated to Third Parties. FTE's which result from work delegated to and carried out by contractors will be separately identified by VERTEX on its invoices provided to NOVARTIS under Section 12.19 hereof.

1.19. [This section has been intentionally left blank.]

1.20. [This section has been intentionally left blank.]

1.21. "JOINT RESEARCH COMMITTEE" or "JRC" shall have the meaning ascribed to it in Section 2.5 of this Research Agreement.

1.22. "JOINT STEERING COMMITTEE" or "JSC" shall have the meaning ascribed to it in Section 2.6 of this Research Agreement.

1.23. "KINASE" shall mean a human enzyme that catalyzes the transfer of a phosphate group from a nucleoside triphosphate to a protein.

1.24. "KINASE TECHNOLOGY" shall mean all data, technical information, know-how, experience, inventions (whether or not patented) trade secrets, processes and methods discovered, developed or applied (with the consent of its owner) and Controlled by either party or its Affiliates, in connection with performance by either party under the Research Program, or in connection with the conduct of a Development Program under the License Agreement prior to termination of the Research Program, that relate to the research, development, utilization, manufacture or use of Compounds, Development Candidates, Drug Product Candidates or Drug Products (other than any such technology which is exclusive to Excluded Kinases); provided, however, that the term Kinase Technology shall not apply to VERTEX's general drug design technology whether in hardware or software form, tangible or intangible.

1.25. "KNOW-HOW" means all Kinase Technology other than inventions which are the subject of Patents; and "LEAD PERIOD" shall have the meaning set forth in Section 4.5(a) hereof.

1.26. "LICENSE AGREEMENT" shall mean the License, Development and Commercialization Agreement, identical in substance to EXHIBIT A to this Research Agreement, to be executed by VERTEX and NOVARTIS with respect to each Drug Product Candidate; and "Notice Period" shall have the meaning set forth in Section 4.1(b) hereof.

1.27. "NOVARTIS KNOW-HOW" shall mean all Know-How of NOVARTIS.

1.28. "NOVARTIS PATENTS" shall mean any Patents controlled by NOVARTIS or its Affiliates claiming Kinase Technology.

1.29. "NOVARTIS KINASE TECHNOLOGY" shall mean all NOVARTIS Patents and NOVARTIS Know-How.

1.30. "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 supplementary protection 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.

1.31. "PERSON" means any individual, corporation, partnership, association, joint-stock company, trust, unincorporated organization or government or political subdivision thereof.

1.32. [This section has been intentionally left blank.]

1.33. [This section has been intentionally left blank.]

1.34. "REFUSED CANDIDATE" shall have the meaning set forth in Section 4.4 hereof.

1.35. "REPLACEMENT CANDIDATE" shall have the meaning set forth in Section 4.5(b) hereof.

1.36. "RESEARCH PLAN" shall have the meaning set forth in Section 2.4.1 hereto.

1.37. (a) "RESEARCH PROGRAM" shall mean all research activities undertaken under this Research Agreement associated with the identification and design of Compounds and Development Candidates as provided herein; including but not limited to identification and initial testing of Compounds; the conduct of activities referenced in the Development Candidate Criteria with respect to Compounds; and selection of Development Candidates from Compounds.

1.37. (b) "RESEARCH TERMINATION DATE" shall mean the earlier of April 30, 2006 or the date upon which the Research Program is terminated under Sections 9.2, 9.3 or 9.5 hereof.

1.38. "RESEARCH YEAR" means a twelve-month period during the term of the Research Program commencing on May 1, and ending on April 30 of each year. The first Research Year hereunder shall be deemed to have commenced on May 1, 2000.

1.39. [This space has been intentionally left blank.]

1.40. "TECHNOLOGY" shall mean NOVARTIS Kinase Technology and VERTEX Kinase Technology.

1.41. "THIRD PARTY" shall mean any person or entity which is not a party or an Affiliate of any party to this Research Agreement.

CONFIDENTIAL TREATMENT REQUESTED

1.42. "THIRD PARTY REFERRAL" shall mean the procedure for resolution of certain disputes hereunder which is set forth in Section 11.2(b) hereof.

1.43. "VERTEX KNOW-HOW" shall mean all Know-How of VERTEX.

1.44. "VERTEX PATENTS" shall mean any Patents Controlled by VERTEX or its Affiliates claiming Kinase Technology.

1.45. "VERTEX KINASE TECHNOLOGY" shall mean all VERTEX Patents and VERTEX Know-How.

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

ARTICLE II
RESEARCH PROGRAM

2.1. COMMENCEMENT.

The Research Program originally commenced on May 1, 2000. VERTEX has principal responsibility for the conduct of the Research Program and NOVARTIS provides consultation, advice and such research effort as may be deemed appropriate by the JRC and accepted by NOVARTIS. The JRC shall review and coordinate all of the parties' efforts with respect to the Research Program.

2.2. TERM.

The Research Program will conclude on May 1, 2006, unless earlier terminated in accordance with the provisions hereof. At the request of either party made during the fourth Research Year, the parties will discuss whether, and upon what basis, the Research Program might be extended on comparable terms beyond its initial 6 year term.

2.3. RESEARCH DILIGENCE.

The common objective of the parties is to identify Development Candidates as soon as practicable for selection by NOVARTIS as Drug Product Candidates and for worldwide development and marketing under the terms of the License Agreement. VERTEX will work diligently and use all reasonable efforts, consistent with prudent business judgment, to identify Development Candidates for acceptance by NOVARTIS as Drug Product Candidates. VERTEX intends to dedicate to the Research Program at least that level of staffing referenced in Section 3.2 hereof, and expects to employ an optimal combination of experience and training in the Field. As a matter of corporate strategy, VERTEX has chosen to dedicate a significant amount of its overall research efforts to work in the Field, and will not change that overall strategy during the term of the Research Program without prior notice to and approval by NOVARTIS.

2.4. RESEARCH PLAN; EARLY DEVELOPMENT PLAN.

2.4.1. General. VERTEX originally prepared an overall research plan for the Research Program which it submitted to the JRC for its review and comment at the first meeting of the JRC after the Effective Date. The research plan has been and will be revised, updated and submitted to the JRC at least annually for its review and comment (as so revised, updated and submitted, the "Research Plan").

CONFIDENTIAL TREATMENT REQUESTED

2.4.2. [This section has been intentionally left blank.]

2.4.3. Plan Review. In developing the Research Plan, VERTEX will take into account the intention of the parties to produce Compounds which meet the Development Candidate Criteria. VERTEX shall not perform any work under this Research Agreement with respect to Excluded Compounds or Excluded Kinases. The Research Plan will be reviewed as necessary at each meeting of the JRC, and at any other time upon the request of either party, and shall be modified as appropriate to reflect material scientific or commercial developments. Any disagreements among the parties with respect to these matters may be referred by either party to the Joint Steering Committee for resolution. Notwithstanding the foregoing, VERTEX shall have the final say with respect to the Research Plan.

2.5. JOINT RESEARCH COMMITTEE.

2.5.1. Composition and Purposes. VERTEX and NOVARTIS have established and will continue to participate in a Joint Research Committee ("JRC") consisting of at least eight (8) representatives (as may be increased or decreased by the JRC), half of whom shall be designated from time to time by each party. If the JRC chooses to designate a Committee Chair, the Chair will be appointed from among the members of the Committee designated by VERTEX. The JRC 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 receive and review reports by VERTEX and its project

teams, which shall be prepared and submitted to the JRC on a quarterly basis within fifteen (15) days after the end of each calendar quarter, such reports summarizing progress during the preceding quarter under the Research Plan; and to review information with respect to the Compounds under investigation (which VERTEX shall provide in form and content at least as extensive as customarily provided to the JRC under the Original Agreement);

(ii) To review a proposal by either party that specified Excluded Compounds or Excluded Kinases be included in the Research Program, or that a Kinase be added to the list of Excluded Kinases; provided that the JRC shall have no authority to include or exclude any Compound or Kinase from the Research Program, and that any such action must be the subject of a formally adopted amendment to this Research Agreement;

(iii) To define as soon as possible the further, more specific Development Criteria (x) for ongoing projects, after the signature of this Research Agreement, or (y) for new projects, after the start of such new research project;

(iv) To review Development Candidates proposed by VERTEX and to assess whether a given Development Candidate proposed by VERTEX meets the Development Criteria;

(v) To review the Research Plan and any proposed revisions thereto;

(vi) [This subsection has been intentionally left blank.]; and

(vii) To discuss matters relating to Patents, as may be presented to the JRC by VERTEX or NOVARTIS.

The party hosting a particular JRC meeting shall prepare and deliver to the members of the JRC, within thirty (30) days after the date of each meeting, minutes of such meeting setting forth, inter alia, all decisions of the JRC, and including a report on the progress of work performed. In case the JRC meets by means of telephone or video conferences, this responsibility shall lie with VERTEX.

2.5.2. DECISION-MAKING.

(i) Each of VERTEX and NOVARTIS shall have one vote on the JRC. The objective of the JRC shall be to reach agreement by consensus on all matters within the scope of the Research Plan. However, in the event of a deadlock with respect to any action (which shall be deemed to have occurred if either party shall request a vote of the JRC on a matter and that vote shall either not be taken within thirty (30) days of the request or if taken shall result in a tie vote) and subject to the procedure set forth in subsection (ii) below as to certain matters, the vote of VERTEX, rendered after reasonable and open discussion among the members of the JRC, shall be final and controlling.

(ii) Notwithstanding the foregoing, with respect to JRC decisions (x) as to the nature and extent of any additional Development Candidate Criteria referenced in Section 2.5.3 hereof, any disagreement between the parties that cannot be resolved within forty-five (45) days by the JRC (as that period may be extended under (iii) below) shall be referred to the JSC for resolution and if not resolved within seven (7) business days after referral, shall be referred for final resolution in good faith by the Chief Executive Officer of VERTEX and the Chief Executive Officer of NOVARTIS, and failing final resolution, there will be no change to the Development Candidate Criteria; or (y) as to whether or not Development Candidate Information provided by VERTEX, pursuant to subsection (iii) below, is complete or as to whether or not a given Compound proposed by VERTEX as a Development Candidate meets the Development Criteria, the matter shall be referred as provided in subsection (x) above to the JRC and the JSC and, failing agreement, the matter shall be referred for final resolution under the provisions of Section 11.2(b) of this Research Agreement.

(iii) In the event that NOVARTIS's representatives on the JRC reasonably believe that the Development Candidate Information with respect to a particular Development Candidate proposed by VERTEX to the JRC is incomplete, NOVARTIS shall provide written notice thereof to VERTEX within fifteen (15) business days after receipt of the Development Candidate Information, and VERTEX shall undertake reasonable efforts to furnish the requested additional Development Candidate Information within fifteen (15) business days after receipt of NOVARTIS's notice hereunder. The 45-day period provided for action by the JRC under subsection (ii) above shall be extended by the amount of time required for VERTEX to provide the requested information, but in any event not in excess of thirty (30) days.

(iv) Notwithstanding any of the foregoing, if VERTEX and NOVARTIS deadlock on any other matters being considered by the JRC which might have a

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significant impact on the time or likely success of the Research Program, the matter shall be referred to the JSC for resolution in accordance with Section 2.6 hereof.

(v) Each party shall retain the rights, powers, and discretion granted to it under this Research Agreement, and the JRC shall not be delegated or vested with any such rights, powers or discretion except as expressly provided in this Research Agreement. The JRC shall not have the power to amend or modify this Research Agreement, which may only be amended or modified as provided in Section 12.15.

2.5.3. ADDITIONAL DEVELOPMENT CANDIDATE CRITERIA. The parties acknowledge that it may be necessary or appropriate to adopt additional Development Candidate Criteria which more specifically define the pre-development characteristics of Compounds which the parties believe may be suitable for development and commercialization under the License Agreement, based upon the Kinase targeted by a specific project under the Research Program and the particular disease indication or indications thought to be addressed by Compounds modulating the Kinase which is the subject of that project. The parties will use good faith efforts through their respective representatives on the JRC to agree on any such additional Development Candidate Criteria as soon as practicable after [***] Any disagreements with respect to the selection of additional Development Candidate Criteria hereunder will be addressed as provided in Section 2.5.2(ii).

2.6. JOINT STEERING COMMITTEE.

2.6.1. Composition and Purposes. VERTEX and NOVARTIS have established and will continue to participate in a Joint Steering Committee ("JSC") which shall consist of an equal number of senior executives as may be designated by each party from time to time. The JSC shall initially have four (4) members. If the JSC chooses to designate a Committee Chair, the Chair will be appointed from among the members of the JSC designated by NOVARTIS. The JSC shall meet annually, or with such other frequency, and at such time and location, as may be established by the Committee, for the following purposes:

(i) General oversight of the entire collaboration between VERTEX and NOVARTIS, including the Research Program and any development and commercialization of a Drug Product Candidate under the License Agreement;

(ii) Periodically review the overall goals and strategy of the Research Program;

(iii) Discuss and attempt to resolve any deadlocked issues submitted to it by the JRC, although the vote of VERTEX's representatives shall prevail if the JSC is unable to reach a consensus on any matter other than matters submitted to the JSC under Section 2.5.2(ii).

2.7. EXCHANGE OF INFORMATION.

2.7.1. VERTEX, and at its sole discretion NOVARTIS, will share information with the JRC, as soon as it is available, necessary to facilitate mutual understanding of the status of the Research Program and decision-making in connection therewith.

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2.7.2. Neither VERTEX nor NOVARTIS shall use Kinase Technology disclosed by the other party (excluding information which is no longer subject to confidentiality restrictions under Article V by reason of the exceptions set forth in Section 5.2) for any purpose, including the filing of patent applications containing such information, without the other party's consent, other than for carrying out the Research Program or discharging its responsibilities under the License Agreement, or as otherwise permitted under the Research Agreement or the License Agreement.

