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

FORM 10-Q

☒ QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
FOR THE QUARTERLY PERIOD ENDED SEPTEMBER 30, 2021

or

❑ 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	**04-3039129**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
50 Northern Avenue, Boston, Massachusetts	**02210**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code **(617) 341-6100**

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

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, $0.01 Par Value Per Share	VRTX	The Nasdaq Global Select Market

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☒ Accelerated filer ☐ Non-accelerated filer ☐ Smaller reporting company ☐ Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

Indicate the number of shares outstanding of each of the issuer's classes of common stock, as of the latest practicable date.

Common Stock, par value $0.01 per share	254,251,938	Outstanding at October 29, 2021

VERTEX PHARMACEUTICALS INCORPORATED
FORM 10-Q
FOR THE QUARTER ENDED SEPTEMBER 30, 2021

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"We," "us," "Vertex" and the "Company" as used in this Quarterly Report on Form 10-Q refer to Vertex Pharmaceuticals Incorporated, a Massachusetts corporation, and its subsidiaries.

"Vertex," "KALYDECO®," "ORKAMBI®," "SYMDEKO®," "SYMKEVI®" and "TRIKAFTA®" are registered trademarks of Vertex. The trademark for "KAFTRIO™" is pending in the United States and registered in the European Union. Other brands, names and trademarks contained in this Quarterly Report on Form 10-Q are the property of their respective owners.

We use the brand name for our products when we refer to the product that has been approved and with respect to the indications on the approved label. Otherwise, including in discussions of our cystic fibrosis development programs, we refer to our compounds by their scientific (or generic) name or VX developmental designation.

Part I. Financial Information

Item 1. Financial Statements

VERTEX PHARMACEUTICALS INCORPORATED
Condensed Consolidated Statements of Operations
(unaudited)
(in thousands, except per share amounts)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Revenues:				
Product revenues, net	$ 1,984,164	$ 1,536,271	$ 5,500,839	$ 4,575,863
Other revenues	—	2,000	1,000	2,000
Total revenues	1,984,164	1,538,271	5,501,839	4,577,863
Costs and expenses:				
Cost of sales	236,512	186,182	656,813	533,199
Research and development expenses	493,751	493,497	2,356,814	1,362,953
Selling, general and administrative expenses	198,189	184,551	584,935	558,613
Change in fair value of contingent consideration	1,200	1,800	(1,100)	12,600
Total costs and expenses	929,652	866,030	3,597,462	2,467,365
Income from operations	1,054,512	672,241	1,904,377	2,110,498
Interest income	1,116	3,100	3,714	19,919
Interest expense	(15,255)	(13,856)	(46,411)	(41,863)
Other income (expense), net	42,368	84,386	(2,234)	139,621
Income before provision for income taxes	1,082,741	745,871	1,859,446	2,228,175
Provision for income taxes	230,813	78,437	287,456	120,718
Net income	$ 851,928	$ 667,434	$ 1,571,990	$ 2,107,457
Net income per common share:				
Basic	$ 3.30	$ 2.56	$ 6.08	$ 8.10
Diluted	$ 3.28	$ 2.53	$ 6.03	$ 7.98
Shares used in per share calculations:				
Basic	257,876	260,392	258,740	260,313
Diluted	259,707	264,079	260,877	264,031

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

VERTEX PHARMACEUTICALS INCORPORATED
Condensed Consolidated Statements of Comprehensive Income
(unaudited)
(in thousands)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Net income	$ 851,928	$ 667,434	$ 1,571,990	$ 2,107,457
Other comprehensive income (loss):				
Unrealized holding (losses) gains on marketable securities, net	(56)	(1,132)	(329)	818
Unrealized gains (losses) on foreign currency forward contracts, net of tax of $(9.6) million, $7.6 million, $(21.2) million and $7.3 million, respectively	34,766	(26,313)	77,011	(27,211)
Foreign currency translation adjustment	1,986	584	3,335	(12,616)
Total other comprehensive income (loss)	36,696	(26,861)	80,017	(39,009)
Comprehensive income	$ 888,624	$ 640,573	$ 1,652,007	$ 2,068,448

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

VERTEX PHARMACEUTICALS INCORPORATED
Condensed Consolidated Balance Sheets
(unaudited)
(in thousands, except per share amounts)

	September 30, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 6,275,698	$ 5,988,187
Marketable securities	685,187	670,710
Accounts receivable, net	1,100,372	885,352
Inventories	333,456	280,777
Prepaid expenses and other current assets	457,827	308,353
Total current assets	8,852,540	8,133,379
Property and equipment, net	1,042,347	958,534
Goodwill	1,002,158	1,002,158
Intangible assets	400,000	400,000
Deferred tax assets	933,839	882,779
Operating lease assets	312,343	325,564
Other assets	75,518	49,394
Total assets	$ 12,618,745	$ 11,751,808
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	$ 127,863	$ 155,139
Accrued expenses	1,584,992	1,404,971
Other current liabilities	201,409	317,423
Total current liabilities	1,914,264	1,877,533
Long-term finance lease liabilities	513,255	539,042
Long-term operating lease liabilities	363,545	350,463
Long-term contingent consideration	188,500	189,600
Other long-term liabilities	108,473	108,355
Total liabilities	3,088,037	3,064,993
Commitments and contingencies	—	—
Shareholders' equity:		
Preferred stock, $0.01 par value; 1,000 shares authorized; none issued and outstanding	—	—
Common stock, $0.01 par value; 500,000 shares authorized, 256,206 and 259,890 shares issued and outstanding, respectively	2,562	2,599
Additional paid-in capital	7,085,950	7,894,027
Accumulated other comprehensive income (loss)	11,537	(68,480)
Retained earnings	2,430,659	858,669
Total shareholders' equity	9,530,708	8,686,815
Total liabilities and shareholders' equity	$ 12,618,745	$ 11,751,808

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

VERTEX PHARMACEUTICALS INCORPORATED
Condensed Consolidated Statements of Shareholders' Equity
(unaudited)
(in thousands)

	Three Months Ended					
	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Retained Earnings (Accumulated Deficit)	Total Shareholders' Equity
	Shares	Amount				
Balance at June 30, 2020	260,124	$ 2,601	$ 7,943,717	$ (14,121)	$ (412,955)	$ 7,519,242
Other comprehensive loss, net of tax	—	—	—	(26,861)	—	(26,861)
Net income	—	—	—	—	667,434	667,434
Repurchase of common stock	(403)	(4)	(108,003)	—	—	(108,007)
Common stock withheld for employee tax obligations	(141)	(1)	(40,527)	—	—	(40,528)
Issuance of common stock under benefit plans	594	5	21,699	—	—	21,704
Stock-based compensation expense	—	—	100,489	—	—	100,489
Balance at September 30, 2020	260,174	$ 2,601	$ 7,917,375	$ (40,982)	$ 254,479	$ 8,133,473
Balance at June 30, 2021	259,114	$ 2,591	$ 7,640,233	$ (25,159)	$ 1,578,731	$ 9,196,396
Other comprehensive income, net of tax	—	—	—	36,696	—	36,696
Net income	—	—	—	—	851,928	851,928
Repurchase of common stock	(3,293)	(33)	(642,240)	—	—	(642,273)
Common stock withheld for employee tax obligations	(144)	(1)	(28,558)	—	—	(28,559)
Issuance of common stock under benefit plans	529	5	12,862	—	—	12,867
Stock-based compensation expense	—	—	103,653	—	—	103,653
Balance at September 30, 2021	256,206	$ 2,562	$ 7,085,950	$ 11,537	$ 2,430,659	$ 9,530,708

	Nine Months Ended					
	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Retained Earnings (Accumulated Deficit)	Total Shareholders' Equity
	Shares	Amount				
Balance at December 31, 2019	258,993	$ 2,589	$ 7,937,606	$ (1,973)	$ (1,852,978)	$ 6,085,244
Other comprehensive loss, net of tax	—	—	—	(39,009)	—	(39,009)
Net income	—	—	—	—	2,107,457	2,107,457
Repurchase of common stock	(1,807)	(18)	(408,015)	—	—	(408,033)
Common stock withheld for employee tax obligations	(727)	(7)	(179,768)	—	—	(179,775)
Issuance of common stock under benefit plans	3,715	37	232,042	—	—	232,079
Stock-based compensation expense	—	—	335,510	—	—	335,510
Balance at September 30, 2020	260,174	$ 2,601	$ 7,917,375	$ (40,982)	$ 254,479	$ 8,133,473
Balance at December 31, 2020	259,890	$ 2,599	$ 7,894,027	$ (68,480)	$ 858,669	$ 8,686,815
Other comprehensive income, net of tax	—	—	—	80,017	—	80,017
Net income	—	—	—	—	1,571,990	1,571,990
Repurchase of common stock	(5,282)	(53)	(1,067,172)	—	—	(1,067,225)
Common stock withheld for employee tax obligations	(633)	(6)	(134,217)	—	—	(134,223)
Issuance of common stock under benefit plans	2,231	22	66,707	—	—	66,729
Stock-based compensation expense	—	—	326,605	—	—	326,605
Balance at September 30, 2021	256,206	$ 2,562	$ 7,085,950	$ 11,537	$ 2,430,659	$ 9,530,708

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

VERTEX PHARMACEUTICALS INCORPORATED
Condensed Consolidated Statements of Cash Flows
(unaudited)
(in thousands)