2.7.3. [This section has been intentionally left blank.]

2.7.4. Neither party shall be entitled to information from the other party concerning [***] However, neither party will apply its rights in any Technology other than [***]

2.8. [This section has been intentionally left blank.]

2.9. FREEDOM-OF-ACTION AND EXCLUSIVITY

2.9.1. NOVARTIS and any of its Affiliates shall be free, by itself/themselves or together with Third Parties, to pursue efforts directed toward the identification, and/or development and/or commercialization of compounds (other than those Compounds which have been the subject of a Development Election procedure pursuant to Section 4.1(b)) free of any obligation to VERTEX under this Research Agreement or the License Agreement (but subject always to intellectual property rights, if any, held by VERTEX and the obligations of NOVARTIS under Sections 5.1 and 5.2).

2.9.2. Subject to the provisions stated in Section 2.4.3, during the term of the Research Program neither VERTEX nor any of its Affiliates will enter into any agreement or collaboration with a Third Party aimed at identifying or developing Compounds in the Field. The foregoing restrictions shall not be applicable to Excluded Compounds or to agreements or collaborations with respect to Excluded Kinases.

2.9.3. [This section has been intentionally left blank.]

2.9.4. [This section has been intentionally left blank.]

2.9.5. [This section has been intentionally left blank.]

2.9.6. [This section has been intentionally left blank.]

ARTICLE III
PAYMENTS

3.1. SIGNATURE PAYMENT BY NOVARTIS.

Upon the Effective Date of this Research Agreement NOVARTIS made an initial non-refundable payment of $15,000,000 to VERTEX.

3.2. STAFFING AND RESEARCH SUPPORT PAYMENTS.

NOVARTIS has made or will make the payments specified below to VERTEX during each Research Year in support of the Research Program under this Research Agreement.

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The required payments are based upon the following assumptions: (a) the average number of FTE's which VERTEX will have employed in the Research Program during a Research Year will be approximately equal to the FTE Level listed in the third column below; and (b) the annual rate per FTE is approximately [***]. If the average FTE level for any Research Year is less than the level specified below for that year (the difference being referred to in this section as an "FTE Shortfall"), then the amount of funding specified below for that Research Year shall be reduced by an amount (the "FTE Shortfall Amount") which bears the same relation to the total funding specified below for that Research Year as the FTE Shortfall bears to the projected FTE Level for that Year. The FTE Shortfall Amount shall be carried over from year to year and applied to compensate VERTEX for FTE Levels in subsequent Research Years which exceed the level for those Years as specified below. In any such subsequent Research Year, VERTEX shall be entitled to receive out of any remaining FTE Shortfall Amount a payment equal to the value (computed with reference to the inflation-adjusted FTE rate specified above) of any FTE's actually employed during that Research Year in excess of the FTE Level specified for that year ("Excess FTE's"). Notwithstanding the foregoing, the FTE Shortfall Amount will not be applied to compensate VERTEX on account of more than 20 Excess FTE's in any one Research Year.

Research
Year
Funding
FTE
Level 1
[***]
[***] 2
[***]
[***] 3

[***]
[***] 4
[***]
[***] 5
[***]
[***] 6
[***]
[***]

Research Year 1 will be deemed to have commenced on May 1, 2000. Payments due for each Research Year shall be made quarterly in advance on or before May 1, August 1, November 1 and February 1 of each Research Year except that the quarterly payment due May 1, 2000 was made within thirty business days after the Effective Date of this Research Agreement. All payments shall be made without deduction for withholding or other similar taxes, in United States dollars to the credit of such bank account as may be designated by VERTEX in writing to NOVARTIS. 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.

3.3. DEVELOPMENT LOAN FACILITY.

The existing development loan facility is hereby terminated. All currently outstanding loans made under the facility will be repaid by VERTEX on or before the earlier of: May 7, 2008, as specified in Section 3.3.3 of the Original Agreement; or the first anniversary of the effective date of any termination of this Research Agreement by NOVARTIS for cause under Section 9.2 hereof. Notwithstanding the foregoing, the provisions of Section 4.8 of this Research

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Agreement will apply as specified therein to repayment of development loans advanced on account of the Compounds known as VX-680 and VX-528.

3.4. RECORDS.

VERTEX shall keep accurate records and books of accounts containing all data reasonably required for the calculation and verification of FTE's employed by VERTEX in the Research Program.

At NOVARTIS's request, VERTEX shall make those records available, no more than once a year, during reasonable working hours, for review by a recognized independent accounting firm acceptable to both parties, at NOVARTIS's expense, for the sole purpose of verifying the accuracy of those records in the calculation of Research Program FTE's. VERTEX shall not, however, be required to retain or make available to NOVARTIS or its accountants, any such records or books of account for any Research Year, beyond thirty-six (36) months from the conclusion of that Research Year. NOVARTIS shall cause the accounting firm to retain all such information in confidence.

In the event of a negative difference between the average number of FTE's stated to be involved in the Research Program and the number of FTE's actually employed, the amount previously advanced to VERTEX and attributable to any such negative difference shall be due and payable to NOVARTIS without delay. If the negative difference is more than [***] in any Research Year, then VERTEX shall also pay the reasonable costs of the independent accountant employed by NOVARTIS in the review. Interest at the rate of [***], assessed from the end of the Research Year to which the negative difference relates, shall be due from VERTEX upon prior written notice.

ARTICLE IV
LICENSE, DEVELOPMENT AND COMMERCIALIZATION RIGHTS

4.1. DEVELOPMENT ELECTION.

(a) NOVARTIS shall have the exclusive right (the "Development Election") to develop and commercialize, under the terms and conditions set forth in the License Agreement and for any and all Indications, (i) each Drug Product Candidate proposed to it by VERTEX as set forth below, and related Back-up Compounds as provided in Section 4.5 hereof and selected by NOVARTIS, and (ii) any Compound or Compounds selected by NOVARTIS, as provided in Section 4.1(d) hereof, from Compounds which have met the Development Candidate Criteria, whether or not any such Compound or Compounds have been proposed as Development Candidates by VERTEX. While the Development Election is in effect, VERTEX will

not grant to any Third Party rights to VERTEX Kinase Technology which are inconsistent with the grant of the Development Election to NOVARTIS hereunder. NOVARTIS's right to exercise Development Elections will expire and NOVARTIS shall no longer have the right to select Drug Candidates hereunder upon the first to occur of:

(1) The Final Termination Date as defined below;

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(2) Termination of the Research Program by VERTEX under Section 9.3 hereof;

(3) Termination of the Research Program by either party hereto for Scientific Cause under Section 9.5 hereof.

If NOVARTIS validly terminates the Research Program for cause under Section 9.2 hereof, the Development Election may nonetheless be exercised for the one-year period after the effective date of the termination for cause, but only with respect to Compounds which have met the Development Candidate Criteria prior to the effective termination date.

(b) VERTEX shall notify NOVARTIS and the JRC each time VERTEX has identified a Compound that, in the reasonable exercise of its scientific and business judgment, is a suitable Development Candidate and meets the Development Candidate Criteria. The corresponding notice shall be accompanied by the Development Candidate Information relating to the Development Candidate and its Back-up Compounds, provided that information concerning Compound structures shall be handled as specified in Section 5.1 hereof. NOVARTIS may, at its sole discretion, exercise its Development Election and accept the Development Candidate as a Drug Product Candidate by delivery of written notice to VERTEX [***]. The total period of time from receipt of notice from VERTEX through [***] shall be referred to as the "Notice Period". Notwithstanding any other provisions of this Research Agreement, the Development Election with respect to any Development Candidate will not expire until the end of the Notice Period with respect to that Development Candidate.

(c) [This subsection has been intentionally left blank.]

(d) VERTEX will submit a final report (the "Final Report") to NOVARTIS covering the period beginning on the Research Termination Date [***] (the "Final Report Period"). The Final Report will contain Development Candidate Information for any Compound that VERTEX believes, in the reasonable exercise of its scientific and business judgment, meets the Development Candidate Criteria [***], along with information with respect to relevant Back-up Compounds. The procedure whereby NOVARTIS may exercise its Development Election and accept any Development Candidate identified in the Final Report, for further development as a Drug Product Candidate, will be the same as that described in subsection (b) above, and the time period from receipt of the Final Report from VERTEX through the end of the 90-day period referenced in that subsection (b) shall be called the "Final Notice Period".

In addition, [***] If NOVARTIS, based on this information, concludes that a given Compound does meet the Development Candidate Criteria, a formal Development Election procedure pursuant to Section 4.1(b) will be initiated for such Compound. If VERTEX disagrees with NOVARTIS's judgment that a given Compound meets the Development Candidate Criteria, the dispute resolution provisions in Section 2.5.2(ii) shall apply.

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The date upon which the Final Report Period, as and if extended by the parties as provided for in Section 4.3 hereof, expires shall be called the "Final Termination Date."

(e) [***]

(f) Promptly following exercise by NOVARTIS of its Development Election, the parties will execute a License Agreement substantially identical to the license agreement attached hereto as Exhibit A. NOVARTIS will develop and commercialize the Drug Product Candidate under the provisions of the License Agreement. If the Development Election has previously been exercised with respect to another Drug Product Candidate and a License Agreement is in effect, then the License Agreement will be amended to reflect the addition of another Drug Product Candidate. Development of each Drug Product Candidate shall proceed immediately after the Development Election is exercised, in accordance with the terms of the License Agreement.

4.2. [This section has been intentionally left blank.]

4.3. EXTENSION OF NOTICE PERIOD AND FINAL NOTICE PERIOD.

NOVARTIS may propose to VERTEX by written notice delivered during [***] the Notice Period with respect to a particular Development Candidate, or the Final Notice Period, with specific reference to one or more Compounds included in the Final Report and meeting the Development Candidate Criteria, that the Notice Period or the Final Notice Period, as the case may be, for a specific Development Candidate or Compound be extended for good reason for a specified time to permit NOVARTIS, at its expense and under its direction, to conduct such additional studies of that Development Candidate or Compound as may be specified in the notice. VERTEX shall discuss this request with NOVARTIS and the parties shall attempt in good faith to reach mutual agreement with respect to the requested extension period and the conduct of additional studies, but failing agreement the applicable Notice Period or Final Notice Period shall expire as specified herein.

4.4. REFUSED CANDIDATE.

4.4.1. If NOVARTIS does not exercise its Development Election within the Notice Period or the Final Notice Period, as applicable, specified in Section 4.1, with respect to a particular Development Candidate proposed by VERTEX, then the Development Election will expire with respect to that Development Candidate (a "Refused Candidate"), and (a) NOVARTIS will relinquish all rights under this Research Agreement and the License Agreement [***] (b) VERTEX may thereafter develop and commercialize the Refused Candidate and any such Excluded Compounds at its expense free of any further obligation to NOVARTIS with respect thereto; and [***], shall be considered Excluded Compounds under the provisions of this Section 4.4.1.

4.4.2. [This section has been intentionally left blank.]

4.5. BACK-UP COMPOUNDS.

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The following provisions will apply with respect to Back-up Compounds to any Drug Product Candidate.

(a) VERTEX RESTRICTIONS ON NOMINATION AND DEVELOPMENT. So long as NOVARTIS is using commercially reasonable efforts with respect to the development of a particular Drug Product Candidate or the commercialization of a particular Drug Product, VERTEX will not (i) propose a Compound for development under the License Agreement which is a Back-up Compound with respect to that Drug Product Candidate or Drug Product, or (ii) until after the period starting on the date on which NOVARTIS has exercised its Development Election for a particular Drug Product Candidate and ending [***] (the "Lead Period"), commence development of that Back-up Compound either directly or together with or through an Affiliate or a Third Party.

(b) TERMINATION OF DEVELOPMENT OR COMMERCIALIZATION. If, prior to the end of the Lead Period with respect to a particular Drug Product or Drug Product Candidate, NOVARTIS ceases to use commercially reasonable efforts to develop or commercialize that Drug Product Candidate or Drug Product, then the restrictions on nomination and development referenced in subsection (a) above will no longer apply with respect to Back-up Compounds for that Drug Product Candidate or Drug Product unless NOVARTIS, without delay, commences another Development Program under the License Agreement with another Compound (a "Replacement Candidate") targeting the same Kinase, which Replacement Candidate is a Back-up Compound associated with the discontinued Drug Product Candidate or Drug Product, and NOVARTIS shall have the right to select for this purpose any such Back-up Compound by providing VERTEX with notice of its Development Election in this regard. Any such Back-up Compound for which NOVARTIS has exercised its Development Election under this subsection (b) shall hereafter be a Drug Product Candidate subject to the terms and conditions of the License

Agreement.

(c) TERMINATION OF RIGHTS TO BACK-UP COMPOUNDS. A Back-up Compound will no longer be subject to NOVARTIS's Development Election under the Research Agreement after the end of the Lead Period applicable to that Back-up Compound, except for Back-up Compounds which (i) subject to subsection (a) above, VERTEX has proposed for development on or before the Final Termination Date, and as to which NOVARTIS has exercised its Development Election hereunder; or (ii) have been or will be selected by NOVARTIS for development before the end of the applicable Lead Period under the provisions of subsection (b) above, or (iii) for which NOVARTIS has exercised or will exercise its Development Election before the end of the applicable Lead Period under the provisions of subsection (d) below.

(d) NOVARTIS RIGHTS TO LICENSE BACK-UP COMPOUNDS. Anytime prior to the expiry of the Lead Period with respect a particular Drug Product Candidate, NOVARTIS may also, by paying in each case the Back-up Election Fee provided under Section 6.1 of the License Agreement, exercise its Development Election with respect to any one or more Back-up Compounds associated with that Drug Product Candidate, provided that Drug Product Candidate, or a Back-up Compound selected pursuant to the provisions of subsection (b) above, is still in active development. Any such Back-up Compound for which NOVARTIS has exercised its

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Development Election under this subsection (d) shall become a "Drug Product Candidate Back-up Candidate" subject to the terms and conditions of the License Agreement.

(e) NOVARTIS OBLIGATIONS WITH RESPECT TO DRUG PRODUCT CANDIDATE BACK-UP CANDIDATES. So long as NOVARTIS is using commercially reasonable efforts, pursuant to the provisions of Sections 3.6 and 5.6 of the License Agreement, with respect to the development of a particular Drug Product Candidate or the commercialization of a particular Drug Product, NOVARTIS shall have no obligation to develop any of the Drug Product Candidate Back-up Candidates associated with that Drug Product Candidate or Drug Product. As soon as NOVARTIS ceases the development of a particular Drug Product Candidate, NOVARTIS's obligations to use diligent, commercially reasonable efforts will immediately shift from the discontinued Drug Product Candidate to an associated Drug Product Candidate Back-up Compound. If NOVARTIS ceases the development of a particular Drug Product Candidate and does not commence development of a Drug Product Candidate Back-up Compound pursuant to the foregoing, the license to the Drug Product Candidate and its Back-up Compounds under the License Agreement will expire and the license rights will revert to VERTEX.

4.6. [This section has been intentionally left blank.]

4.7. DRUG SUBSTANCE.

As soon as practicable after the exercise of its Development Election with respect to a Drug Product Candidate, VERTEX will deliver to NOVARTIS, if so requested by NOVARTIS, all drug substance for that Candidate in VERTEX's possession, if any, to the extent it is usable in connection with development of that Candidate. NOVARTIS will reimburse VERTEX for the Manufacturing Cost (as such term is defined in the License Agreement) of that material within thirty (30) days of receipt of VERTEX's invoice therefor.

4.8. SPECIAL PROVISIONS REGARDING VX-680, VX-528 AND VX-608.

The parties acknowledge that VERTEX is currently pursuing three Development Candidates which have been designated as VX-608, VX-680 and VX-528.

(a) VX-608. VX-608 will be governed by this Research Agreement and will be subject to the Development Election. The Notice Period with respect to VX-608 shall be deemed to have commenced on the later of (i) the date on which this Research Agreement is entered into, or (ii) the date by which NOVARTIS is in possession of the Development Candidate Information. If NOVARTIS exercises its Development Election with respect to VX-608 during the Notice Period, that Compound will become a Drug Product Candidate hereunder, and NOVARTIS will undertake all future development of VX-608 under the terms of the License Agreement. The Development Election Payment will be made to VERTEX and [***]. If NOVARTIS fails to exercise its Development Election with respect to VX-608 during the Notice Period, then VX-608 will become a Refused Candidate hereunder and the provisions of Section 4.4 will be applicable thereafter. Any outstanding development loan will be repaid in accordance with Section 3.3 hereof.

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(b) VX-680 AND VX-528. The Compounds designated by VERTEX as VX-680 and VX-528 are in early development under the provisions of the Original Agreement, and the terms of the Original Agreement shall continue to govern the rights and obligations of VERTEX and NOVARTIS with respect to VX-680 and VX-528 only, with the following modifications: (i) Section 6.4 of the original License Agreement which is part of the Original Agreement shall not be applicable; (ii) if VERTEX develops VX-680 to Proof of Concept under the Original Agreement and NOVARTIS declines to exercise its Development Election at that time, it will have no Second Opportunity to do so, and all rights to VX-680 and VX-528 will revert to VERTEX free and clear of any further obligation to NOVARTIS; and (iii) NOVARTIS will have no obligation to make further development loans to VERTEX on account of VX-680 or VX-528.

At its sole discretion exercisable by notice in writing from VERTEX to NOVARTIS delivered on or before June 30, 2004, VERTEX may elect to consider VX-680 and VX-528 as Development Candidates which have become Refused Candidates under the Research Agreement, and the terms and conditions of the Research Agreement as they apply to any Refused Candidate shall thereafter apply in the case of VX-680 and VX-528. Contemporaneously with the aforementioned notice, VERTEX shall repay to NOVARTIS that portion of the total amount of any development loan previously advanced by NOVARTIS to VERTEX on account of either Compound, which is unspent and uncommitted as of the notice date. The balance of any development loan shall be repaid as provided in Section 3.3 hereof.

ARTICLE V
CONFIDENTIALITY

5.1. UNDERTAKING.

During the term of this Research 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 Kinase Technology and NOVARTIS Kinase Technology.

(a) 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.

(b) 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 Drug Candidates, 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,

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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.

(c) 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.

(d) NOVARTIS will ensure that information with respect to the chemical structure of any Development Candidate which is delivered to NOVARTIS under Section 4.1(b) hereof as part of the Development Candidate Information with respect to that Development Candidate and its associated Back-up Compounds

will be distributed or otherwise made known only to [***] The foregoing limitation on distribution of information will cease being applicable at such time as NOVARTIS exercises its Development Election with respect to that Development Candidate.

5.2. EXCEPTIONS.

Notwithstanding the foregoing, the provisions of Section 5.1 hereof shall not apply to knowledge, information, documents or materials which the receiving party can conclusively establish:

(a) have entered the public domain without such party's breach of any obligation owed to the disclosing party;

(b) are permitted to be disclosed by the prior written consent of the disclosing party;

(c) 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;

(d) are disclosed by the disclosing party to a Third Party without restrictions on its disclosure;

(e) are independently developed by the receiving party without breach of this Research Agreement; or

(f) 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.

Either VERTEX or NOVARTIS may at any time, by notice in writing to the other party, waive any or all of the confidentiality obligations to which the other party is subject hereunder, for any length of time or with respect to any specific information.

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5.3. PUBLICITY.

The parties will agree upon the timing and content of any initial press release or other public communications relating to this First Revised and Restated Agreement and the transactions contemplated herein.

(a) 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 Research Agreement or concerning the transactions described herein shall be made, either directly or indirectly, by VERTEX or NOVARTIS, 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.

(b) 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.

5.4. SURVIVAL.

The provisions of this Article V shall survive the termination of this Research Agreement and shall extend for a period of five (5) years thereafter.

ARTICLE VI
PUBLICATION

Each of NOVARTIS 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 V hereof, (ii) information that if

published would have an adverse effect on a patent application covering the subject matter of this Research Agreement 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 Candidate. 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 V of this Research 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 JSC for resolution. If the JSC is unable to reach agreement on the matter within

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thirty (30) days after such referral, the matter shall be referred by the JSC to the Chief Executive Officer of NOVARTIS 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 two (2) weeks of referral by the JSC as aforesaid, then the decision of the publishing party as to publication of any information generated by it, subject always to the confidentiality provisions of Article V hereof, shall be final, provided that such decision shall be exercised with reasonable regard for the interests of the non-publishing party. 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.

This Article VI shall terminate with the termination of this Research Agreement, but the provisions of Article V hereof shall continue to govern the disclosure by one party, whether by publication or otherwise, of Confidential Information of the other, during the period set forth in Section 5.4.

ARTICLE VII
INDEMNIFICATION

7.1. INDEMNIFICATION BY VERTEX.

VERTEX will indemnify and hold NOVARTIS 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 Compound, a Development Candidate, a Drug Product Candidate or a Drug Product by VERTEX or its Affiliates or their representatives, agents, authorized sublicensees or subcontractors under this Research 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 Research Agreement; and

(c) provided however, that the foregoing indemnification shall not apply to any Loss to the extent such Loss is caused by the negligent or willful misconduct of NOVARTIS or its Affiliates.

7.2. INDEMNIFICATION BY NOVARTIS.

NOVARTIS 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 Compound, a Development Candidate, a Drug Product Candidate or a Drug Product by

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NOVARTIS or its Affiliates or their representatives, agents, authorized sublicensees or subcontractors under this Research 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 NOVARTIS of any of its covenants, representations or warranties set forth in this Research Agreement; and

(c) 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.

7.3. CLAIMS PROCEDURES.

Each Party entitled to be indemnified by the other Party (an "Indemnified Party") pursuant to Section 7.1 or 7.2 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:

(a) 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

(b) The failure of any Indemnified Party to give notice as provided herein shall not relieve the Indemnifying Party of its obligations under this Research Agreement to the extent that the failure to give notice did not result in harm to the Indemnifying Party.

(c) 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.

(d) 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.

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7.4. COMPLIANCE.

The parties shall comply fully with all applicable laws and regulations in connection with their respective activities under this Research Agreement.

ARTICLE VIII
PATENTABLE INVENTIONS

8.1. OWNERSHIP.

All inventions made and all Know-How generated exclusively by either party or its Affiliates (directly or through others acting on its behalf) prior to and during the term of this Research Agreement shall be owned by the party making the invention or generating the Know-How claimed, or if such invention is made jointly (a "Joint Invention"), shall be owned jointly, all as determined in accordance with United States laws of inventorship.

8.2. PREPARATION.

VERTEX shall take responsibility for the preparation, filing, prosecution and maintenance of all VERTEX Patents, and any patents and patent applications claiming Joint Inventions, and NOVARTIS shall take responsibility for the preparation, filing, prosecution and maintenance of all NOVARTIS Patents. VERTEX shall provide the JRC with periodic reports listing, by name, Patents filed by VERTEX in the United States and other jurisdictions, along with a general summary of the claims made and the jurisdictions of filing. In good time, before the deadline for foreign filing of any patent application filed in the United States, VERTEX will notify NOVARTIS whether it intends to foreign file such patent application, and if it intends to do so, in what countries it proposes to foreign file. Upon timely written notice from NOVARTIS, VERTEX will file in such additional countries -- all being countries in which NOVARTIS would customarily file its own cases dealing with similar subject matter -- as NOVARTIS shall request.

8.3. COSTS.

(a) During the Research Program. NOVARTIS shall reimburse VERTEX for [***]. If the full amount of any reimbursement commitment is not applied in any Research Year, the unused balance may be carried over from year to year during the Research Program.

(b) After the Research Program. Upon expiration of the Research Program, the parties shall determine which Patents covering Drug Product Candidates and Drug Products, and Development Candidates and Back-up Compounds as to which the Development Election is still applicable (until it expires), are included in the Kinase Technology, and thereafter [***]. Either party may at any time thereafter elect, by written notice to the other party, to discontinue support for one or more such Patents (a "Discontinued Patent") and shall not be responsible for any costs relating to a Discontinued Patent which are incurred more than sixty (60) days after receipt of that notice by the other party. In such case, the other party may elect at its sole discretion to continue preparation, filing, prosecution or maintenance of the Discontinued Patent at its sole expense. The party so continuing shall own any such Patent, and if the party electing to discontinue support is the owner of the Discontinued Patent, it shall execute such documents of transfer or assignment and perform such acts as may be reasonably necessary to transfer ownership of the Discontinued Patent to the other party and enable that party to file or to

continue prosecution or maintenance, if the other party elects to do so. Discontinuance may be on a country-by-country basis or for a Patent series in total.

ARTICLE IX
TERM AND TERMINATION

9.1. TERM.

9.1.1. This Research Agreement shall have retroactive effect to the Effective Date, replacing and superceding the rights and obligations of the parties under the Original Agreement, except that the terms of the Original Agreement shall be deemed to govern the rights and obligations of the parties with respect to the Compounds known as VX-680 and VX-528, pursuant to the provisions of Section 4.8 of this Research Agreement. This Research Agreement will extend until the Final Termination Date as defined herein, unless earlier terminated by either party hereto in accordance with this Research Agreement, or unless extended by mutual agreement of the parties; provided that the Agreement will be deemed to continue in effect with respect to any Drug Product Candidate during the Lead Period with respect to that Candidate, but only insofar as necessary to enable NOVARTIS to exercise its Development Election under Section 4.5 hereof with respect to any Back-up Compounds for that Drug Product Candidate.

9.2. TERMINATION OF THE RESEARCH PROGRAM BY NOVARTIS FOR CAUSE.

Upon written notice to VERTEX, NOVARTIS may at its sole discretion unilaterally terminate the Research Program and this Research Agreement upon the occurrence of any of the following events:

(a) VERTEX shall materially breach any of its material obligations, such as its obligations under Section 3.2 hereof, under this Research Agreement or the License Agreement, and such material breach shall not have been remedied or steps initiated to remedy the same to NOVARTIS's reasonable satisfaction, within sixty (60) days after NOVARTIS 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 Majeure, strike, labor dispute or any other events over which it has no control.

In the event of any valid termination under this Section 9.2, NOVARTIS shall not be required to make any payments under Section 3.2 hereof which are not due and payable prior to receipt by VERTEX of the notice of breach referenced under Section 9.2(a) or receipt by VERTEX of the notice of termination pursuant to Section 9.2(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.

9.3. TERMINATION OF THE RESEARCH PROGRAM BY VERTEX FOR CAUSE.

VERTEX may at its sole discretion terminate this Research Agreement upon written notice to NOVARTIS upon the occurrence of any of the following events:

(a) NOVARTIS shall materially breach any of its material obligations under this Research 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 NOVARTIS; or

(b) NOVARTIS shall cease to function as a going concern by suspending or discontinuing its business for any reason except for interruptions caused by Force Majeure, 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.

9.4. [This section has been intentionally left blank.]

9.5. TERMINATION FOR SCIENTIFIC CAUSE.

Either party may terminate this Research Agreement upon six months' prior written notice to the other party, if the terminating party can demonstrate to the reasonable satisfaction of the other party that, by reason of scientific developments unknown on the Effective Date, the Research Program is unlikely to produce any Compounds that can achieve a commercially viable therapeutic effect through an effect on a Kinase target.

9.6. EFFECT OF TERMINATION.

(a) Except where explicitly provided elsewhere herein, termination of this Research Agreement for any reason, or expiration of this Research 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 Research Agreement, including obligations of confidentiality under Article V hereof, the indemnification provisions of Article VII hereof and the rights and obligations of the parties during the Lead Period under Sections 4.1 and 4.5 with respect to a particular Drug Product Candidate and related Back-up Compounds.