	Nine Months Ended September 30,	
	2021	**2020**
Cash flows from operating activities:		
Net income	$ 1,571,990	$ 2,107,457
Adjustments to reconcile net income to net cash provided by operating activities:		
Stock-based compensation expense	322,792	332,434
Depreciation expense	91,768	80,160
(Decrease) increase in fair value of contingent consideration	(1,100)	12,600
Deferred income taxes	(112,654)	65,110
Gains on equity securities	(4,993)	(140,866)
Other non-cash items, net	20,588	52,371
Changes in operating assets and liabilities:		
Accounts receivable, net	(231,166)	(151,191)
Inventories	(65,827)	(94,907)
Prepaid expenses and other assets	(107,672)	(264,909)
Accounts payable	(22,043)	16,153
Accrued expenses	254,157	451,084
Other liabilities	(67,333)	296,477
Net cash provided by operating activities	1,648,507	2,761,973
Cash flows from investing activities:		
Purchases of available-for-sale debt securities	(447,759)	(246,937)
Maturities of available-for-sale debt securities	452,133	184,419
Purchases of property and equipment	(173,285)	(212,109)
Investment in equity securities and notes receivable	(37,991)	(19,327)
Sale of equity securities	—	149,595
Net cash used in investing activities	(206,902)	(144,359)
Cash flows from financing activities:		
Issuances of common stock under benefit plans	67,289	234,854
Repurchases of common stock	(1,057,225)	(408,033)
Payments in connection with common stock withheld for employee tax obligations	(134,223)	(179,775)
Payments on finance leases	(34,592)	(31,378)
Proceeds from finance leases	12,647	8,642
Other financing activities	4,339	(4,399)
Net cash used in financing activities	(1,141,765)	(380,089)
Effect of changes in exchange rates on cash	(8,472)	2,779
Net increase in cash, cash equivalents and restricted cash	291,368	2,240,304
Cash, cash equivalents and restricted cash—beginning of period	5,988,845	3,120,681
Cash, cash equivalents and restricted cash—end of period	$ 6,280,213	$ 5,360,985
Supplemental disclosure of cash flow information:		
Cash paid for interest	$ 42,698	$ 40,769
Cash paid for income taxes	$ 381,533	$ 81,684

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

A. Basis of Presentation and Accounting Policies

Basis of Presentation

The accompanying condensed consolidated financial statements are unaudited and have been prepared by Vertex Pharmaceuticals Incorporated ("Vertex" or the "Company") in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP").

The condensed consolidated financial statements reflect the operations of the Company and its wholly-owned subsidiaries. All material intercompany balances and transactions have been eliminated. The Company operates in one segment, pharmaceuticals. The Company has reclassified certain items from the prior year's condensed consolidated financial statements to conform to the current year's presentation.

Certain information and footnote disclosures normally included in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2020 (the "2020 Annual Report on Form 10-K") have been condensed or omitted. These interim financial statements, in the opinion of management, reflect all normal recurring adjustments necessary for a fair presentation of the financial position and results of operations for the interim periods ended September 30, 2021 and 2020.

The results of operations for the interim periods are not necessarily indicative of the results of operations to be expected for the full fiscal year. These interim financial statements should be read in conjunction with the audited financial statements for the year ended December 31, 2020, which are contained in the Company's 2020 Annual Report on Form 10-K.

Use of Estimates

The preparation of condensed consolidated financial statements in accordance with U.S. GAAP requires management to make certain estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the condensed consolidated financial statements, and the amounts of revenues and expenses during the reported periods. The Company bases its estimates on historical experience and various other assumptions, including in certain circumstances future projections that management believes to be reasonable under the circumstances. Actual results could differ from those estimates. Changes in estimates are reflected in reported results in the period in which they become known.

Recently Adopted and Issued Accounting Standards

Income Taxes

In 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740)* ("ASU 2019-12"), which simplifies the accounting for income taxes. ASU 2019-12 became effective on January 1, 2021. The adoption of ASU 2019-12 did not have a significant impact on the Company's condensed consolidated financial statements.

For a discussion of other recent accounting pronouncements please refer to Note A, "Nature of Business and Accounting Policies," in the Company's 2020 Annual Report on Form 10-K.

Summary of Significant Accounting Policies

The Company's significant accounting policies are described in Note A, "Nature of Business and Accounting Policies," in its 2020 Annual Report on Form 10-K.

B. Revenue Recognition

Disaggregation of Revenue

Revenues by Product

Product revenues, net consisted of the following:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
	(in thousands)			
TRIKAFTA/KAFTRIO	$ 1,555,772	$ 960,308	$ 4,004,600	$ 2,773,256
SYMDEKO/SYMKEVI	81,415	156,178	339,969	501,066
ORKAMBI	184,561	225,919	624,224	692,038
KALYDECO	162,416	193,866	532,046	609,503
Total product revenues, net	$ 1,984,164	$ 1,536,271	$ 5,500,839	$ 4,575,863

Product Revenues by Geographic Location

Total net product revenues by geographic region, based on the location of the customer, consisted of the following:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
	(in thousands)			
United States	$ 1,382,892	$ 1,222,565	$ 3,893,245	$ 3,620,467
Outside of the United States				
Europe	518,826	251,366	1,382,701	766,438
Other	82,446	62,340	224,893	188,958
Total product revenues outside of the United States	601,272	313,706	1,607,594	955,396
Total product revenues, net	$ 1,984,164	$ 1,536,271	$ 5,500,839	$ 4,575,863

Contract Liabilities

The Company had contract liabilities of $104.1 million and $191.5 million as of September 30, 2021 and December 31, 2020, respectively, related to annual contracts with government-owned and supported customers in international markets that limit the amount of annual reimbursement the Company can receive. Upon exceeding the annual reimbursement amount, products are provided free of charge, which is a material right. These contracts include upfront payments and fees. The Company defers a portion of the consideration received for shipments made up to the annual reimbursement limit as a portion of “Other current liabilities.” The deferred amount is recognized as revenue when the free products are shipped. The Company’s product revenue contracts include performance obligations that are one year or less.

The Company’s contract liabilities at the end of each fiscal year relate to contracts with annual reimbursement limits in international markets in which the annual period associated with the contract is not the same as the Company’s fiscal year. In these markets, the Company recognizes revenues related to performance obligations satisfied in previous years; however, these revenues do not relate to any performance obligations that were satisfied more than 12 months prior to the beginning of the current year.

C. Collaborative Arrangements

The Company has entered into numerous agreements pursuant to which it collaborates with third parties on research, development and commercialization programs, including in-license and out-license agreements.

The Company's in-license and out-license agreements that had a significant impact on its financial statements for the three and nine months ended September 30, 2021 and 2020, or were new or materially revised during the nine months ended September 30, 2021, are described below. Additional in-license and out-license agreements were described in Note B, "Collaborative Arrangements," of the Company's 2020 Annual Report on Form 10-K.

In-license Agreements

The Company has entered into a number of in-license agreements in order to advance and obtain access to technologies and services related to its research and early-development activities. The Company is generally required to make an upfront payment upon execution of the license agreement; development, regulatory and commercialization milestones payments upon the achievement of certain product research, development and commercialization objectives; and royalty payments on future sales, if any, of commercial products resulting from the collaboration.

Pursuant to the terms of its in-license agreements, the Company's collaborators typically lead the discovery efforts and the Company leads all preclinical, development and commercialization activities associated with the advancement of any drug candidates and funds all expenses.

The Company typically can terminate its in-license agreements by providing advance notice to its collaborators; the required length of notice is dependent on whether any product developed under the license agreement has received marketing approval. The Company's license agreements may be terminated by either party for a material breach by the other, subject to notice and cure provisions. Unless earlier terminated, these license agreements generally remain in effect until the date on which the royalty term and all payment obligations with respect to all products in all countries have expired.

The Company's "Research and development expenses" included $26.8 million and $986.8 million for the three and nine months ended September 30, 2021, respectively, and $80.1 million and $143.3 million for the three and nine months ended September 30, 2020, respectively, related to upfront and milestone payments pursuant to its in-license agreements.

CRISPR Therapeutics AG - CRISPR-Cas9 Gene-editing Therapies

In 2015, the Company entered into a strategic collaboration, option and license agreement (the "CRISPR Agreement") with CRISPR Therapeutics AG and its affiliates ("CRISPR") to collaborate on the discovery and development of potential new treatments aimed at the underlying genetic causes of human diseases using CRISPR-Cas9 gene-editing technology. The Company had the exclusive right to license certain targets. In 2019, the Company elected to exclusively license three targets, including cystic fibrosis, pursuant to the CRISPR Agreement. For each of the three targets that the Company elected to license, CRISPR has the potential to receive up to an additional $410.0 million in development, regulatory and commercial milestones as well as royalties on net product sales.

In 2017, the Company entered into a joint development and commercialization agreement with CRISPR pursuant to the terms of the CRISPR Agreement (the "Original CTX001 JDCA"), under which the Company and CRISPR were co-developing and preparing to co-commercialize CTX001 for the treatment of hemoglobinopathies, including treatments for sickle cell disease and beta thalassemia.

In the second quarter of 2021, the Company and CRISPR amended and restated the Original CTX001 JDCA (the "A&R JDCA"), pursuant to which the parties agreed to, among other things, (a) adjust the governance structure for the collaboration and adjust the responsibilities of each party thereunder; (b) adjust the allocation of net profits and net losses between the parties; and (c) exclusively license (subject to CRISPR's reserved rights to conduct certain activities) certain intellectual property rights to the Company relating to the products that may be researched, developed, manufactured and commercialized under such agreement.

Pursuant to the A&R JDCA, the Company is now leading global development, manufacturing and commercialization of CTX001, with support from CRISPR. Subject to the terms and conditions of the A&R JDCA, the Company also has the right

to conduct all research, development, manufacturing and commercialization activities relating to the product candidates and products under the A&R JDCA (including CTX001) throughout the world subject to CRISPR's reserved right to conduct certain activities.

In connection with the amendment and restatement of this agreement, the Company made a $900.0 million upfront payment to CRISPR in the second quarter of 2021. The Company concluded that it did not have any alternative future use for the acquired in-process research and development and recorded this upfront payment to "Research and development expenses." CRISPR has the potential to receive an additional one-time $200.0 million milestone payment upon receipt of the first marketing approval of CTX001 from the U.S. Food or Drug Administration or the European Commission.

The Company and CRISPR shared equally all expenses incurred under the Original CTX001 JDCA. On July 1, 2021, with respect to CTX001, the net profits and net losses incurred pursuant to the A&R JDCA began to be allocated 60% to the Company and 40% to CRISPR, while all other product candidates and products continued to have net profits and net losses shared equally between the parties. The Company concluded that the Original CTX001 JDCA and the A&R JDCA are cost-sharing arrangements, which result in the net impact of the arrangements being recorded in "Research and development expenses" in its condensed consolidated statements of operations. During the three and nine months ended September 30, 2021 and 2020, the Company recognized the following amounts in total related to these agreements:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
	(in thousands)			
Total research and development expenses incurred under the Original CTX001 JDCA and A&R JDCA	$ 58,659	$ 28,623	$ 147,448	$ 66,720
Vertex's share recognized in research and development expenses in condensed consolidated statement of operations	35,195	14,311	79,590	33,360

Moderna, Inc.

In 2016, the Company entered into a strategic collaboration and licensing agreement with Moderna, Inc. ("Moderna"), pursuant to which the parties are seeking to identify and develop messenger ribonucleic acid ("mRNA") therapeutics for the treatment of CF.

In September 2020, the Company entered into a new strategic collaboration and licensing agreement with Moderna (the "2020 Moderna Agreement") aimed at the discovery and development of lipid nanoparticles and mRNAs that can deliver gene-editing therapies to lung cells for the treatment of CF. Pursuant to the 2020 Moderna Agreement, Moderna received an upfront payment of $75.0 million and is eligible to receive up to $380.0 million in development, regulatory and commercial milestones as well as royalties on net product sales. The Company determined that substantially all of the fair value of the 2020 Moderna Agreement was attributable to in-process research and development and no substantive processes were acquired that would constitute a business. The Company concluded that it did not have any alternative future use for the acquired in-process research and development and recorded the upfront payment to "Research and development expenses" in the third quarter of 2020.

Out-license Agreements

The Company has entered into licensing agreements pursuant to which it has out-licensed rights to certain drug candidates to third-party collaborators. Pursuant to these out-license agreements, the Company's collaborators become responsible for all costs related to the continued development of such drug candidates and obtain development and commercialization rights to these drug candidates. Depending on the terms of the agreements, the Company's collaborators may be required to make upfront payments, milestone payments upon the achievement of certain product research and development objectives and may also be required to pay royalties on future sales, if any, of commercial products resulting from the collaboration. The termination provisions associated with these collaborations are generally the same as those described above related to the Company's in-license agreements. None of the Company's out-license agreements had a significant impact on the Company's condensed consolidated statement of operations during the three and nine months ended September 30, 2021 and 2020.

Cystic Fibrosis Foundation

The Company has a research, development and commercialization agreement that was originally entered into in 2004 with the Cystic Fibrosis Foundation, as successor in interest to the Cystic Fibrosis Foundation Therapeutics, Inc. This agreement was most recently amended in 2016. Pursuant to the agreement, as amended, the Company agreed to pay royalties ranging from low-single digits to mid-single digits on potential sales of certain compounds first synthesized and/or tested between March 1, 2014 and August 31, 2016, including elexacaftor, and tiered royalties ranging from single digits to sub-teens on covered compounds first synthesized and/or tested during a research term on or before February 28, 2014, including KALYDECO (ivacaftor), ORKAMBI (lumacaftor in combination with ivacaftor) and SYMDEKO/SYMKEVI (tezacaftor in combination with ivacaftor). For combination products, such as ORKAMBI, SYMDEKO/SYMKEVI and TRIKAFTA/KAFTRIO (elexacaftor/tezacaftor/ivacaftor and ivacaftor), sales are allocated equally to each of the active pharmaceutical ingredients in the combination product.

D. Earnings Per Share

Basic net income per common share is based upon the weighted-average number of common shares outstanding during the period. Diluted net income per common share utilizing the treasury-stock method is based upon the weighted-average number of common shares outstanding during the period plus additional weighted-average common equivalent shares outstanding during the period when the effect is dilutive.

The following table sets forth the computation of basic and diluted net income per common share for the periods ended:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
	(in thousands, except per share amounts)			
Net income	$ 851,928	$ 667,434	$ 1,571,990	$ 2,107,457
Basic weighted-average common shares outstanding	257,876	260,392	258,740	260,313
Effect of potentially dilutive securities:				
Stock options	971	1,887	1,124	1,936
Restricted stock units (including PSUs)	841	1,788	1,003	1,765
Employee stock purchase program	19	12	10	17
Diluted weighted-average common shares outstanding	259,707	264,079	260,877	264,031
Basic net income per common share	$ 3.30	$ 2.56	$ 6.08	$ 8.10
Diluted net income per common share	$ 3.28	$ 2.53	$ 6.03	$ 7.98

The Company did not include the securities in the following table in the computation of the net income per common share because the effect would have been anti-dilutive during each period:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
	(in thousands)			
Stock options	1,060	23	711	303
Unvested restricted stock units (including PSUs)	204	252	440	229

E. Fair Value Measurements

The following fair value hierarchy is used to classify assets and liabilities based on observable inputs and unobservable inputs used in order to determine the fair value of the Company's financial assets and liabilities:

Level 1:	Quoted prices in active markets for identical assets or liabilities. An active market for an asset or liability is a market in which transactions for the asset or liability occur with sufficient frequency and volume to provide pricing information on an ongoing basis.
Level 2:	Observable inputs other than Level 1 inputs. Examples of Level 2 inputs include quoted prices in active markets for similar assets or liabilities and quoted prices for identical assets or liabilities in markets that are not active.
Level 3:	Unobservable inputs based on the Company's assessment of the assumptions that market participants would use in pricing the asset or liability.

The Company's investment strategy is focused on capital preservation. The Company invests in instruments that meet the credit quality standards outlined in the Company's investment policy. This policy also limits the amount of credit exposure to any one issue or type of instrument. The Company maintains strategic investments separately from the investment policy that governs its other cash, cash equivalents and marketable securities as described in Note F, "Marketable Securities and Equity Investments." Additionally, the Company utilizes foreign currency forward contracts intended to mitigate the effect of changes in foreign exchange rates on its condensed consolidated statement of operations.

During the three and nine months ended September 30, 2021 and 2020, the Company did not record any other-than-temporary impairment charges related to its financial assets.

The following tables set forth the Company's financial assets and liabilities subject to fair value measurements by level within the fair value hierarchy (and does not include $2.7 billion and $2.8 billion of cash as of September 30, 2021 and December 31, 2020, respectively):

	As of September 30, 2021				As of December 31, 2020			
	Total	Level 1	Level 2	Level 3	Total	Level 1	Level 2	Level 3
	(in thousands)							
Financial instruments carried at fair value (asset positions):								
Cash equivalents:								
Money market funds	$ 3,578,764	$ 3,578,764	$ —	$ —	$ 3,141,053	$ 3,141,053	$ —	$ —
Commercial paper	31,998	—	31,998	—	—	—	—	—
Marketable securities:								
Corporate equity securities	218,764	218,764	—	—	195,781	15,650	180,131	—
U.S. Treasury securities	46,539	46,539	—	—	—	—	—	—
Government-sponsored enterprise securities	69,002	69,002	—	—	80,063	80,063	—	—
Corporate debt securities	95,359	—	95,359	—	231,598	—	231,598	—
Commercial paper	255,523	—	255,523	—	163,268	—	163,268	—
Prepaid expenses and other current assets:								
Foreign currency forward contracts	34,300	—	34,300	—	—	—	—	—
Other assets:								
Foreign currency forward contracts	4,781	—	4,781	—	—	—	—	—
Total financial assets	$ 4,335,030	$ 3,913,069	$ 421,961	$ —	$ 3,811,763	$ 3,236,766	$ 574,997	$ —
Financial instruments carried at fair value (liability positions):								
Other current liabilities:								
Foreign currency forward contracts	$ (4,356)	$ —	$ (4,356)	$ —	$ (59,184)	$ —	$ (59,184)	$ —
Long-term contingent consideration	(188,500)	—	—	(188,500)	(189,600)	—	—	(189,600)
Other long-term liabilities:								
Foreign currency forward contracts	(29)	—	(29)	—	(4,283)	—	(4,283)	—
Total financial liabilities	$ (192,885)	$ —	$ (4,385)	$ (188,500)	$ (253,067)	$ —	$ (63,467)	$ (189,600)

Please refer to Note F, "Marketable Securities and Equity Investments," for the carrying amount and related unrealized gains (losses) by type of investment.