(b) Upon termination or expiration of this Research Agreement, NOVARTIS and VERTEX will retain exclusive rights to their respective Kinase Technology (including intellectual property), except NOVARTIS shall hold those rights to VERTEX Technology provided in any License Agreement in effect on the Final Termination Date covering Drug Product Candidates selected by NOVARTIS, and shall hold those rights to Back-up Compounds and Drug Product Candidate Back-up Compounds provided in Sections 4.1(e) and 4.5.

ARTICLE X
REPRESENTATIONS AND WARRANTIES

10.1. REPRESENTATIONS AND WARRANTIES OF VERTEX.

VERTEX represents and warrants to NOVARTIS as follows: (a) Authorization. This Research 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, bankruptcy, reorganization, moratorium and other laws relating to or affecting creditors'

rights generally and by general equitable principles.

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The execution, delivery and performance of this Research 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 Kinase Technology relating to the Field and to grant the licenses herein. The granting of the Development Election to NOVARTIS 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 Research Agreement or their respective agents, VERTEX is not aware of any issued patents or pending patent applications that, if issued, would be infringed by the development, manufacture, use or sale of any Compound, Development Candidate or Drug Product Candidate pursuant to this Research Agreement.

10.2. REPRESENTATIONS AND WARRANTIES OF NOVARTIS.

NOVARTIS represents and warrants to VERTEX as follows:

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

The execution, delivery and performance of this Research Agreement have been duly authorized by all necessary action on the part of NOVARTIS, its officers and directors.

(b) Third Party Rights. NOVARTIS owns or possesses adequate licenses or other rights to use all NOVARTIS Kinase Technology relating to the Field in accordance with the provisions of this Research Agreement.

(c) Third Party Patents. Except as disclosed in writing between the parties to this Research Agreement or their respective agents, NOVARTIS is not aware of any issued patents or pending patent applications that, if issued, would be infringed by the development, manufacture, use or sale of any Compound, Development Candidate or Drug Product Candidate pursuant to this Research Agreement.

ARTICLE XI
DISPUTE RESOLUTION

11.1. GOVERNING LAW, AND JURISDICTION.

This Research Agreement shall be governed and construed in accordance with the internal laws of the State of New York.

11.2. 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 Research Agreement, or the collaborative effort contemplated hereby, the parties shall, and either party may, initially refer such dispute to the JSC, and failing resolution of the controversy or claim within thirty (30) days after such referral, the matter shall be referred

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to the Chief Executive Officer of VERTEX and the Chief Executive Officer of NOVARTIS 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 date of initial referral of the matter to the JSC, either party shall be free to initiate proceedings in any court having requisite

jurisdiction.

(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 Research 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 NOVARTIS as provided below. The "Referral Matter" shall consist solely of disagreements concerning whether a particular Compound has satisfied all of the applicable Development Candidate Criteria. Within thirty (30) days after delivery of the above-referenced written request, each party will appoint one person who is not an Affiliate of the party appointing that person, and who is 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 thirty (30) day period referenced above, then the appointee who has been designated by the other party 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 XII
MISCELLANEOUS PROVISIONS

12.1. OFFICIAL LANGUAGE.

English shall be the official language of this Research Agreement and the License Agreement, and all communications between the parties hereto shall be conducted in that language.

12.2. WAIVER.

No provision of this Research 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.

12.3. 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.

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12.4. SEVERABILITY.

Should one or more provisions of this Research 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 Research 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 Research Agreement shall nevertheless not affect the validity of the Agreement as a whole, unless the invalid provisions are of such essential importance for this Research Agreement that it may be reasonably presumed that the parties would not have entered into this Research Agreement without the invalid provisions.

12.5. 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 NOVARTIS or VERTEX under this Research Agreement, the party, if any, not so affected, shall have the right, at its option, to suspend or terminate this Research 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, are not successful after a reasonable period of time in producing mutually acceptable modifications to this Research Agreement.

12.6. GOVERNMENT APPROVALS.

Each party will obtain any government approval required in its country of domicile to enable this Research 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.

12.7. EXPORT CONTROLS.

This Research Agreement is made subject to any restrictions concerning the export of materials and Technology from the United States which may be imposed upon or related to either party to this Research Agreement from time to time by the Government of the United States. Furthermore, NOVARTIS will not export, directly or indirectly, any VERTEX Kinase Technology or any Bulk Drug Substance, Drug Product Candidates or Drug Products utilizing such Technology 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.

12.8. ASSIGNMENT.

This Research 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 Research 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 12.8 shall, at the option of the non-assigning party,

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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. This Research Agreement shall be binding upon and enforceable against the successor to or any permitted assignees from either of the parties hereto.

12.9. 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. The use of subcontractors by either party shall not increase the financial obligations of the other party hereunder in any respect.

12.10. COUNTERPARTS.

This Research 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.

12.11. NO AGENCY.

Nothing herein contained shall be deemed to create an agency, joint venture, amalgamation, partnership or similar relationship between NOVARTIS and VERTEX. Notwithstanding any of the provisions of this Research Agreement, neither party to this Research 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 Research 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.

12.12. NOTICE.

All communications between the parties with respect to any of the provisions of this Research 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 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 NOVARTIS, at:

NOVARTIS PHARMA AG
Business Development and Licensing
P.O. Box
CH-4002
Basel, Switzerland
Attention: Victor A. Hartmann, Vice President

with a copy to: Legal Services, at the address referenced above

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if to VERTEX, at:

Vertex Pharmaceuticals Incorporated
130 Waverly Street
Cambridge, MA U.S.A. 02139-4211
Attention: President

with a copy to: Legal Department
Attention: General Counsel

12.13. 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.

12.14. AUTHORITY.

The undersigned represent that they are authorized to sign this Research Agreement on behalf of the parties hereto. The parties each represent that no provision of this Research 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 Research Agreement.

12.15. ENTIRE AGREEMENT.

This Research Agreement, together with the Original Agreement insofar as it remains applicable, as set forth in the Recitals, in Section 4.8 and elsewhere herein, with respect to VX-680 and VX-528 only, and the respective License Agreements thereto, 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.

12.16. STANDSTILL.

During [***] neither NOVARTIS nor any of its Affiliates will acquire or hold, or without the prior approval of the VERTEX Board of Directors, will propose to acquire or hold, at any time, of record or beneficially, more than [***] of the outstanding voting securities of VERTEX, nor will NOVARTIS participate in a group (as the term "group" is referenced in Section 14(d) of the U.S. Securities Exchange Act of 1934 and Regulations promulgated thereunder) which acquires or holds, or proposes to acquire or hold, such amount of securities during the referenced time period; provided that NOVARTIS shall not be required to reduce its share holdings if its ownership percentage increase above [***] by reason of the actions of VERTEX, including without limitation any recapitalization or repurchase of shares by VERTEX. Notwithstanding the foregoing: (A) if a tender offer directed toward the acquisition of more than [***] of the voting securities of VERTEX is commenced by a Third Party who is not then or during the pendency of that tender offer a member of a "group" in which NOVARTIS is participating, then NOVARTIS may during the pendency of that tender offer commence a competing tender offer, and may thereafter complete that offer in accordance with its terms (as revised from time to time), notwithstanding any limitation on the acquisition or holding of VERTEX shares as set forth above; provided that if any such tender offer by NOVARTIS is not completed or is withdrawn, the provisions of this Section 12.16 shall thereafter apply to any

subsequent share acquisitions by NOVARTIS as if the previous tender offer had not occurred; (B) if VERTEX shall make a public announcement that it intends to enter into a transaction which will result in the acquisition of a controlling interest in VERTEX's voting securities by a Third Party which is not a member of a "group" that includes NOVARTIS, then at any time thereafter and during the period ending with the closing of any such transaction or the public announcement of its termination, NOVARTIS may make a competing proposal for a transaction with VERTEX or for VERTEX's shares, and the provisions of the first sentence of this Section 12.16 shall not operate to prevent the completion of any such proposal or require the sale or divestiture of any VERTEX shares acquired by NOVARTIS during that period; and (C) if a Third Party which is not a member of a "group" that includes NOVARTIS, should acquire more than [***] of VERTEX's voting securities, then, during such period as that Third Party owns more than [***] of VERTEX's voting securities, NOVARTIS is entitled to increase its holdings of VERTEX's voting securities, by purchase from Third Parties, to an amount which will not exceed, at the time of the share purchase by NOVARTIS, the amount owned by such Third Party. This limitation shall not be applicable if the provisions set forth in (A) above, otherwise apply.

12.17. NOTICE OF PHARMACEUTICAL SIDE-EFFECTS.

During the term of this Research Agreement, the parties shall keep each other promptly and fully informed and will promptly notify appropriate authorities in accordance with applicable law, after receipt of information with respect to any serious adverse event (as defined by the ICH Harmonized Tripartite Guideline on Clinical Safety Data Management), directly or indirectly attributable to the use or application of Compounds, a Development Candidate, Bulk Drug Substance, a Drug Product Candidate or a Drug Product.

12.18. INFLATION ADJUSTMENT.

All payments required to be made to VERTEX hereunder (except any royalty payments required to be made under the provisions of Section 6.3 of the License Agreement) shall be adjusted at the beginning of each Research Year (commencing at the beginning of Research Year 2) to reflect the impact of inflation since the Effective Date of the Agreement, as measured by the biotech worker inflation rate defined and reported in the Radford Survey (Radford/AON Consulting Inc., San Francisco, CA), or other mutually acceptable index. Notwithstanding the foregoing, no adjustment shall be required in any Research Year in which the appropriate inflation adjustment, if applied, would result in a change of less than [***] in the relevant payment amount.

12.19. INVOICE REQUIREMENT.

Any amounts payable to VERTEX hereunder (except any royalty payments required to be made under the provisions of Section 6.3 of the License Agreement) shall be made within thirty days after receipt by NOVARTIS, or its nominee designated for that purpose in advance by NOVARTIS in writing to VERTEX, of an invoice covering such payment, which invoice shall conform to the extent reasonably practicable to the form of invoice contained in Exhibit B to this Research Agreement.

12.20. HARDSHIP.

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If as a result of unforeseen events or developments relating to the subject matter of this Research Agreement, the performance of this Research Agreement shall cause inequitable economic hardship for one party which runs counter to the objectives of this Research Agreement and which the other party cannot reasonably and in good faith expect the first party to bear unrelieved, the parties will meet and seek in good faith to find equitable means of amending this Research Agreement to reestablish a fair and reasonable economic balance under this Research Agreement between the parties hereto.

VERTEX PHARMACEUTICALS INCORPORATED

By: /s/ Kenneth S. Boger

Kenneth S. Boger
Title: Senior Vice President and
General Counsel

NOVARTIS PHARMA AG

By: /s/ Stephanie Lassarat

Title: Senior Legal Counsel

By: /s/ W. Steiger

Title: Head of Administration, NIBR Basil

Schedule 1.13

Excluded Compounds and Excluded Kinases

Excluded Kinases

	SWISSPROT Designation
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
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[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]

Excluded Compounds

[***]

Schedule 1.13

CONFIDENTIAL TREATMENT REQUESTED

Schedule 2.4.3

Development Candidate Criteria

[***]

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

CONFIDENTIAL TREATMENT REQUESTED

Exhibit A

FORM OF LICENSE, DEVELOPMENT AND COMMERCIALIZATION AGREEMENT

CONFIDENTIAL TREATMENT REQUESTED

EXHIBIT B

FORM OF INVOICE

[COMPANY Letterhead]

[Date]

Novartis Pharma AG
Zentraler Faktureneingang
Attn: Ms. R. Aschwanden
Lichtstrasse 35
CH - 4002 Basel
Switzerland

Dear Ms. Aschwanden

Re: [COMPANY] License Agreement for [PRODUCT]

This is an invoice requesting payment in connection the above-captioned Agreement between [COMPANY] and Novartis Pharma AG.

Novartis Contract Code No:	[will be assigned within Novartis following execution]
Novartis Cost Centre:	630926 / 393120
SPECIFICATION:	[PLEASE SPECIFY THE EVENT FOR WHICH THE INVOICE IS DUE, AND ADD ANY COPIES OF INVOICES FROM THIRD PARTIES IN CASE REIMBURSEMENT FOR THIRD PARTY WORK IS AGREED TO]
Amount and Currency:	[self-explanatory]
Bank address and Account No:	[insert the name and address of the bank to which the payment should be sent and the account number to which it should be credited]

Sincerely yours,

[COMPANY]

First Revised and Restated
Research and Early Develoment Agreement -- Confidential
Exhibit B

CONFIDENTIAL TREATMENT

EXHIBIT A

LICENSE, DEVELOPMENT AND COMMERCIALIZATION AGREEMENT

BETWEEN

VERTEX PHARMACEUTICALS INCORPORATED

AND

NOVARTIS PHARMA AG

LICENSE, DEVELOPMENT AND COMMERCIALIZATION AGREEMENT

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LICENSE AND DEVELOPMENT AGREEMENT

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LICENSE, DEVELOPMENT AND COMMERCIALIZATION 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 NOVARTIS PHARMA AG (hereinafter "NOVARTIS"), a Swiss corporation with principal offices at Lichtstrasse 35, CH-4056 Basel, Switzerland.