Fair Value of Corporate Equity Securities

The Company classifies its investments in publicly traded corporate equity securities as "Marketable securities" on its condensed consolidated balance sheets. Generally, the Company's investments in the common stock of these publicly traded companies are valued based on Level 1 inputs because they have readily determinable fair values. However, certain of the Company's investments in publicly traded companies have been or continue to be valued based on Level 2 inputs due to transfer restrictions associated with these investments. Please refer to Note F, "Marketable Securities and Equity Investments," for further information on these investments.

Fair Value of Contingent Consideration

In 2019, the Company acquired Exonics Therapeutics, Inc. ("Exonics"), a privately-held company focused on creating transformative gene-editing therapies to repair mutations that cause DMD and other severe neuromuscular diseases, including DM1. The Company's Level 3 contingent consideration liabilities are related to $678.3 million of development and regulatory milestones potentially payable to Exonics' former equity holders. The Company bases its estimates of the probability of achieving the milestones relevant to the fair value of contingent payments on industry data attributable to rare diseases. The discount rates used in the valuation model for contingent payments, which were between 0.3% and 2.2% as of September 30, 2021, represent a measure of credit risk and market risk associated with settling the liabilities. Significant

judgment is used in determining the appropriateness of these assumptions at each reporting period. Due to the uncertainties associated with development and commercialization of drug candidates in the pharmaceutical industry and the effects of changes in other assumptions including discount rates, the Company expects its estimates regarding the fair value of contingent consideration to change in the future, resulting in adjustments to the fair value of the Company's contingent consideration liabilities, and the effect of any such adjustments could be material.

The following table represents a rollforward of the fair value of the Company's contingent consideration liabilities:

	Nine Months Ended September 30, 2021
	(in thousands)
Balance at December 31, 2020	$ 189,600
Decrease in fair value of contingent payments	(1,100)
Balance at September 30, 2021	$ 188,500

F. Marketable Securities and Equity Investments

A summary of the Company's cash equivalents and marketable securities, which are recorded at fair value (and do not include $2.7 billion and $2.8 billion of cash as of September 30, 2021 and December 31, 2020, respectively), is shown below:

	As of September 30, 2021				As of December 31, 2020			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
	(in thousands)							
Cash equivalents:								
Money market funds	$ 3,578,764	$ —	$ —	$ 3,578,764	$ 3,141,053	$ —	$ —	$ 3,141,053
Commercial paper	31,997	1	—	31,998	—	—	—	—
Total cash equivalents	$ 3,610,761	$ 1	$ —	$ 3,610,762	$ 3,141,053	$ —	$ —	$ 3,141,053
Marketable securities:								
U.S. Treasury securities	$ 46,536	$ 4	$ (1)	$ 46,539	$ —	$ —	$ —	$ —
Government-sponsored enterprise securities	68,996	8	(2)	69,002	80,046	17	—	80,063
Corporate debt securities	95,385	26	(52)	95,359	231,263	377	(42)	231,598
Commercial paper	255,501	40	(18)	255,523	163,286	19	(37)	163,268
Total marketable debt securities	466,418	78	(73)	466,423	474,595	413	(79)	474,929
Corporate equity securities	69,418	150,263	(917)	218,764	51,427	144,354	—	195,781
Total marketable securities	$ 535,836	$ 150,341	$ (990)	$ 685,187	$ 526,022	$ 144,767	$ (79)	$ 670,710

Available-for-sale debt securities were classified on the Company's condensed consolidated balance sheets at fair value as follows:

	As of September 30, 2021	As of December 31, 2020
	(in thousands)	
Cash and cash equivalents	$ 3,610,762	$ 3,141,053
Marketable securities	466,423	474,929
Total	$ 4,077,185	$ 3,615,982

Available-for-sale debt securities by contractual maturity were as follows:

	As of September 30, 2021	As of December 31, 2020
	(in thousands)	
Matures within one year	$ 4,014,441	$ 3,526,185
Matures after one year through five years	62,744	89,797
Total	$ 4,077,185	$ 3,615,982

The Company has a limited number of available-for-sale debt securities in insignificant loss positions as of September 30, 2021, which it does not intend to sell and has concluded it will not be required to sell before recovery of the amortized costs for the investments at maturity. The Company did not record any charges for other-than-temporary declines in the fair value of available-for-sale debt securities or gross realized gains or losses in the three and nine months ended September 30, 2021 and 2020.

The Company records changes in the fair value of its investments in corporate equity securities to “Other income (expense), net” on its condensed consolidated statements of operations. During the three and nine months ended September 30, 2021 and 2020, the Company’s net unrealized gains on corporate equity securities held at the conclusion of each period were as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
	(in thousands)			
Net unrealized gains	$ 46,679	$ 69,834	$ 4,993	$ 102,317

During the nine months ended September 30, 2020, the Company received proceeds of $149.6 million related to the sale of the common stock of publicly traded companies, which had a total original weighted-average cost basis of $51.3 million. There were no sales of the common stock of publicly traded companies during the nine months ended September 30, 2021.

As of September 30, 2021, the carrying value of the Company’s equity investments without readily determinable fair values, which are recorded in “Other assets” on its condensed consolidated balance sheets, was $35.9 million.

G. Accumulated Other Comprehensive Income (Loss)

The following table summarizes the changes in accumulated other comprehensive income (loss) by component:

	Foreign Currency Translation Adjustment	Unrealized Holding Gains (Losses), Net of Tax		Total
		On Available-For-Sale Debt Securities	On Foreign Currency Forward Contracts	
	(in thousands)			
Balance at December 31, 2020	$ (15,678)	$ 334	$ (53,136)	$ (68,480)
Other comprehensive income (loss) before reclassifications	3,335	(329)	46,175	49,181
Amounts reclassified from accumulated other comprehensive (loss) income	—	—	30,836	30,836
Net current period other comprehensive income (loss)	3,335	(329)	77,011	80,017
Balance at September 30, 2021	$ (12,343)	$ 5	$ 23,875	$ 11,537
Balance at December 31, 2019	$ (895)	$ 503	$ (1,581)	$ (1,973)
Other comprehensive (loss) income before reclassifications	(12,616)	818	(20,913)	(32,711)
Amounts reclassified from accumulated other comprehensive loss	—	—	(6,298)	(6,298)
Net current period other comprehensive (loss) income	(12,616)	818	(27,211)	(39,009)
Balance at September 30, 2020	$ (13,511)	$ 1,321	$ (28,792)	$ (40,982)

H. Hedging

Foreign currency forward contracts - Designated as hedging instruments

The Company maintains a hedging program intended to mitigate the effect of changes in foreign exchange rates for a portion of the Company's forecasted product revenues denominated in certain foreign currencies. The program includes foreign currency forward contracts that are designated as cash flow hedges under U.S. GAAP having contractual durations from one to eighteen months. The Company recognizes realized gains and losses for the effective portion of such contracts in "Product revenues, net" in its condensed consolidated statements of operations in the same period that it recognizes the product revenues that were impacted by the hedged foreign exchange rate changes.

The Company formally documents the relationship between foreign currency forward contracts (hedging instruments) and forecasted product revenues (hedged items), as well as the Company's risk management objective and strategy for undertaking various hedging activities, which includes matching all foreign currency forward contracts that are designated as cash flow hedges to forecasted transactions. The Company also formally assesses, both at the hedge's inception and on an ongoing basis, whether the foreign currency forward contracts are highly effective in offsetting changes in cash flows of hedged items on a prospective and retrospective basis. If the Company were to determine that a (i) foreign currency forward contract is not highly effective as a cash flow hedge, (ii) foreign currency forward contract has ceased to be a highly effective hedge or (iii) forecasted transaction is no longer probable of occurring, the Company would discontinue hedge accounting treatment prospectively. The Company measures effectiveness based on the change in fair value of the forward contracts and the fair value of the hypothetical foreign currency forward contracts with terms that match the critical terms of the risk being hedged. As of September 30, 2021, all hedges were determined to be highly effective.

The Company considers the impact of its counterparties' credit risk on the fair value of the foreign currency forward contracts. As of September 30, 2021 and December 31, 2020, credit risk did not change the fair value of the Company's foreign currency forward contracts.

The following table summarizes the notional amount in U.S. dollars of the Company's outstanding foreign currency forward contracts designated as cash flow hedges under U.S. GAAP:

Foreign Currency	As of September 30, 2021	As of December 31, 2020
	(in thousands)	
Euro	$ 1,194,338	$ 745,099
British pound sterling	277,815	160,427
Australian dollar	95,970	99,922
Canadian dollar	87,259	86,468
Swiss Franc	41,335	—
Total foreign currency forward contracts	$ 1,696,717	$ 1,091,916

Foreign currency forward contracts - Not designated as hedging instruments

The Company also enters into foreign currency forward contracts with contractual maturities of less than one month, which are designed to mitigate the effect of changes in foreign exchange rates on monetary assets and liabilities, including intercompany balances. These contracts are not designated as hedging instruments under U.S. GAAP. The Company recognizes realized gains and losses for such contracts in "Other income (expense), net" in its condensed consolidated statements of operations each period. As of September 30, 2021, the notional amount of the Company's outstanding foreign currency forward contracts where hedge accounting under U.S. GAAP is not applied was $306.2 million.

During the three and nine months ended September 30, 2021 and 2020, the Company recognized the following related to foreign currency forward contracts in its condensed consolidated statements of operations:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
	(in thousands)			
Designated as hedging instruments - Reclassified from AOCI				
Product revenues, net	$ (5,224)	$ (7,249)	$ (39,342)	$ 8,039
Not designated as hedging instruments				
Other income (expense), net	$ (400)	$ 25,897	$ (9,350)	$ 15,724
Total reported in the Condensed Consolidated Statement of Operations				
Product revenues, net	$ 1,984,164	$ 1,536,271	$ 5,500,839	$ 4,575,863
Other income (expense), net	$ 42,368	$ 84,386	$ (2,234)	$ 139,621

The following table summarizes the fair value of the Company's outstanding foreign currency forward contracts designated as cash flow hedges under U.S. GAAP included on its condensed consolidated balance sheets:

As of September 30, 2021			
Assets		Liabilities	
Classification	Fair Value	Classification	Fair Value
	(in thousands)		
Prepaid expenses and other current assets	$ 34,300	Other current liabilities	$ (4,356)
Other assets	4,781	Other long-term liabilities	(29)
Total assets	$ 39,081	Total liabilities	$ (4,385)

As of December 31, 2020			
Assets		**Liabilities**	
Classification	**Fair Value**	**Classification**	**Fair Value**
	(in thousands)		
Prepaid expenses and other current assets	$ —	Other current liabilities	$ (59,184)
Other assets	—	Other long-term liabilities	(4,283)
Total assets	$ —	Total liabilities	$ (63,467)

As of September 30, 2021, the Company expects the amounts that are related to foreign exchange forward contracts designated as cash flow hedges under U.S. GAAP recorded in “Prepaid expenses and other current assets” and “Other current liabilities” to be reclassified to earnings within twelve months.

The following table summarizes the potential effect of offsetting derivatives by type of financial instrument designated as cash flow hedges under U.S. GAAP on the Company’s condensed consolidated balance sheets:

	As of September 30, 2021				
	Gross Amounts Recognized	**Gross Amounts Offset**	**Gross Amounts Presented**	**Gross Amounts Not Offset**	**Legal Offset**
Foreign currency forward contracts			**(in thousands)**		
Total assets	$ 39,081	$ —	$ 39,081	$ (4,385)	$ 34,696
Total liabilities	(4,385)	—	(4,385)	4,385	—

	As of December 31, 2020				
	Gross Amounts Recognized	**Gross Amounts Offset**	**Gross Amounts Presented**	**Gross Amounts Not Offset**	**Legal Offset**
Foreign currency forward contracts			**(in thousands)**		
Total assets	$ —	$ —	$ —	$ —	$ —
Total liabilities	(63,467)	—	(63,467)	—	(63,467)

I. Inventories

Inventories consisted of the following:

	As of September 30, 2021	**As of December 31, 2020**
	(in thousands)	
Raw materials	$ 45,990	$ 46,232
Work-in-process	192,650	161,324
Finished goods	94,816	73,221
Total	$ 333,456	$ 280,777

J. Stock-based Compensation Expense and Share Repurchase Programs

Stock-based compensation expense

During the three and nine months ended September 30, 2021 and 2020, the Company recognized the following stock-based compensation expense:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
	(in thousands)			
Stock-based compensation expense by type of award:				
Restricted stock units (including PSUs) and restricted stock	$ 89,458	$ 84,043	$ 279,131	$ 279,611
Stock options	7,875	13,221	29,580	47,334
ESPP share issuances	6,321	3,225	17,895	8,565
Stock-based compensation expense related to inventories	(658)	(950)	(3,814)	(3,076)
Total stock-based compensation expense included in costs and expenses	$ 102,996	$ 99,539	$ 322,792	$ 332,434
Stock-based compensation expense by line item:				
Cost of sales	$ 1,599	$ 1,250	$ 4,570	$ 3,998
Research and development expenses	60,995	60,770	196,412	203,732
Selling, general and administrative expenses	40,402	37,519	121,810	124,704
Total stock-based compensation expense included in costs and expenses	102,996	99,539	322,792	332,434
Income tax effect	(21,556)	(35,295)	(73,663)	(130,692)
Total stock-based compensation expense, net of tax	$ 81,440	$ 64,244	$ 249,129	$ 201,742

Share repurchase programs

In 2019, the Company's Board of Directors approved a share repurchase program (the "2019 Share Repurchase Program"), pursuant to which the Company repurchased $500.0 million of its common stock in 2019 and 2020. During the nine months ended September 30, 2020, the Company repurchased 1,806,587 shares of its common stock under the 2019 Share Repurchase Program for an aggregate of $408.0 million.

In November 2020, the Company's Board of Directors approved a share repurchase program (the "2020 Share Repurchase Program"), pursuant to which the Company repurchased $500.0 million of its common stock in 2020 and the first quarter of 2021. During the three months ended March 31, 2021, the Company repurchased 1,988,941 shares of its common stock under the 2020 Share Repurchase Program for an aggregate of $424.9 million.

On June 23, 2021, the Company's Board of Directors approved a new share repurchase program (the "2021 Share Repurchase Program"), pursuant to which the Company is authorized to repurchase up to $1.5 billion of its common stock by December 31, 2022. During the three months ended September 30, 2021, the Company repurchased 3,293,161 shares of its common stock under the 2021 Share Repurchase Program for an aggregate of $642.2 million. As of September 30, 2021, a total of $857.8 million remained available under this program.

K. Income Taxes

The Company is subject to U.S. federal, state, and foreign income taxes. During the three and nine months ended September 30, 2021 and 2020, the Company recorded the following provisions for income taxes and effective tax rates as compared to its income before provision for income taxes:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
	(in thousands, except percentages)			
Income before provision for income taxes	$ 1,082,741	$ 745,871	$ 1,859,446	$ 2,228,175
Provision for income taxes	230,813	78,437	287,456	120,718
Effective tax rate	21 %	11 %	15 %	5 %

The Company's effective tax rate for the three months ended September 30, 2021 was similar to the U.S. statutory rate. The Company's effective tax rate for the nine months ended September 30, 2021 was lower than the U.S. statutory rate primarily due to a $99.7 million discrete tax benefit associated with an increase in the U.K.'s corporate tax rate from 19% to 25%, which was enacted in June 2021 and will become effective in April 2023.

The Company's effective tax rate for the three months ended September 30, 2020 was lower than the U.S. statutory rate primarily due to a discrete tax benefit associated with an increase in the U.K.'s corporate tax rate from 17% to 19%, which was enacted and became effective in July 2020. The Company's effective tax rate for the nine months ended September 30, 2020 was lower than the U.S. statutory rate due to a discrete tax benefit of $209.0 million associated with an intra-entity transfer of intellectual property rights to the U.K., a discrete benefit related to the write-off of a long-term intercompany receivable, the increase in the U.K.'s corporate tax rate from 17% to 19% noted above and excess tax benefits related to stock-based compensation.

As part of the U.S. Tax Cut and Jobs Act of 2017, the Company is subject to a territorial tax system, under which it must establish an accounting policy to provide for tax on Global Intangible Low Taxed Income ("GILTI") earned by certain foreign subsidiaries. The Company has elected to treat the impact of GILTI as a current tax expense in its provision for income taxes.

The Company has reviewed the tax positions taken, or to be taken, in its tax returns for all tax years currently open to examination by a taxing authority. Unrecognized tax benefits represent the aggregate tax effect of differences between tax return positions and the benefits recognized in the consolidated financial statements. As of September 30, 2021 and December 31, 2020, the Company had $89.0 million and $75.8 million, respectively, of net unrecognized tax benefits, which would affect the Company's tax rate if recognized. The Company does not expect that its unrecognized tax benefits will materially change within the next twelve months.

As of September 30, 2021, foreign earnings have been retained by foreign subsidiaries for indefinite reinvestment. Upon repatriation of those earnings, in the form of dividends or otherwise, the Company could be subject to withholding taxes payable to the various foreign countries.

The Company files U.S. federal income tax returns and income tax returns in various state, local and foreign jurisdictions. The Company has various income tax audits ongoing at any time throughout the world. The Company is no longer subject to any tax assessment from an income tax examination in the U.S. or any other major taxing jurisdiction before 2011, except where the Company has net operating losses or tax credit carryforwards that originate before 2011.

L. Commitments and Contingencies

Revolving Credit Facilities

The Company and certain of its subsidiaries have entered into two credit agreements (the "Credit Agreements") with Bank of America, N.A., as administrative agent and the lenders referred to therein (the "Lenders"). The Credit Agreements

were not drawn upon at closing and the Company has not drawn upon them to date. Amounts drawn pursuant to the Credit Agreements, if any, will be used for general corporate purposes. Any amounts borrowed under the Credit Agreements will bear interest, at the Company's option, at either a base rate or a Eurocurrency rate, in each case plus an applicable margin based on the Company's consolidated leverage ratio (the ratio of the Company's total consolidated funded indebtedness to the Company's consolidated EBITDA for the most recently completed four fiscal quarter period).

In September 2019, the Company and certain of its subsidiaries entered into a $500.0 million unsecured revolving facility (the "2019 Credit Agreement") with the Lenders, which matures on September 17, 2024. Under the 2019 Credit Agreement, the applicable margins on base rate loans range from 0.125% to 0.500% and the applicable margins on Eurocurrency loans range from 1.125% to 1.500%. The 2019 Credit Agreement provides a sublimit of $50.0 million for letters of credit.

In September 2020, the Company and certain of its subsidiaries entered into a $2.0 billion unsecured revolving facility (the "2020 Credit Agreement") with the Lenders, which matures on September 18, 2022. Under the 2020 Credit Agreement, the applicable margins on base rate loans range from 0.500% to 0.875% and the applicable margins on Eurocurrency loans range from 1.500% to 1.875%. The 2020 Credit Agreement does not support letters of credit.