INTRODUCTION

WHEREAS, VERTEX and NOVARTIS are parties to a certain First Revised and Restated Research Agreement dated January __, 2004 (the "Research Agreement") which revised and restated a certain Research and Early Development Agreement dated May 8, 2000 (the "Original Agreement"), under which VERTEX is attempting to design novel, small-molecule compounds targeting the Kinase protein

superfamily; and

WHEREAS, NOVARTIS may elect to develop and commercialize compounds proposed by VERTEX under the Research Agreement; and

WHEREAS, in accordance with the Research Agreement NOVARTIS has elected to develop and commercialize the Drug Product Candidates designated on SCHEDULE 1.12 hereto, and the parties therefore wish to execute this License, Development and Commercialization Agreement, which is identical in substance to the agreement attached as Exhibit A to the Research Agreement, to memorialize the provisions specific to development and commercialization of Drug Product Candidates;

WHEREAS, the parties have special rights and obligations with respect to Back-up Compounds to the Drug Product Candidates (as defined in the Research Agreement); and

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

ARTICLE I
DEFINITIONS

For purposes of this Agreement, the terms defined in this Article 1 shall have the following meanings whether used in their singular or plural forms. Use of the singular shall include the plural and vice versa, unless the context requires otherwise:

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, more

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than 50% of the voting stock of any other Person. For the avoidance of any doubt, the Novartis Institute for Functional Genomics, Inc. and The Friedrich Miescher Institute, as currently operated, are not Affiliates of NOVARTIS for the purposes of this Agreement.

1.1.1. "CHANGE OF CONTROL" shall mean (a) a transaction which results in the voting securities of VERTEX immediately prior to such transaction ceasing to represent more than fifty percent (50%) of the combined voting power of the surviving entity immediately after such transaction; (b) any Third Party (other than any trustee or other fiduciary holding securities under an employee benefit plan, or any corporation or other entity owned directly or indirectly by the stockholders of such party in substantially the same portion as their ownership of stock of such party) becoming the beneficial owner of more than fifty percent (50%) of the combined voting power of the outstanding securities of VERTEX; or (c) a sale to a Third Party of all or substantially all of the business of VERTEX necessary for VERTEX's performance under this Agreement.

1.2. "GLOBAL BRAND TEAM" or "GBT" shall have the meaning set forth in Section 5.2 hereof; and "BACK-UP COMPOUND" shall have the meaning set forth in Section 1.1.1 of the Research Agreement.

1.3. [This section has been intentionally left blank.]

1.4. "BULK DRUG SUBSTANCE" shall mean a Drug Product Candidate in bulk crystal, powder or other form suitable for incorporation in a Drug Product.

1.5. "CONTROLLED" shall mean the legal authority or right of a party hereto to grant a license or sublicense of intellectual property rights to another party hereto, or to otherwise disclose proprietary or trade secret information to such other party, without breaching the terms of any agreement with a Third Party, infringing upon the intellectual property rights of a Third Party, or misappropriating the proprietary or trade secret information of a Third Party.

1.6. [This section has been intentionally left blank.]

1.7. (a) "DEVELOPMENT CANDIDATE" shall have the meaning ascribed to it in the Research Agreement.

(b) "DEVELOPMENT ELECTION FEE" and "BACK-UP ELECTION FEE" shall each have the meaning ascribed to it in Section 6.1 hereof.

1.8. "DEVELOPMENT PLAN" shall have the meaning ascribed to it in Section

3.2.2 hereof.

1.9. "DEVELOPMENT PROGRAM" shall mean activities associated with development of a Drug Product Candidate which are conducted by or at the direction of NOVARTIS after the Development Election has been exercised with respect to that Drug Product Candidate, including but not limited to (a) manufacture and formulation of Drug Product Candidates for use in pre-clinical, non-clinical and clinical studies; (b) pre-clinical and non-clinical animal studies performed in accordance with GLP (or the applicable equivalent); (c) planning, implementation, evaluation and administration of human clinical trials; (d) manufacturing process development, scale-up and commercial manufacture of Drug Product; (e) preparation and submission of

applications for Regulatory Approval; and (f) post-market surveillance of approved drug indications, as required or agreed as part of a marketing approval by any governmental regulatory authority.

1.10. [This Section has been intentionally left blank.]

1.11. "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.

1.12. "DRUG PRODUCT CANDIDATE" shall mean any Development Candidate or Drug Product Candidate Back-up Candidate listed from time to time on Schedule 1.12 hereof, as to which NOVARTIS has exercised the Development Election under the Research Agreement and which has become a subject of this License Agreement in accordance with the provisions thereof; and "Drug Product Candidate Back-up Candidate" shall have the meaning set forth in Section 7.4 of this Agreement.

1.13. "EFFECTIVE DATE" shall mean the effective date of this Agreement as set forth on the first page hereof.

1.14. [This section has been intentionally left blank.]

1.15. "FIELD" shall mean the treatment or prevention of conditions or diseases in humans, principally by affecting a Kinase other than an Excluded Kinase.

1.16. "FIRST COMMERCIAL SALE" shall mean the first sale of a Drug Product by NOVARTIS or an Affiliate or sublicensee of NOVARTIS 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.

1.17. "FILING OUTSIDE THE U.S." shall mean any application or regulatory filing to be made hereunder with a regulatory authority outside the United States, for approval to manufacture and sell Drug Product(s) outside the U.S., and any correspondence, approvals or governmental licenses relating thereto.

1.18. [This section has been intentionally left blank.]

1.19. "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 regulations or standards of countries outside the United States as may be applicable to activities conducted hereunder; and "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 regulations or standards of countries outside the United States as may be applicable to activities conducted hereunder.

1.20. "INDICATION" shall mean a recognized disease or condition, an important manifestation of a disease or condition, or symptom associated with a disease or syndrome for

which use of a Drug Product is indicated, as would be identified in the Drug Product's label under applicable FDA regulations or the foreign equivalent thereof.

1.21. "IND" shall mean the investigational new drug application relating to a Drug Product Candidate 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 Filing(s) Outside the U.S. (such as a CTX in

the European Union).

1.22. "INTERNATIONAL PROJECT TEAM" or "IPT" shall have the meaning set forth in Section 3.2.1 hereof.

1.23. "JOINT STEERING COMMITTEE" or "JSC" shall have the meaning set forth in Section 2.6 of the Research Agreement.

1.24. "KNOW-HOW" means all proprietary material and information including 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 Controlled by a Party or its Affiliates and that relate to the 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; provided however, that for the purposes of the definition of VERTEX Know-How only, the term "Know-How" shall not include VERTEX's general drug design technology, whether in software or hardware, tangible or intangible, form; and "Lead Period" shall mean the period starting on date this Agreement is effective with respect to a particular Drug Product Candidate and ending on the second anniversary thereafter.

1.25. "MAJOR MARKETS" shall mean those countries listed on SCHEDULE 1.25 hereto.

1.26. "MANUFACTURING COST" shall mean [***].

1.27. "NET SALES" with respect to any Drug Product shall mean the gross amount invoiced by NOVARTIS and any NOVARTIS Affiliate, licensee or sublicensee for that Drug Product sold to Third Parties in bona fide, arms-length transactions, less [***]; all as determined in accordance with NOVARTIS' usual and customary accounting methods, which are in accordance with generally accepted accounting principles (GAAP).

1.27.1. In the case of any sale or other disposal of a Drug Product between or among NOVARTIS and its Affiliates, licensees and sublicensees, for resale, Net Sales shall be calculated as above only on the value charged or invoiced on the first arm's-length sale thereafter to a Third Party;

1.27.2. In the case of any sale which is not invoiced or is delivered before invoice, Net Sales shall be calculated at the time of shipment or when the Drug Product is paid for, if paid for before shipment or invoice;

1.27.3. In the case of any 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 value of the consideration received or the fair market price (if higher) of the Drug Product in the country of sale or disposal;

1.27.4. In the event the Drug Product is sold in a finished dosage form containing the Drug Product in combination with one or more other active ingredients (a "Combination Product"), the Net Sales of the Drug Product, for the purposes of determining royalty payments, shall be determined by [***].

1.28. "NOVARTIS KNOW-HOW" shall mean all Know-How of NOVARTIS.

1.29. "NOVARTIS PATENTS" shall mean any Patents Controlled by NOVARTIS or any of its Affiliates claiming Bulk Drug Substance, a Drug Product Candidate or a Drug Product, or a formulation or prodrug thereof, discovered or identified by NOVARTIS or its Affiliates during the course of the Research Program or a Development Program, or a method of making or using Bulk Drug Substance, a Drug Product Candidate or a Drug Product, or a prodrug thereof, or an improvement to the subject matter of a Patent covering any of the foregoing. A list of NOVARTIS Patents is appended hereto as Schedule 1.29 and will be updated periodically to reflect additions thereto during the term of this Agreement. NOVARTIS shall keep VERTEX periodically informed in writing of all NOVARTIS Patents.

1.30. "NOVARTIS TECHNOLOGY" shall mean all NOVARTIS Patents and all NOVARTIS Know-How which is applied by NOVARTIS to the development, manufacture or use of Bulk Drug Substance, a Drug Product Candidate or a Drug Product.

1.31. "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 supplementary protection 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.

1.32. "PERSON" shall mean any individual, corporation, partnership, association. joint-stock company, trust, unincorporated organization or government or political subdivision thereof.

1.33. "PIVOTAL REGISTRATION STUDY" shall mean a human clinical trial conducted for inclusion in (i) that portion of the FDA submission and approval process which provides for the continued trials of a Drug Candidate on sufficient numbers of patients to generate safety and efficacy data to support Regulatory Approval in the proposed therapeutic indication, as more fully defined in 21 CFR. ss. 312.21(c), and (ii) equivalent submissions with similar requirements in other countries.

1.34. "REGULATORY APPROVAL" shall mean, with respect to any country, all authorizations by the appropriate governmental entity or entities necessary for commercial sale of a Drug Product in that country including, without limitation and where applicable, approval of labeling, price, reimbursement and manufacturing. "Regulatory Approval" in the United States

shall mean final approval of a new drug application pursuant to 21 CFR ss. 314, permitting marketing of the applicable Drug Product in interstate commerce in the United States. "Regulatory Approval" in the European Union shall mean final approval of a Marketing Authorization Application pursuant to Council Directive 75/319/EEC, as amended, or Council Regulation 2309/93/EEC, as amended.

1.35. "RESEARCH AGREEMENT" shall mean that certain First Revised and Restated Research and Early Development Agreement between VERTEX and NOVARTIS dated February 3, 2004. 1.36. [This section has been intentionally left blank.]

1.37. [This section has been intentionally left blank.]

1.38. "TECHNOLOGY" shall mean VERTEX Technology and NOVARTIS Technology.

1.39. "TERRITORY" shall mean all the countries in the world.

1.40. "THIRD PARTY" shall mean any person or entity which is not a party or an Affiliate of any party to this Agreement.

1.41. [This section has been intentionally left blank.]

1.42. "VALID PATENT CLAIM" shall mean either (a) a claim of an issued and unexpired Patent which has not been revoked or held permanently unenforceable or invalid by a decision of a court or other governmental agency of competent jurisdiction, unappealable or unappealed within the time allowed for appeal, and which has not been admitted to be invalid or unenforceable through reissue or disclaimer or otherwise, or (b) a claim of a pending patent application which claim was filed in good faith and has not been abandoned or finally disallowed without the possibility of appeal or refiling of said application.

1.43. "VERTEX KNOW-HOW" shall mean all Know-How of VERTEX.

1.44. "VERTEX PATENTS" shall mean any Patents Controlled by VERTEX or any of its Affiliates claiming Bulk Drug Substance, a Drug Product Candidate or a Drug Product, or a formulation or prodrug thereof, discovered or identified by VERTEX or its Affiliates during the course of the Research Program and the Development Program, or a method of making or using Bulk Drug Substance, a Drug Product Candidate or a Drug Product, or a prodrug thereof, or an improvement to the subject matter of a Patent covering any of the foregoing. A list of VERTEX Patents is appended hereto as Schedule 1.44 and will be updated periodically to reflect additions thereto during the term of this Agreement.

1.45. "VERTEX TECHNOLOGY" shall mean all VERTEX Patents and all VERTEX Know-How.

1.46. The term "EUROPEAN UNION" shall mean those countries which are now or later become members of the European Union.

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 NOVARTIS.

(a) Subject to the other provisions of this Agreement, VERTEX hereby grants to NOVARTIS an exclusive worldwide license under VERTEX Technology to the extent useful to permit NOVARTIS 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, as provided herein, Bulk Drug Substance, Drug Product Candidates and Drug Products worldwide. NOVARTIS shall have the right to sublicense under this Agreement. Subject to the provisions of this Agreement, VERTEX shall have the right to use VERTEX Technology to discharge its obligations and exercise its rights under this Agreement. VERTEX retains all rights to VERTEX Technology except to the extent explicitly granted to NOVARTIS hereunder.

(b) NOVARTIS may subcontract its rights to manufacture Bulk Drug Substance, Drug Product Candidates, and Drug Product and may contract with reputable organizations to conduct or assist in the conduct of human clinical trials and the evaluation of trials data, after prior notice to, but without the consent of, VERTEX. NOVARTIS shall be responsible to VERTEX for the performance of any of its sublicensees or subcontractors under any provisions of this Agreement for which NOVARTIS is responsible. NOVARTIS shall not permit any subcontractors or sublicensees to use VERTEX Technology without provisions safeguarding confidentiality at least equivalent to those provided in this Agreement. Any such provisions will allow VERTEX the right to directly enforce the obligations of confidentiality with respect to VERTEX Technology in possession of the Third Party.

(c) The license set forth in subsection (a) above may be [***] upon reasonable and customary terms and conditions mutually agreeable to the parties. [***]

2.2. GRANT TO VERTEX. Subject to the other provisions of this Agreement, NOVARTIS hereby grants to VERTEX a non-exclusive, worldwide license or (as appropriate) sublicense under NOVARTIS Technology, only to the extent necessary to permit VERTEX to carry out the activities which it is permitted to undertake in this Agreement. VERTEX shall not sublicense such license to the NOVARTIS Technology without the consent of NOVARTIS (which shall not be unreasonably withheld). Any permitted sublicense will contain provisions safeguarding confidentiality at least equivalent to those provided in this Agreement, which will allow NOVARTIS the right to directly enforce the obligations of confidentiality with respect to

NOVARTIS Technology in possession of the Third Party. NOVARTIS retains all rights to NOVARTIS Technology except to the extent explicitly granted to VERTEX hereunder.