Subject to satisfaction of certain conditions, the Company may request that the borrowing capacity for each of the Credit Agreements be increased by an additional $500.0 million. Any amounts borrowed pursuant to the Credit Agreements are guaranteed by certain of the Company's existing and future domestic subsidiaries, subject to certain exceptions.

The Credit Agreements contain customary representations and warranties and affirmative and negative covenants, including financial covenants to maintain (x) subject to certain limited exceptions, a consolidated leverage ratio of 3.50 to 1.00, subject to an increase to 4.00 to 1.00 following a material acquisition and (y) a consolidated interest coverage ratio of 2.50 to 1.00, in each case measured on a quarterly basis. As of September 30, 2021, the Company was in compliance with the covenants described above. The Credit Agreements also contain customary events of default. In the case of a continuing event of default, the administrative agent would be entitled to exercise various remedies, including the acceleration of amounts due under outstanding loans.

Direct costs related to the Credit Agreements are recorded over the term of the Credit Agreements and were not material to the Company's financial statements.

Guaranties and Indemnifications

As permitted under Massachusetts law, the Company's Articles of Organization and By-laws provide that the Company will indemnify certain of its officers and directors for certain claims asserted against them in connection with their service as an officer or director. The maximum potential amount of future payments that the Company could be required to make under these indemnification provisions is unlimited. However, the Company has purchased directors' and officers' liability insurance policies that could reduce its monetary exposure and enable it to recover a portion of any future amounts paid. No indemnification claims currently are outstanding, and the Company believes the estimated fair value of these indemnification arrangements is minimal.

The Company customarily agrees in the ordinary course of its business to indemnification provisions in agreements with clinical trial investigators and sites in its drug development programs, sponsored research agreements with academic and not-for-profit institutions, various comparable agreements involving parties performing services for the Company and its real estate leases. The Company also customarily agrees to certain indemnification provisions in its drug discovery, development and commercialization collaboration agreements. With respect to the Company's clinical trials and sponsored research agreements, these indemnification provisions typically apply to any claim asserted against the investigator or the investigator's institution relating to personal injury or property damage, violations of law or certain breaches of the Company's contractual obligations arising out of the research or clinical testing of the Company's compounds or drug candidates. With respect to lease agreements, the indemnification provisions typically apply to claims asserted against the landlord relating to personal injury or property damage caused by the Company, to violations of law by the Company or to certain breaches of the Company's contractual obligations. The indemnification provisions appearing in the Company's collaboration agreements are similar to those for the other agreements discussed above, but in addition provide some limited indemnification for its collaborator in the event of third-party claims alleging infringement of intellectual property rights. In

each of the cases above, the indemnification obligation generally survives the termination of the agreement for some extended period, although the Company believes the obligation typically has the most relevance during the contract term and for a short period of time thereafter. The maximum potential amount of future payments that the Company could be required to make under these provisions is generally unlimited. The Company has purchased insurance policies covering personal injury, property damage and general liability that reduce its exposure for indemnification and would enable it in many cases to recover all or a portion of any future amounts paid. The Company has never paid any material amounts to defend lawsuits or settle claims related to these indemnification provisions. Accordingly, the Company believes the estimated fair value of these indemnification arrangements is minimal.

Other Contingencies

The Company has certain contingent liabilities that arise in the ordinary course of its business activities. The Company accrues a reserve for contingent liabilities when it is probable that future expenditures will be made, and such expenditures can be reasonably estimated. Other than the Company's contingent consideration liabilities discussed in Note E, "Fair Value Measurements," there were no material contingent liabilities accrued as of September 30, 2021 or December 31, 2020.

M. Additional Cash Flow Information

The cash, cash equivalents and restricted cash at the beginning and ending of each period presented in the Company's condensed consolidated statements of cash flows consisted of the following:

	Nine Months Ended September 30,			
	2021		2020	
	Beginning of period	End of period	Beginning of period	End of period
	(in thousands)			
Cash and cash equivalents	$ 5,988,187	$ 6,275,698	$ 3,109,322	$ 5,358,087
Prepaid expenses and other current assets	658	4,515	8,004	2,898
Other assets	—	—	3,355	—
Cash, cash equivalents and restricted cash per condensed consolidated statement of cash flows	$ 5,988,845	$ 6,280,213	$ 3,120,681	$ 5,360,985

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

OVERVIEW

We invest in scientific innovation to create transformative medicines for people with serious diseases with a focus on specialty markets. We have four approved medicines to treat cystic fibrosis, or CF, a life-threatening genetic disease, and are focused on increasing the number of people with CF eligible and able to receive our medicines through label expansions, approval of new medicines, and expanded reimbursement. We are broadening our pipeline into additional disease areas through internal research efforts and accessing external innovation through business development transactions.

Our triple combination regimen, TRIKAFTA/KAFTRIO (elexacaftor/tezacaftor/ivacaftor and ivacaftor), was approved in 2019 in the United States, or U.S., and in 2020 in the European Union, or E.U. Collectively, our four medicines are approved to treat the majority of the approximately 83,000 people with CF in North America, Europe and Australia. We are evaluating our medicines in additional patient populations, including younger children, with the goal of having small molecule treatments for up to 90% of people with CF. We are also pursuing genetic therapies to address the remaining 10% of people with CF who are not eligible for our small molecule correctors.

Beyond CF, we continue to research and develop small molecule drug candidates for the treatment of serious diseases, including alpha-1 antitrypsin, or AAT, deficiency, APOL1-mediated kidney diseases, and pain. We are also focused on developing cell and genetic therapies for various diseases in our pipeline, including sickle cell disease, or SCD, beta thalassemia, type 1 diabetes, or T1D, Duchenne muscular dystrophy, or DMD, myotonic dystrophy, or DM1, and CF. We are evaluating CTX001, a genetic therapy, as a potential treatment for SCD and transfusion-dependent beta thalassemia, or TDT, the most severe form of beta thalassemia, in collaboration with CRISPR Therapeutics AG, or CRISPR. In T1D, we are pursuing two programs for the transplant of functional islets into patients: transplantation of islet cells alone, using immunosuppression to protect the implanted cells, and implantation of the islet cells inside a novel immunoprotective device.

Financial Highlights

Revenues

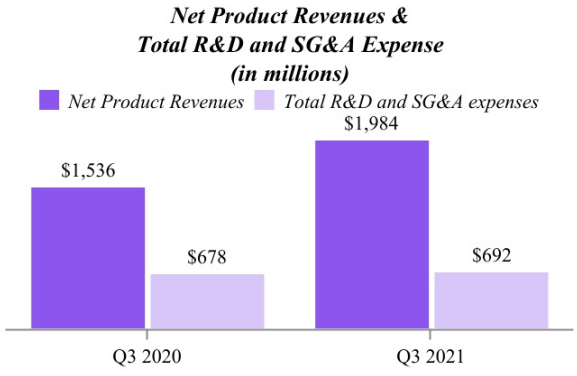
In the third quarter of 2021, our net product revenues continued to increase due to the uptake of KAFTRIO in Europe and continued performance of TRIKAFTA in the U.S.

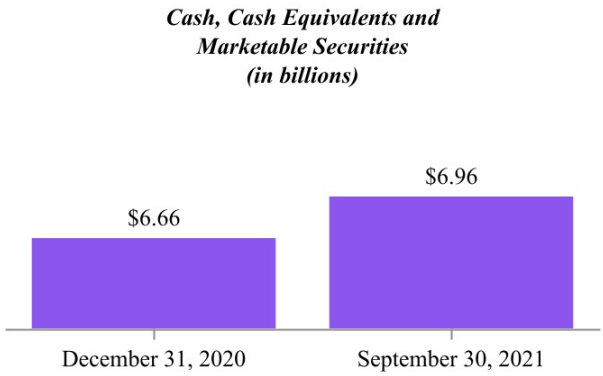
Expenses

Our total R&D and SG&A expenses increased to $691.9 million in the third quarter of 2021 as compared to $678.0 million in the third quarter of 2020. In the third quarter of 2021, cost of sales was 12% of our net product revenues.

Cash

Our cash, cash equivalent and marketable securities increased to $6.96 billion as of September 30, 2021 as compared to $6.66 billion as of December 31, 2020 primarily due to our net product revenues and profitability, offset by repurchases of our common stock, and a $900.0 million payment we made to CRISPR in connection with an amendment to our CTX001 collaboration.





Business Updates

Cystic Fibrosis Marketed Products

We expect to continue to grow our CF business by increasing the number of people with CF eligible and able to receive our medicines. Recent progress in our CF business is included below.

- We have signed a letter of intent with the pan-Canadian Pharmaceutical Alliance regarding the public reimbursement of TRIKAFTA for eligible people with CF. We have reached multiple provincial reimbursement agreements across Canada providing approximately 90% of Canadian patients 12 years of age and older and covered by government insurance with reimbursed access to TRIKAFTA.
- Our application for approval of TRIKAFTA in children 6 through 11 years of age has been accepted for priority review by Health Canada.
- TRIKAFTA/KAFTRIO is now approved and reimbursed or accessible in more than 20 countries outside the U.S., including Italy, France and Canada.

Pipeline

We continue to advance a pipeline of potentially transformative small molecule, and cell and genetic therapies aimed at treating serious diseases. Recent and anticipated progress in activities supporting these efforts is included below.

Cystic Fibrosis

- We recently initiated our Phase 3 clinical trials evaluating the new once-daily investigational triple combination of VX-121/tezacaftor/VX-561 (deutivacaftor).
- In collaboration with Moderna, Inc., we are seeking to discover and develop CF mRNA therapeutics designed to treat the underlying cause of CF by enabling cells in the lungs to produce functional CF transmembrane conductance regulator, or CFTR, protein for the treatment of the 10% of patients who do not produce any CFTR protein. We are conducting enabling studies and expect to submit an Investigational New Drug Application, or IND, for this program in 2022.