2.3. INFORMATION TRANSFER.

(a) Neither party shall be entitled to information from the other party concerning know-how or technology discovered or developed by that party outside the Research Program under the Research Agreement or outside a Development Program under this Agreement ("Excluded Technology"), or otherwise unrelated to research or development of Drug Product Candidates or Drug Products under this Agreement. However, neither party will apply its rights in any Excluded Technology other than Excluded Technology claiming Excluded Compounds or the use thereof (and will use good faith efforts to prevent its licensees, if any, from applying similar rights acquired by license) to block or impede the use of the Kinase Technology as permitted hereunder by the other party or its assignees or licensees.

(b) VERTEX shall deliver to NOVARTIS all information Controlled by it and requested by NOVARTIS relating to Drug Product Candidates which is necessary or useful for exercise by NOVARTIS 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 Drug Product Candidates whether in human or machine readable form.

(c) NOVARTIS shall deliver to VERTEX all information Controlled by it and requested by VERTEX which is necessary or useful for exercise by VERTEX of the assistance rights under Section 3.5.

ARTICLE III
DEVELOPMENT

3.1. COMMENCEMENT OF DEVELOPMENT PROGRAM. NOVARTIS shall promptly and diligently commence and pursue a Development Program with respect to each Drug Product Candidate as soon as practicable after exercise by NOVARTIS of its Development Election with respect to that Drug Product Candidate.

3.2. INTERNATIONAL PROJECT TEAM.

3.2.1. FORMATION AND RESPONSIBILITIES. As soon as practicable after the exercise by NOVARTIS of its Development Election with respect to a Drug Product Candidate, NOVARTIS will establish an International Project Team ("IPT") which shall include one representative designated by VERTEX from time to time; provided, however, an IPT shall no longer

include a representative designated by VERTEX in case of a Change of Control of VERTEX. Additional IPT's, which shall also include one VERTEX representative, may be established from time to time in connection with the development of additional Drug Product Candidates. The IPT (or its successor organization, as designated by NOVARTIS) will be the principal organization through which the development of a Drug Product Candidate is planned, administered, evaluated and completed, subject to appropriate review and approval at senior management levels as required by NOVARTIS from time to time. In addition to the VERTEX member, the IPT will typically have members from the various functional groups (e.g., research, preclinical safety, clinical, regulatory, marketing) which are or will be expected to be involved in development and launch of the Drug Product Candidate and Drug Product. NOVARTIS will appoint the IPT Chair. The IPT will typically meet every four to six weeks, depending on the level of current development activity, and will be responsible for preparation and implementation of the Development Plan described in Section 3.2.2 below with respect to each Drug Product Candidate.

3.2.2. DEVELOPMENT PLAN. The IPT shall prepare and oversee the implementation of the overall Development Plan for each Drug Product Candidate. The Development Plan shall, among other things, detail, schedule and fully describe the proposed toxicology studies, clinical trials, regulatory plans, clinical trial and commercial material requirements, and process development and manufacturing plans for each Drug Product Candidate, along with relevant budget information for the described items, and will outline the key elements involved in obtaining Regulatory Approval in each country where the Drug Product is to be marketed. The parties expect that development tasks will be advanced in parallel rather than serially where practicable and appropriate, if doing so would be likely to advance the ultimate date of Regulatory Approval and launch and is otherwise commercially reasonable.

3.2.3. MEETING MATERIALS. The IPT will consider all information that is material to an assessment of the status, direction and progress of the Development Program, including all clinical trials protocols, data and reports. The IPT Leader will ensure that full and complete minutes are prepared and distributed to each member of the IPT promptly after each meeting. Those minutes shall contain a full report on the activities of the IPT during its meeting. VERTEX's representative on the IPT will receive all documents and information distributed or communicated

to members of the IPT generally, and may review copies of all other information relative to the development of a Drug Product Candidate unless the IPT Leader denies access to that information for good reason.

3.2.4. [This section has been intentionally left blank.]

3.3. DEVELOPMENT RESPONSIBILITY AND COSTS. Except as provided in Section 3.5 below, NOVARTIS will have sole responsibility for, and bear the cost of conducting, the Development Program with respect to each Drug Product Candidate.

3.4. REGULATORY APPROVALS. NOVARTIS shall be solely responsible for preparing and submitting registration dossiers for Regulatory Approval of Drug Product Candidates in the Territory.

3.4.1. NOVARTIS Ownership. All Regulatory Approvals shall be held by and in the name of NOVARTIS, and NOVARTIS shall own all submissions in connection therewith, provided that VERTEX shall have a right of reference to all or any part of the submissions if the "Assistance Rights" become effective under Section 3.5 hereof.

3.4.2. Principal Interface. All formulary or marketing approvals shall also be obtained by and in the name of NOVARTIS, and NOVARTIS 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 3.4.3.

3.4.3. Regulatory Meetings. To the extent not prohibited by law or regulation, VERTEX shall have the right, after consultation with NOVARTIS and unless VERTEX's presence would impede the regulatory approval process, to have one representative participate in all material meetings between representatives of NOVARTIS and any of the FDA, the EMEA and Koseisho (MHW Japan).

(a) NOVARTIS will undertake to provide VERTEX with information reasonably in advance of the meeting sufficient to ensure that the VERTEX representative is adequately informed about the issues to be presented at any such meeting.

(b) VERTEX may request NOVARTIS to provide VERTEX with a copy of any correspondence between the FDA, the EMEA and Koseisho that relates to any material issues involving Regulatory Approval of a Drug Product Candidate, and NOVARTIS shall provide that information upon request, unless NOVARTIS has good reason to withhold any such correspondence, in which case it will notify VERTEX of that reason promptly.

(c) Notwithstanding the foregoing, NOVARTIS will have sole discretion as to the regulatory strategy and decision-making for any Drug Product Candidate or Drug Product.

3.5. ASSISTANCE RIGHTS. If NOVARTIS is not using commercially reasonable efforts, pursuant to the provisions of Sections 3.6 and 5.6 of this Agreement, to conduct development

activities ("Development Work") on the critical path provided for in the then current Development Plan and if, as a consequence thereof, such Development Work is materially delayed, and if VERTEX believes that delay to be unreasonable under the circumstances,] VERTEX may request the JSC to review and discuss the matter and a special meeting of the JSC will be convened for that purpose within [***] of VERTEX's written request. If within [***] after review by [***] NOVARTIS is unwilling or unable to cure the delay, then VERTEX may propose, by written notice to NOVARTIS, undertake that particular Development Work at its own expense. VERTEX shall be free to do so commencing [***] after delivery of its notice to NOVARTIS unless [***]

3.5.1. Notwithstanding the foregoing, if the Development Work is

terminated or delayed as a result of [***] then VERTEX may [***]

3.5.2. If VERTEX pursues its Assistance Rights:

(a) REGULATORY ACTIONS. NOVARTIS will continue to make any necessary and appropriate regulatory filings with respect to the Development Work and will, if required for VERTEX to exercise its Assistance Rights effectively, transfer to VERTEX at VERTEX's expense any IND material (or equivalents thereof) relevant to such Development Work.

(b) MANUFACTURE OF CLINICAL SUPPLY OF DRUG PRODUCT CANDIDATE. NOVARTIS will supply VERTEX (for up to two years) with the necessary clinical supply of Drug Product Candidate required to perform such Development Work in accordance with NOVARTIS' then current scale of manufacturing at NOVARTIS' Manufacturing Cost and upon such other reasonable and customary terms as to shipment, delivery and similar matters as may be agreed.

(c) MILESTONES. If NOVARTIS elects to resume the Development Program for a Drug Product Candidate, it will provide VERTEX with ninety (90) days prior notice thereof, and will reimburse VERTEX for the actual direct cost of the Development Work of good quality, if such work conforms with the requirements of the relevant Development Plan. NOVARTIS will pay VERTEX interest on the reimbursable costs incurred by VERTEX in the conduct of the Development Work, at a rate compounded quarterly equal to the thirty-day London InterBank Offered Rate ("LIBOR") for the local currency in which payment is made, as quoted in The Financial Times as determined on the date the Development Work is first undertaken by VERTEX and on the last Business Day of each calendar quarter thereafter.

3.6. REASONABLE EFFORTS IN DEVELOPMENT. NOVARTIS will use diligent, commercially reasonable efforts consistent with those used by NOVARTIS for its own compounds of similar commercial potential to develop Drug Product Candidates into Drug Products. NOVARTIS will promptly notify VERTEX in writing if it should determine that development of any Drug Product Candidate or Drug Product is not technically feasible or commercially justifiable, specifying in reasonable detail the reasons for that determination.

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ARTICLE IV
MANUFACTURING AND SUPPLY

4.1. SUPPLY OF BULK DRUG SUBSTANCE AND DRUG PRODUCT. NOVARTIS will be responsible for manufacturing and supply of all Bulk Drug Substance, Drug Product Candidates and Drug Product as necessary for the conduct of the Development Plan and for all commercial purposes in the Territory. Pursuant to the provisions of Section 4.7 of the Research Agreement, the parties will agree on reasonable and appropriate measures by which manufacturing previously being undertaken by VERTEX shall be transitioned to NOVARTIS following the exercise of its Development Election with respect to a particular Drug Product Candidate. The objective of both parties will be to accomplish a smooth and timely transition. Any Bulk Drug Substance provided to NOVARTIS during the transition period will be supplied at VERTEX's reasonable Manufacturing Cost.

4.2. [This section has been intentionally left blank.]

4.3. FORMULATION AND PACKAGING. In all events, NOVARTIS will be responsible for formulation and packaging of Drug Products.

ARTICLE V
COMMERCIALIZATION

5.1. MARKETING AND PROMOTION. NOVARTIS shall have exclusive rights to market, sell and distribute all Drug Products in the Territory. NOVARTIS will book all sales of Drug Products and will report those sales to VERTEX as specified in Section 6.5 of this Agreement.

5.2. GLOBAL BRAND TEAM. Not later than six months prior to the commencement of Phase III Clinical Trials for any Drug Product Candidate, NOVARTIS will form a Global Brand Team ("GBT"), which will include one representative designated by VERTEX; provided, however, [***]. Additional GBT's,

which shall also include one VERTEX representative, may be established from time to time in connection with the marketing of additional Drug Product Candidates. The GBT (or its successor organization, as designated by NOVARTIS) will be the principal organization through which the marketing of a Drug Product is planned, administered, evaluated and effected, subject to appropriate review at senior management levels as required by NOVARTIS. NOVARTIS will appoint the chair of the GBT, who will normally be the Brand Director. The GBT will periodically meet as necessary, depending on the level of marketing activity at the time.

5.2.1. MARKETING PLANS. The Global Brand Team will prepare and oversee the implementation of a detailed marketing plan (a "Marketing Plan") for the launch of each Drug Product, addressing the overall branding and branding elements as well as the key promotional product claims. The GBT will select an external agency or agencies which will be charged with the execution of some components of the Marketing Plan. The Marketing Plan will contain among other things budgets, schedules, product positioning, pricing, market research plans and results and other customary planning and marketing material with respect to marketing and

launch of the Drug Product. The Marketing Plan will be periodically updated to reflect changes in market information, sales performance and forecasts, sales force deployment, communication plans and information concerning competition and competitors.

5.2.2. LOCAL PRODUCT TEAMS. Local Product Teams will be established in each country to prepare and execute the product launch for a Drug Product within the framework of the Marketing Plan. .

5.2.3. CAMPAIGNS AND PROMOTIONAL MATERIALS. The GBT will review all general product campaigns (including target audience and principal messages) and may from time to time review the principal promotional material to be used in connection with the marketing and sale of a Drug Product.

5.2.4. [This section has been intentionally left blank.]

5.3. [This section has been intentionally left blank.]

5.4. [This section has been intentionally left blank.]

5.5. CO-LABELING. To the extent not prohibited by law or regulation and subject to any required Regulatory Approval, Drug Products (including labels, packaging and inserts) and all promotional materials for the same, sold in North America, the countries of the European Union and Japan will bear both NOVARTIS' and VERTEX's company names and logos with equal prominence (including equal sized type face), or if equal prominence is prohibited by law, with such prominence as may otherwise be permitted by law. To the extent not prohibited by law or regulation and subject to any required Regulatory Approval, Drug Products (including labels, packaging and inserts) and all promotional materials for the same, sold in the rest of the world will include VERTEX's company name (in the English alphabet) and logo with the designation: "under license from" ; provided, however, that this provision shall no longer apply in case of a Change of Control of VERTEX. Any trademark for a Drug Product will be selected by, and will be the property of, NOVARTIS.

5.5.1. REVIEW OF REGULATORY FILINGS. NOVARTIS will permit VERTEX to review all material regulatory filings which relate to product labeling, and all proposed labels, packaging, package inserts, and promotional materials required under the Agreement to bear VERTEX's name, if permitted by law, prior to the filing of any such materials with any regulatory authority; provided, however, that this provision shall no longer apply in case of a Change of Control of VERTEX.

5.5.2. REGULATORY COMMUNICATIONS.

(a) NOVARTIS will permit VERTEX to participate with NOVARTIS in material communications with regulatory officials which concern the matters referenced in this Section 5.5; provided, however, [***].

(b) NOVARTIS will immediately inform VERTEX of any material regulatory communications received by NOVARTIS which might operate to restrict VERTEX's rights under this Section 5.5.2, and will cooperate with any reasonable request of VERTEX aimed at facilitating approval by a regulatory authority for co-labeling consistent with this provision.

5.6. DUE DILIGENCE. NOVARTIS 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 of its products of comparable market potential. Following the First Commercial Sale of a Drug Product and until the expiration of this Agreement, NOVARTIS shall endeavor to keep Drug Products reasonably available to the public in each of the Major Markets. NOVARTIS shall promptly notify VERTEX if it shall determine that the marketing and sale of a Drug Product in any country is not commercially reasonable or economically profitable or if for other unforeseen reasons further commercial support of the Drug Product in certain territories is no longer prudent or practical. In determining whether NOVARTIS 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.

ARTICLE VI
PAYMENTS

6.1. DEVELOPMENT ELECTION PAYMENT. NOVARTIS will pay to VERTEX a milestone payment in the amount of [***] (a "Development Election Fee") each time NOVARTIS exercises its Development Election with respect to a Development Candidate. Each time NOVARTIS exercises its Development Election under Section 4.1 of the Research Agreement with respect to a Compound which is a Back-up Compound to a Drug Product Candidate, NOVARTIS will pay to VERTEX a milestone payment in the amount of [***] (the "Back-up Election Fee"); [***].

6.2. DEVELOPMENT MILESTONE PAYMENTS BY NOVARTIS.

6.2.1. NOVARTIS will make the following payments to VERTEX upon the achievement of any of the following milestones with respect to a Drug Product Candidate:

CONFIDENTIAL TREATMENT REQUESTED

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

6.2.2. [This section has been intentionally left blank.]

6.2.3. All payments shall be made by wire transfer in United States dollars ("Dollars") to the credit of such bank account as may be designated by VERTEX in writing to NOVARTIS. 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.

6.2.4. If a Drug Product Candidate is abandoned during the term of this Agreement for any scientific or medical reasons after any one or more of the foregoing milestone payments are made, and if a Back-up Compound to that Drug Product Candidate is developed to replace the abandoned Drug Product Candidate for the same Indications, then no milestone payment shall be required with respect to the Back-up Compound to the extent that that milestone payment has already been made with respect to the abandoned Drug Product Candidate.

6.3. ROYALTIES. NOVARTIS shall pay to VERTEX the following annual

royalties on Net Sales of each Drug Product in the Territory.

[***]

[***]

[***]

6.3.1. THIRD PARTY ROYALTIES: If NOVARTIS is required to pay royalties to any Third Party in order to exercise its rights to sell a Drug Product in a country, then [***] payable to such Third Party in any calendar quarter for such Drug Product in such country shall be deductible from the royalties payable to VERTEX under this Agreement in respect of sales of that Drug Product in such country for the same calendar quarter, provided that in no

event shall the net royalty rate payable fall below [***], as a result of the application of this Sections 6.3.1 and 6.3.2.

6.3.2. UNLICENSED COMPETITION: If in any country a Third Party sells a pharmaceutical product which is a "generic version" of a Drug Product being sold in that country (a "Third Party Product") -- where "generic version" means a pharmaceutical product (other than a product originally sold as a Drug Product) that includes the same active ingredient as that used in a Drug Product-- then for the period in which the sales of such Third Party Product in such country are at least [***], the royalties payable to VERTEX by NOVARTIS on sales of such Product in such country for such period shall be [***] in Section 6.3 , but in no event shall the royalties owed for such Drug Product in such country, when combined with any royalty reduction provided under Section 6.3.1 hereof, reduce the royalties payable on Net Sales of such Drug Product in that country by more than [***]

6.4. [This section has been intentionally left blank.]

6.5. SALES REPORTS.

(a) During the term of this Agreement and after the First Commercial Sale of a Drug Product, NOVARTIS 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 NOVARTIS and each Affiliate and sublicensee; (ii) the royalties, payable in Dollars, which shall have accrued under Section 6.3 hereof in respect of such sales and the basis of calculating those royalties; (iii) withholding taxes, if any, required by law to be deducted in respect of any such sales; (iv) 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; and (v) 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 NOVARTIS' 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 NOVARTIS, generally, in its external financial reporting, as reviewed and approved by its independent auditors and will be in conformity with NOVARTIS' usual and customary general accounting principles consistently applied. If any sublicensee 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. NOVARTIS 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 thirtieth (30th) day

following the close of each reporting period, although NOVARTIS shall

also provide VERTEX with a "flash" report of Net Sales, only, within ten (10) business days after the end of each month. NOVARTIS shall keep accurate records in sufficient detail to enable the amounts due hereunder to be determined and to be verified by VERTEX.

(b) Amounts shown to have accrued by each sales report provided for under subsection 6.5(a), above, 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 Products are sold, NOVARTIS or its sublicensees 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, NOVARTIS shall permit an independent accountant of national prominence selected by VERTEX, to have access during normal business hours to those records of NOVARTIS as may be reasonably necessary to verify the accuracy of the sales reports furnished by NOVARTIS pursuant to this Section 6.5, in respect of any calendar year ending not more than thirty-six (36) months prior to the date of such notice. NOVARTIS shall include in each sublicense entered into by it pursuant to this Agreement a provision requiring the sublicensee to keep and maintain adequate records of sales made pursuant to such sublicense and to grant access to such records by the aforementioned independent accountant for the reasons specified in this Section 6.5. 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 NOVARTIS and its sublicensees shall be released from any liability or accountability with respect to payments for such year. The report prepared by such independent accountant, a copy of which shall be sent or otherwise provided to NOVARTIS by such independent accountant at the same time it is sent or otherwise provided to VERTEX, shall contain the conclusions of such independent 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 accountant's report shows any underpayment, NOVARTIS shall remit or shall cause its sublicensees to remit to VERTEX within thirty (30) days after NOVARTIS' receipt of such report, (i) the amount of such underpayment and (ii) if such underpayment exceeds [***] owed for the calendar year then being audited, the reasonable and necessary fees and expenses of such independent accountant performing the audit, subject to reasonable substantiation thereof. Any overpayments shall be fully creditable against amounts payable in subsequent payment periods. VERTEX agrees that all information subject to review under this Section 6.5 or under any sublicense 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 NOVARTIS to VERTEX not occasioned by Force Majeure, interest at the rate of [***], assessed from the thirty-first day after the due date of the payment, shall be due from NOVARTIS upon prior written notice.

6.6. 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 NOVARTIS 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 NOVARTIS' request shall sign a usual and customary exemption application and in addition shall apply for a tax refund at the request of NOVARTIS from any tax authority to which NOVARTIS has paid withholding tax on account of any payments made by NOVARTIS to VERTEX hereunder.

ARTICLE VII
BACK-UP COMPOUNDS

Notwithstanding the provisions under the Research Agreement with respect to Back-up Compounds and for the sake of clarity, it is reminded that the parties agreed the following with respect to Back-up Compounds in Section 4.5 of the Research Agreement.

7.1 VERTEX RESTRICTIONS ON NOMINATION AND DEVELOPMENT. So long as NOVARTIS is using commercially reasonable efforts with respect to the development of a particular Drug Product Candidate or the commercialization of a particular Drug Product, pursuant to Sections 3.6 and 5.6 hereof, VERTEX will not (i) propose a Compound for development under the License Agreement which is a Back-up Compound with respect to that Drug Product Candidate or Drug Product, or (ii) until after the period starting on the date on which NOVARTIS has exercised its Development Election for a particular Drug Product Candidate and ending [***] (the "Lead Period"), commence development of that Back-up Compound

either directly or together with or through an Affiliate or a Third Party.

7.2 TERMINATION OF DEVELOPMENT OR COMMERCIALIZATION. If, prior to the end of the Lead Period with respect to a particular Drug Product or Drug Product Candidate, pursuant to Sections 3.6 and 5.6 hereof, NOVARTIS ceases to use commercially reasonable efforts to develop or commercialize that Drug Product Candidate or Drug Product, then the restrictions on nomination and development referenced in Section 7.1 above will no longer apply with respect to Back-up Compounds for that Drug Product Candidate or Drug Product unless NOVARTIS, without delay, commences another Development Program under the License Agreement with another Compound (a "Replacement Candidate") targeting the same Kinase, which Replacement Candidate is a Back-up Compound associated with the discontinued Drug Product Candidate or Drug Product, and NOVARTIS shall have the right to select for this purpose any such Back-up Compound by providing VERTEX with notice of its Development Election in this regard. Any such Back-up Compound for which NOVARTIS has exercised its Development Election under this Section 7.2 shall hereafter be a Drug Product Candidate subject to the terms and conditions of this Agreement.

7.3. TERMINATION OF RIGHTS TO BACK-UP COMPOUNDS. A Back-up Compound will no longer be subject to NOVARTIS' Development Election under the Research Agreement after the

end of the Lead Period applicable to that Back-up Compound, except for Back-up Compounds which (i) subject to Section 7.1 above, VERTEX has proposed for development on or before the Final Termination Date, and as to which NOVARTIS has exercised its Development Election hereunder; or (ii) have been or will be selected by NOVARTIS for development before the end of the applicable Lead Period under the provisions of Section 7.2 above, or (iii) for which NOVARTIS has exercised or will exercise its Development Election before the end of the applicable Lead Period under the provisions of Section 7.4 below.

7.4 NOVARTIS RIGHTS TO LICENSE BACK-UP COMPOUNDS. Anytime prior to the expiry of the Lead Period with respect a particular Drug Product Candidate, NOVARTIS may also, by paying in each case the Back-up Election Fee provided under Section 6.1 of the this Agreement, exercise its Development Election with respect to any one or more Back-up Compounds associated with that Drug Product Candidate, provided that Drug Product Candidate, or a Back-up Compound selected pursuant to the provisions of Section 7.2 above, is still in active development. Any such Back-up Compound for which NOVARTIS has exercised its Development Election under Section 7.4 shall become a "Drug Product Candidate Back-up Candidate" subject to the terms and conditions of this Agreement.

7.5 NOVARTIS OBLIGATIONS WITH RESPECT TO DRUG PRODUCT CANDIDATE BACK-UP CANDIDATES. So long as NOVARTIS is using commercially reasonable efforts, pursuant to the provisions of Sections 3.6 and 5.6 of this Agreement, with respect to the development of a particular Drug Product Candidate or the commercialization of a particular Drug Product, NOVARTIS shall have no obligation to develop any of the Drug Product Candidate Back-up Candidates associated with that Drug Product Candidate or Drug Product. As soon as NOVARTIS ceases the development of a particular Drug Product Candidate, NOVARTIS' obligations to use diligent, commercially reasonable efforts will immediately shift from the discontinued Drug Product Candidate to an associated Drug Product Candidate Back-up Compound. If NOVARTIS ceases the development of a particular Drug Product Candidate and does not commence development of a Drug Product Candidate Back-up Compound pursuant to the foregoing, the license to the Drug Product Candidate and its Back-up Compounds under this Agreement will expire and the license rights will revert to VERTEX.

ARTICLE VIII
INTELLECTUAL PROPERTY

8.1. PATENTABLE INVENTIONS AND KNOW-HOW.

8.1.1. OWNERSHIP. Any inventions made and all Know-How generated by either party or its Affiliates during the term of this Agreement, and Controlled by such party, relating to the manufacture or use of Bulk Drug Substance, a Drug Product Candidate or a Drug Product, or a prodrug thereof, will be disclosed to the other party promptly after the disclosing party recognizes

the significance thereof. 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.

8.1.2. 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 NOVARTIS. NOVARTIS shall be responsible for the preparation, filing, prosecution and maintenance of all patents and patent applications included in NOVARTIS Patents. In each case the responsible party shall consult from time to time with the other party with respect thereto. VERTEX shall provide NOVARTIS with periodic reports listing the jurisdictions in which the VERTEX Patents licensed hereunder have been filed. Subject to the next succeeding sentences, VERTEX will file patent applications with respect to those VERTEX Patents in such other countries as NOVARTIS shall request in writing, all such other countries being countries in which NOVARTIS would customarily file its own cases dealing with similar subject matters. 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.

8.1.3. COSTS. Costs incurred in the preparation, prosecution and maintenance of Patents shall be borne by each party as set forth in Section 8.3 of the Research Agreement.

8.2. INFRINGEMENT CLAIMS BY THIRD PARTIES.

8.2.1. NOTICE. 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.

8.2.2. THIRD PARTY LICENSES. In the event that practicing the Technology in connection with the manufacture, use or sale of a Drug Product in any country would infringe a Third Party's patent, then VERTEX will use reasonable efforts to obtain a license under the Third Party's patents with a right to sublicense to NOVARTIS, under terms reasonably acceptable to both VERTEX and NOVARTIS, and VERTEX and NOVARTIS will [***]

8.2.3. DISCONTINUED SALES, LICENSE OR DEFENSE OF SUIT. If the required license is either unavailable or its terms are unacceptable both to VERTEX and to NOVARTIS, then NOVARTIS 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 [***] Provided that NOVARTIS is conducting the defense of the Infringement Claim or the prosecution of such declaratory judgment actions, [***]. The costs and expenses of all suits brought by a party under this Section 8.2.3 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 NOVARTIS. [***] No settlement or consent judgment or other voluntary final disposition of a suit under this Section 8.2 may be entered into without the joint consent of VERTEX and NOVARTIS (which consent shall not be unreasonably withheld).

8.3. INFRINGEMENT CLAIMS AGAINST THIRD PARTIES.

8.3.1. VERTEX and NOVARTIS each agree to take reasonable actions to protect their respective patents and technology from infringement and from unauthorized possession or use.

8.3.2. If any VERTEX Patents or NOVARTIS Patents are infringed or VERTEX Know-How or NOVARTIS 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 8.3.2 shall be reimbursed to such party and 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 NOVARTIS. [***] No settlement or consent judgment or other voluntary final disposition of a suit under this Section 8.3 may be entered into without the joint consent of VERTEX and NOVARTIS (which consent shall not be unreasonably withheld).

8.4. NOTICE OF CERTIFICATION. VERTEX and NOVARTIS 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 VERTEX Patent or a NOVARTIS 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 NOVARTIS of its decision not to bring suit within twenty-one (21) days after receipt of notice of such certification. NOVARTIS may then, but is not required to, bring suit against the party that filed the certification. Any suit by NOVARTIS or VERTEX shall either be in the name of NOVARTIS or in the name of VERTEX, or jointly by NOVARTIS 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.