Beta Thalassemia and Sickle Cell Disease

- We and our collaborator, CRISPR, are evaluating the use of a non-viral ex vivo CRISPR gene-editing therapy, CTX001, for the treatment of TDT and severe SCD. This approach aims to edit a person’s hematopoietic stem cells to produce fetal hemoglobin in red blood cells, which has the potential to reduce or eliminate symptoms associated with the diseases.
- Data presented to date support the potential profile of CTX001 as a one-time functional cure for people with TDT and severe SCD, showing consistent and durable benefit across all treated patients. CTX001 safety data to date is generally consistent with an autologous stem cell transplant and myeloablative conditioning.
- Target enrollment has been achieved in the ongoing clinical trials evaluating CTX001 in TDT and severe SCD. We anticipate submissions for regulatory approval of CTX001 in late 2022.

Type 1 Diabetes

- We are developing cell therapies designed to replace insulin-producing islet cells that are destroyed in people with T1D, with the goal of delivering a potential functional cure.
- VX-880 is a stem cell-derived, allogeneic, fully differentiated, insulin-secreting islet cell replacement therapy, using standard immunosuppression to protect the implanted cells. Our Phase 1/2 clinical trial evaluating VX-880 as a potential treatment for T1D is ongoing at multiple clinical sites in the U.S. and the Clinical Trial Application has been approved in Canada. In October 2021, we announced positive Day 90 data for the first T1D patient in the Phase 1/2 clinical trial of VX-880.

- We are pursuing a second program in which these stem cell-derived, fully differentiated, insulin-secreting islet cells are encapsulated and implanted in an immunoprotective device. We are conducting IND-enabling studies, and we expect to submit an IND for this cells and device program in 2022.

APOL1-Mediated Kidney Diseases

- We are evaluating the potential of oral, small molecule inhibitors of APOL1 function to treat people with APOL1-mediated kidney diseases.
- Enrollment is complete in the Phase 2 proof-of-concept clinical trial evaluating VX-147 for treatment of people with APOL1-mediated focal segmental glomerulosclerosis with reduction of proteinuria as the primary endpoint. We expect results from this clinical trial in the fourth quarter of 2021 and expect that these results will inform the potential progression of VX-147 into pivotal clinical trials in the broader population of people with APOL1-mediated non-diabetic proteinuric kidney diseases.

Pain

- NaV1.8 is a genetically and pharmacologically validated novel target for the treatment of pain. We previously have demonstrated clinical proof-of-concept with a small molecule investigational treatment targeting NaV1.8 in multiple pain indications including acute pain, neuropathic pain and musculoskeletal pain. We have discovered multiple selective small molecule inhibitors of NaV1.8 with the objective of creating a new class of medicines that have the potential to be highly effective for both acute and chronic pain, without the limitations of opioids and other existing pain medications.
- Two Phase 2 dose ranging acute pain clinical trials evaluating VX-548 are underway; one following bunionectomy surgery and the other following abdominoplasty surgery. We expect to have data from the clinical trials evaluating VX-548 following bunionectomy and abdominoplasty surgeries in the first quarter of 2022.

Alpha-1 Antitrypsin Deficiency

- We are evaluating multiple preclinical compounds with the potential to correct the misfolding of Z-AAT protein in the liver, in order to increase the systemic levels of functional AAT. Misfolded Z-AAT protein is the root cause of AAT deficiency and our small molecule corrector program targets both the liver and lung manifestations of the disease.
- We plan to advance one or more novel small molecule Z-AAT correctors into the clinic in 2022.

Investments in External Innovation

- In the third quarter of 2021, we entered into a new collaboration with Arbor Biotechnologies, Inc., or Arbor, to enhance efforts in developing ex vivo engineered cell therapies for multiple serious diseases using Arbor's proprietary CRISPR gene-editing technology.
- In October 2021, we entered into a collaboration with Mammoth Biosciences, Inc., or Mammoth, to develop in vivo gene-editing therapies for two diseases using Mammoth's next-generation CRISPR systems.

COVID-19

We continue to monitor the impacts of the COVID-19 global pandemic on our business. COVID-19 has not affected our supply chain or the demand for our medicines, and we believe that we will be able to continue to supply all of our approved medicines to patients globally. We adjusted our business operations in response to COVID-19 and have continued to monitor local COVID-19 trends and government guidance for each of our site locations. We are utilizing a phased, site-specific approach to assess and permit employee access to our sites. Currently, our sites are open to certain employees where appropriate and permitted by local laws and guidelines.

Research

We continue to invest in our research programs and foster scientific innovation in order to identify and develop transformative medicines. Our strategy is to combine transformative advances in the understanding of human disease and the

science of therapeutics in order to identify and develop new medicines. We believe that pursuing research in diverse areas allows us to balance the risks inherent in drug development and may provide drug candidates that will form our pipeline in future years. To supplement our internal research programs, we acquire technologies and programs and collaborate with biopharmaceutical and technology companies, leading academic research institutions, government laboratories, foundations and other organizations, as needed, to advance research in our areas of therapeutic interest and to access technologies needed to execute on our strategy.

Drug Discovery and Development

Discovery and development of a new pharmaceutical product is a difficult and lengthy process that requires significant financial resources along with extensive technical and regulatory expertise. Potential drug candidates are subjected to rigorous evaluations, driven in part by stringent regulatory considerations, designed to generate information concerning efficacy, side effects, proper dosage levels and a variety of other physical and chemical characteristics that are important in determining whether a drug candidate should be approved for marketing as a pharmaceutical product. Most chemical compounds that are investigated as potential drug candidates never progress into development, and most drug candidates that do advance into development never receive marketing approval. Our investments in drug candidates are subject to considerable risks. We closely monitor the results of our discovery, research, clinical trials and nonclinical studies and frequently evaluate our drug development programs in light of new data and scientific, business and commercial insights, with the objective of balancing risk and potential. This process can result in rapid changes in focus and priorities as new information becomes available and as we gain additional understanding of our ongoing programs and potential new programs, as well as those of our competitors. For example, in June 2021, we decided not to progress VX-864, a drug candidate for the treatment of AAT deficiency, into late-stage development based on data obtained from a Phase 2 clinical trial.

If we believe that data from a completed registration program support approval of a drug candidate, we submit an New Drug Application or Biologics License Application to the FDA requesting approval to market the drug candidate in the U.S. and seek analogous approvals from comparable regulatory authorities in jurisdictions outside the U.S. To obtain approval, we must, among other things, demonstrate with evidence gathered in nonclinical studies and well-controlled clinical trials that the drug candidate is safe and effective for the disease it is intended to treat and that the manufacturing facilities, processes and controls for the manufacture of the drug candidate are adequate. The FDA and ex-U.S. regulatory authorities have substantial discretion in deciding whether or not a drug candidate should be granted approval based on the benefits and risks of the drug candidate in the treatment of a particular disease, and could delay, limit or deny regulatory approval. If regulatory delays are significant or regulatory approval is limited or denied altogether, our financial results and the commercial prospects for the drug candidate involved will be harmed.

Regulatory Compliance

Our marketing of pharmaceutical products is subject to extensive and complex laws and regulations. We have a corporate compliance program designed to actively identify, prevent and mitigate risk through the implementation of compliance policies and systems and through the promotion of a culture of compliance. Among other laws, regulations and standards, we are subject to various U.S. federal and state laws, and comparable laws in other jurisdictions, pertaining to health care fraud and abuse, including anti-kickback and false claims laws, and laws prohibiting the promotion of drugs for unapproved or off-label uses. Anti-kickback laws generally make it illegal for a prescription drug manufacturer to knowingly and willfully solicit, offer, receive or pay any remuneration in return for or to induce the referral of business, including the purchase or prescription of a particular drug that is reimbursed by a state or federal health care program. False claims laws prohibit anyone from knowingly or willfully presenting for payment to third-party payors, including Medicare and Medicaid, claims for reimbursed drugs or services that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. We are subject to laws and regulations that regulate the sales and marketing practices of pharmaceutical manufacturers, as well as laws such as the U.S. Foreign Corrupt Practices Act, which govern our international business practices with respect to payments to government officials. In addition, we are subject to various data protection and privacy laws and regulations in the U.S., E.U., U.K., Canada, Australia and other jurisdictions.

We expect to continue to devote substantial resources to maintain, administer and expand these compliance programs globally.

Reimbursement

Sales of our products depend, to a large degree, on the extent to which our products are reimbursed by third-party payors, such as government health programs, commercial insurance and managed health care organizations. Reimbursement for our products, including our potential pipeline therapies, cannot be assured and may take significant periods of time to obtain. We dedicate substantial management and other resources in order to obtain and maintain appropriate levels of reimbursement for our products from third-party payors, including governmental organizations in the U.S. and ex-U.S. markets.

In the U.S., we have worked successfully with third party payors in order to promptly obtain appropriate levels of reimbursement for our CF medicines. We plan to continue to engage in discussions with numerous commercial insurers and managed health care organizations, along with government health programs that are typically managed by authorities in the individual states, to ensure that payors recognize the significant benefits that our medicines provide and provide patients with appropriate levels of access to our medicines.