8.5. PATENT TERM EXTENSIONS. The parties shall cooperate in good faith with each other in gaining patent term extension wherever applicable to VERTEX Patents and NOVARTIS Patents covering Drug Product Candidates or Drug Products. NOVARTIS 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 IX
REPRESENTATIONS AND WARRANTIES

9.1. REPRESENTATIONS AND WARRANTIES OF VERTEX. VERTEX represents and warrants to NOVARTIS as follows:

9.1.1. 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.

9.1.2. NO THIRD PARTY RIGHTS. Except as previously disclosed in writing to NOVARTIS on or before the date set forth on the first page hereof, (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 NOVARTIS hereunder does not violate any right known to VERTEX of any Third Party.

9.1.3. NO THIRD PARTY PATENTS. Except as disclosed in writing by VERTEX to NOVARTIS 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 issued patent or 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.

9.1.4. MAINTENANCE OF PATENTS AND LICENSES. Subject to the provisions of Section 8.1.2 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 NOVARTIS hereunder.

9.2. REPRESENTATIONS AND WARRANTIES OF NOVARTIS. NOVARTIS represents and warrants to VERTEX as follows:

9.2.1. AUTHORIZATION. This Agreement has been duly executed and delivered by NOVARTIS and constitutes the valid and binding obligation of NOVARTIS, enforceable against NOVARTIS 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 NOVARTIS, its officers and directors.

9.2.2. NO THIRD PARTY RIGHTS. Except as previously disclosed in writing to VERTEX on or before the date set forth on the first page hereof,

(a) NOVARTIS owns or possesses adequate licenses or other rights to use all NOVARTIS Technology, and to grant the licenses herein; and (b) the granting of the licenses to VERTEX hereunder does not violate any right known to NOVARTIS of any Third Party.

9.2.3. NO THIRD PARTY PATENTS. Except as disclosed in writing by NOVARTIS to VERTEX or its agents, to NOVARTIS' 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 NOVARTIS is not aware of any issued patent or 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.

9.2.4. MAINTENANCE OF PATENTS AND LICENSES. Subject to the provisions of Section 8.1.2 with respect to Discontinued

Patents, NOVARTIS 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 X
CONFIDENTIALITY

10.1. UNDERTAKING. During the term of this Agreement, each party shall keep confidential, and other than as provided herein shall not use or disclose, directly or indirectly, any trade secrets, confidential or proprietary information, or any other knowledge, information, documents or materials, owned, developed or possessed by the other party, whether in tangible or intangible form, the confidentiality of which such other party takes reasonable measures to protect, including but not limited to VERTEX Technology and NOVARTIS Technology.

10.1.1. 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.

10.1.2. 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.

10.1.3. 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.

10.2. EXCEPTIONS. Notwithstanding the foregoing, the provisions of Section 10.1 hereof shall not apply to knowledge, information, documents or materials which the receiving party can conclusively establish:

10.2.1. have entered the public domain without such party's breach of any obligation owed to the disclosing party;

10.2.2. are permitted to be disclosed by the prior written consent of the disclosing party;

10.2.3. 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;

10.2.4. are disclosed by the disclosing party to a Third Party without restrictions on its disclosure;

10.2.5. are independently developed by the receiving party without breach of this Agreement; or

10.2.6. 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.

10.3. PUBLICITY. The parties will agree upon the timing and content of any initial press release or other public communications relating to this Agreement and the transactions contemplated herein.

10.3.1. 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 NOVARTIS, 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.

10.3.2. 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.

10.4. SURVIVAL. The provisions of this Article X shall survive the termination of this Agreement and shall extend for a period of five (5) years thereafter.

ARTICLE XI
PUBLICATION

NOVARTIS reserves the sole right to publish or publicly present the results of the Development Program and information concerning Drug Product Candidates and Back-up Compounds (collectively, the "Results"), subject to the following terms and conditions. NOVARTIS will submit a draft of any proposed manuscript or speech to VERTEX for comments at least thirty (30) days prior to submission for publication or oral presentation. VERTEX shall notify NOVARTIS in writing within fifteen (15) days of receipt of such draft whether such draft contains (i) information of VERTEX which it considers to be confidential under the provisions of Article IX hereof, or (ii) information that if published would have an adverse effect on a patent application covering the subject matter of this Agreement which VERTEX intends to file,. In any such notification, VERTEX shall indicate with specificity its suggestions regarding the manner and degree to which NOVARTIS may disclose such information. In the case of item (ii) above, VERTEX may request a delay and NOVARTIS 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, NOVARTIS may not publish confidential information of VERTEX without its consent in violation of Article IX of this Agreement. The parties agree that authorship of any publication will be determined based on the customary standards then being applied in the relevant scientific journal.

This Article XI shall terminate with the termination of this Agreement, but the provisions of Article X hereof shall continue to govern the disclosure by one party, whether by publication or otherwise, of Confidential Information of the other, during the period set forth in Section 10.4.

ARTICLE XII
DISPUTE RESOLUTION

12.1. GOVERNING LAW, AND JURISDICTION. This Agreement shall be governed and construed in accordance with the internal laws of the State of New York.

12.2. DISPUTE RESOLUTION PROCESS. Except 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, and either party may, initially refer such dispute to the Joint Steering Committee, and failing resolution of the controversy or claim within thirty (30) days after such referral, the matter shall be referred to the Chief Executive Officer of VERTEX and the Chief Executive Officer of NOVARTIS 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 date of initial referral of the matter to the JSC, either party shall be free to initiate proceedings in any court having requisite jurisdiction.

ARTICLE XIII
TERM AND TERMINATION

13.1. TERM. The term of this Agreement shall extend with respect to a Drug Product in a particular country until the later of: (a) the last to expire of any VERTEX Patents containing a Valid Patent Claim covering the Drug Product or its use or manufacture in that country; or (b) if there is no such Valid Patent Claim under a VERTEX Patent in a particular country, ten (10) years from

the earlier of the date Regulatory Approval is received in that country for sale of the Drug Product, or the date of First Commercial Sale of the Drug Product in that country.

13.2. 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 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.

13.3. 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 upon the occurrence 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.

13.4. TERMINATION BY NOVARTIS. NOVARTIS may terminate this Agreement at any time with respect to one or more Drug Product Candidates or Drug Products, upon [***] prior written notice to VERTEX if [***]. In such event NOVARTIS, at the request of VERTEX,

shall assign or otherwise transfer to VERTEX all of its regulatory filings with respect to the Drug Product Candidate or Drug Product as to which NOVARTIS has terminated this Agreement.

13.5. EFFECT OF TERMINATION.

(a) 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.

(b) For each country, at the end of the Agreement term as provided in Section 13.1 hereof in respect of a Drug Product, NOVARTIS shall have a perpetual, nonexclusive, transferable, paid-up, royalty-free license under VERTEX Technology, in each case which is in existence at the end of such Agreement term, to use, make, have made and sell that Drug Product in that country and to make or have made Drug Product for use and sale in that country.

ARTICLE XIV
INDEMNIFICATION

14.1. INDEMNIFICATION BY VERTEX. VERTEX will indemnify and hold NOVARTIS 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:

14.1.1. the development, manufacture, use, storage or handling of 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

14.1.2. the breach by VERTEX of any of its covenants, representations or warranties set forth in this Agreement; and

14.1.3. provided however, that the foregoing indemnification shall not apply to any Loss to the extent such Loss is caused by the negligent or willful misconduct of NOVARTIS or its Affiliates.

14.2. INDEMNIFICATION BY NOVARTIS. NOVARTIS 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:

CONFIDENTIAL TREATMENT REQUESTED

14.2.1. the development, manufacture, use, sale, storage or handling of a Drug Product Candidate or a Drug Product by NOVARTIS 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

14.2.2. the breach by NOVARTIS of any of its covenants, representations or warranties set forth in this Agreement; and

14.2.3. 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.

14.3. CLAIMS PROCEDURES. Each Party entitled to be indemnified by the other Party (an "Indemnified Party") pursuant to Section 14.1 or 14.2 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

14.3.1. 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.

14.3.2. 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.

14.3.3. 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.

CONFIDENTIAL TREATMENT REQUESTED

14.4. COMPLIANCE. The parties shall comply fully with all applicable laws and regulations in connection with their respective activities under this

Agreement.

14.5. INSURANCE. Each party shall use all commercially reasonable efforts to maintain insurance, including product liability insurance, with respect to its activities hereunder.

14.5.1. 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.

14.5.2. Either party may satisfy its obligations under this Section through self-insurance to the same extent.

14.5.3. At such time as a Drug Product is being manufactured by a party for commercial sale, that party shall name the other party as an additional insured on any such policies.

ARTICLE XV
MISCELLANEOUS PROVISIONS

15.1. NOTICE OF PHARMACEUTICAL SIDE-EFFECTS. During the term of this Agreement, 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 event (as defined by the ICH Harmonized Tripartite Guideline on Clinical Safety Data Management), directly or indirectly attributable to the use or application of a Development Candidate, Bulk Drug Substance, a Drug Product Candidate or a Drug Product.

15.2. 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.

15.3. 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.

15.4. REGISTRATION OF LICENSE. NOVARTIS 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 Valid Patent Claim. Upon request by NOVARTIS, VERTEX agrees promptly to execute any "short form" licenses submitted to it by NOVARTIS 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.

CONFIDENTIAL TREATMENT REQUESTED

15.5. 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.

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

15.7. GOVERNMENT APPROVALS. NOVARTIS 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.

15.8. 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 15.8 shall, at the option of the non-assigning 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. This Agreement shall be binding upon and enforceable against the successor to or any permitted assignee from either of the parties hereto.

15.9. 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 of omission) which such party is prohibited hereunder from committing directly. The use of subcontractors by either party shall not increase the financial obligations of the other party hereunder in any respect.

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

15.11. NO AGENCY. Nothing herein contained shall be deemed to create an agency, joint venture, amalgamation, partnership or similar relationship between NOVARTIS 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.

15.12. 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 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 NOVARTIS, at:
NOVARTIS PHARMA AG
Business Development and Licensing
P.O. Box
CH-4002
Basel, Switzerland
Attention: Victor A. Hartmann, Vice President

with a copy to: Legal Services, at the address referenced above

and

if to VERTEX, at:
Vertex Pharmaceutical Incorporated
130 Waverly Street
Cambridge, MA U.S.A. 02139-4211

Attention: President

with a copy to:
Legal Department
Attention: General Counsel

15.13. 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.

15.14. 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.

15.15. 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.

15.16. INFLATION ADJUSTMENT. All payments required to be made to VERTEX hereunder (except any royalty payments required to be made under the provisions of Section 6.3 hereof) shall be adjusted at the beginning of each calendar year to reflect the impact of inflation since the date of execution of the Revised and Restated Research Agreement, as measured by the biotech worker inflation rate defined and reported in the Radford Survey (Radford/AON Consulting Inc., San Francisco, CA), or other mutually acceptable index. Notwithstanding the foregoing, no adjustment shall be required in any calendar year in which the appropriate inflation adjustment, if applied, would result in a change of less than [***].

15.17. INVOICE REQUIREMENT. Any amounts payable to VERTEX hereunder (except any royalty payments required to be made under the provisions of Section 6.3 hereof) shall be made within thirty days after receipt by NOVARTIS, or its nominee designated for that purpose in advance by NOVARTIS in writing to VERTEX, of an invoice covering such payment, which invoice shall conform to the extent reasonably practicable to the form of invoice contained in Exhibit B to the Research Agreement.

15.18. HARDSHIP. If as a result of unforeseen events or developments relating to the subject matter of this Agreement, the performance of this Agreement shall cause inequitable economic hardship for one party which runs counter to the objectives of this Agreement and which the other party cannot reasonably and in good faith expect the first party to bear unrelieved, the parties will meet and seek in good faith to find equitable means of amending this Agreement to reestablish a fair and reasonable economic balance under this Agreement between the parties hereto.

CONFIDENTIAL TREATMENT REQUESTED

IN WITNESS WHEREOF, the parties hereto have caused this Agreement to be executed by their duly authorized representatives as of the day and year first above written.

VERTEX PHARMACEUTICALS INCORPORATED

By:

Kenneth S. Boger
Title: Senior Vice President and General Counsel

NOVARTIS PHARMA AG

By:

Title:

By:

Title:

CONFIDENTIAL TREATMENT REQUESTED

SCHEDULE 1.12

LIST OF DRUG PRODUCT CANDIDATES

To be supplied

CONFIDENTIAL TREATMENT REQUESTED

SCHEDULE 1.25

LIST OF MAJOR MARKETS

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License, Development and Commercialization Agreement--Confidential

CONFIDENTIAL TREATMENT REQUESTED

SCHEDULE 1.29

NOVARTIS PATENTS

- ---

License, Development and Commercialization Agreement--Confidential

CONFIDENTIAL TREATMENT REQUESTED

SCHEDULE 1.44

VERTEX PATENTS

- ---

License, Development and Commercialization Agreement--Confidential

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Exhibit 31.1

SECTION 302 CEO CERTIFICATION

I, Joshua S. Boger, certify that:

1. I have reviewed this annual report on Form 10-K/A of Vertex Pharmaceuticals Incorporated;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report; and

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report.

Date: September 8, 2004

/s/ JOSHUA S. BOGER

Joshua S. Boger
Chairman and Chief Executive Officer

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Exhibit 31.2

SECTION 302 CFO CERTIFICATION

I, Ian F. Smith, certify that:

1. I have reviewed this annual report on Form 10-K/A of Vertex Pharmaceuticals Incorporated;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report; and

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report.

Date: September 8, 2004

/s/ IAN F. SMITH

Ian F. Smith
Senior Vice President and
Chief Financial Officer

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