In Europe and other ex-U.S. markets, we seek government reimbursement for our medicines on a country-by-country basis. This is necessary for each new medicine, as well as for label expansions for our current medicines. We have obtained broad reimbursement for our CF medicines in ex-U.S. markets. TRIKAFTA/KAFTRIO is reimbursed or accessible in more than 20 countries outside the U.S., including England, Ireland, Italy, France and Canada. We expect to continue to focus significant resources to obtain expanded reimbursement for our CF medicines and pipeline therapies in ex-U.S. markets.

Strategic Transactions

Acquisitions

As part of our business strategy, we seek to acquire drugs, drug candidates and other technologies and businesses that have the potential to complement our ongoing research and development efforts. In 2019, we invested significantly in business development transactions designed to augment our pipeline, including the acquisition of Semma Therapeutics, Inc., or Semma, a privately-held company focused on the use of stem cell-derived human islets as a treatment for T1D, and Exonics Therapeutics, Inc., or Exonics, a privately-held company focused on creating transformative gene-editing therapies to repair mutations that cause DMD and other severe neuromuscular diseases, including DM1. We expect to continue to identify and evaluate potential acquisitions and may include larger transactions or later-stage assets.

Collaboration and Licensing Arrangements

We enter into arrangements with third parties, including collaboration and licensing arrangements, for the development, manufacture and commercialization of drugs, drug candidates and other technologies that have the potential to complement our ongoing research and development efforts. We expect to continue to identify and evaluate collaboration and licensing opportunities that may be similar to or different from the collaborations and licenses that we have engaged in previously.

In-License Agreements

We have entered into collaborations with biotechnology and pharmaceutical companies in order to acquire rights or to license drug candidates or technologies that enhance our pipeline and/or our research capabilities. Over the last several years, we entered into collaboration agreements with a number of companies, including Arbor, CRISPR, Kymera Therapeutics, Inc., Mammoth, Moderna, Inc., and Obsidian Therapeutics, Inc. Generally, when we in-license a technology or drug candidate, we make upfront payments to the collaborator, assume the costs of the program and/or agree to make contingent payments, which could consist of milestone, royalty and option payments. Most of these collaboration payments are expensed as research and development expenses; however, depending on many factors, including the structure of the collaboration, the significance of the in-licensed drug candidate to the collaborator’s operations and the other activities in which our collaborators are engaged, the accounting for these transactions can vary significantly. In the nine months ended September 30, 2021 and 2020, our research and development expenses included $986.8 million and $143.3 million, respectively, related to upfront and milestones payments pursuant to our collaboration agreements. In the nine months ended September 30, 2021, these payments were primarily related to the $900.0 million upfront payment we made to CRISPR in the second quarter of 2021.

Joint Development and Commercialization Agreement with CRISPR

In 2017, we entered into a joint development and commercialization agreement, or JDCA, with CRISPR pursuant to which we are developing and preparing to commercialize CTX001 for TDT and SCD. This JDCA was entered into following our exercise of an option to co-develop and co-commercialize the hemoglobinopathies program that was contained in the collaboration agreement that we entered into with CRISPR in 2015.

In April 2021, we and CRISPR entered into an amended and restated joint development and commercialization agreement, or the A&R JDCA. In June 2021, we made a $900.0 million upfront payment to CRISPR in connection with the closing of the transactions contemplated by the A&R JDCA, which we recorded to research and development expenses. Under the terms of the A&R JDCA, we are leading worldwide development, manufacturing and commercialization of CTX001. Additionally, 60% of the net profits and net losses for CTX001 are allocated to us and 40% of the net profits and net losses for CTX001 are allocated to CRISPR. CRISPR may earn an additional one-time $200.0 million milestone payment upon regulatory approval of CTX001.

Out-License Agreements

We also have out-licensed internally developed programs to collaborators who are leading the development of these programs. These out-license arrangements include our agreement with Merck KGaA, Darmstadt, Germany, which licensed oncology research and development programs from us in early 2017. Pursuant to these out-licensing arrangements, our collaborators are responsible for the research, development and commercialization costs associated with these programs, and we are entitled to receive contingent milestone and/or royalty payments. As a result, we do not expect to incur significant expenses in connection with these programs and have the potential for future collaborative and royalty revenues resulting from these programs.

Please refer to Note C, “Collaborative Arrangements,” for further information regarding our in-license agreements and out-license agreements.

Strategic Investments

In connection with our business development activities, we have periodically made equity investments in our collaborators. As of September 30, 2021, we held strategic equity investments in public companies and certain private companies, and we plan to make additional strategic equity investments in the future. While we invest the majority of our cash, cash equivalents and marketable securities in instruments that meet specific credit quality standards and limit our exposure to any one issue or type of instrument, our strategic investments are maintained and managed separately from our other cash, cash equivalents and marketable securities. Any changes in the fair value of equity investments with readily determinable fair values (including publicly traded securities) are recorded to other income (expense), net in our condensed consolidated statement of operations.

In the nine months ended September 30, 2021 and 2020, we recorded within other income (expense), gains of $5.0 million and $140.9 million, respectively, related to changes in the fair value of our strategic investments, and from sales of certain equity investments. As of September 30, 2021, the fair value of our investments in publicly traded companies was $218.8 million. To the extent that we continue to hold strategic investments, particularly strategic investments in publicly traded companies, we will record other income (expense) related to these strategic investments on a quarterly basis. Due to the volatility of the global markets, including as a result of COVID-19, and the high volatility of stocks in the biotechnology industry, we expect the value of these strategic investments to fluctuate and that the increases or decreases in the fair value of these strategic investments will continue to have material impacts on our net income (expense) and our profitability on a quarterly and/or annual basis.

RESULTS OF OPERATIONS

	Three Months Ended September 30,		Increase/(Decrease)		Nine Months Ended September 30,		Increase/(Decrease)	
	2021	2020	$	%	2021	2020	$	%
	(in thousands, except percentages and per share amounts)							
Revenues	$ 1,984,164	$ 1,538,271	$ 445,893	29%	$ 5,501,839	$ 4,577,863	$ 923,976	20%
Operating costs and expenses	929,652	866,030	63,622	7%	3,597,462	2,467,365	1,130,097	46%
Income from operations	1,054,512	672,241	382,271	57%	1,904,377	2,110,498	(206,121)	(10)%
Other non-operating income (expense), net	28,229	73,630	(45,401)	(62)%	(44,931)	117,677	(162,608)	**
Provision for income taxes	230,813	78,437	152,376	194%	287,456	120,718	166,738	138%
Net income	$ 851,928	$ 667,434	$ 184,494	28%	$ 1,571,990	$ 2,107,457	$ (535,467)	(25)%
Net income per diluted common share	$ 3.28	$ 2.53			$ 6.03	$ 7.98		
Diluted shares used in per share calculations	259,707	264,079			260,877	264,031		

** Not meaningful

Net Income

Our net income increased in the third quarter of 2021 as compared to the third quarter of 2020 primarily due to increased revenues resulting from the continued uptake of KAFTRIO in Europe and strong performance of TRIKAFTA in the U.S., including the launch of TRIKAFTA in children with CF 6 through 11 years of age. Our increased revenues were partially offset by increased cost of sales consistent with increased product revenues, changes in the fair value of our strategic investments and an increased provision for income taxes.

Our net income decreased in the nine months ended September 30, 2021 as compared to the nine months ended September 30, 2020 primarily due to the $900.0 million upfront payment we made to CRISPR in the second quarter of 2021 in connection with the amendment of our CTX001 collaboration. Changes in the fair value of our strategic investments, increased cost of sales consistent with increased product revenues and an increased provision for income taxes also decreased our net income. These decreases to our net income were partially offset by increased revenues resulting from the uptake of KAFTRIO in Europe and strong performance of TRIKAFTA in the U.S.

Revenues

	Three Months Ended September 30,		Increase/(Decrease)		Nine Months Ended September 30,		Increase/(Decrease)	
	2021	2020	$	%	2021	2020	$	%
	(in thousands, except percentages)							
Product revenues, net	$ 1,984,164	$ 1,536,271	$ 447,893	29%	$ 5,500,839	$ 4,575,863	$ 924,976	20%
Other revenues	—	2,000	(2,000)	N/A	1,000	2,000	(1,000)	(50)%
Total revenues	$ 1,984,164	$ 1,538,271	$ 445,893	29%	$ 5,501,839	$ 4,577,863	$ 923,976	20%

Product Revenues, Net

	Three Months Ended September 30,		Increase/(Decrease)		Nine Months Ended September 30,		Increase/(Decrease)	
	2021	2020	$	%	2021	2020	$	%
	(in thousands, except percentages)							
TRIKAFTA/KAFTRIO	$ 1,555,772	$ 960,308	$ 595,464	62%	$ 4,004,600	$ 2,773,256	$ 1,231,344	44%
SYMDEKO/SYMKEVI	81,415	156,178	(74,763)	(48)%	339,969	501,066	(161,097)	(32)%
ORKAMBI	184,561	225,919	(41,358)	(18)%	624,224	692,038	(67,814)	(10)%
KALYDECO	162,416	193,866	(31,450)	(16)%	532,046	609,503	(77,457)	(13)%
Total product revenues, net	$ 1,984,164	$ 1,536,271	$ 447,893	29%	$ 5,500,839	$ 4,575,863	$ 924,976	20%

In the third quarter and nine months ended September 30, 2021, our net product revenues increased by $447.9 million and $925.0 million, respectively, as compared to the third quarter and nine months ended September 30, 2020. The increase in our net product revenues in the third quarter and nine months ended September 30, 2021 was primarily due to the continued uptake of KAFTRIO, which was approved in the E.U. in the third quarter of 2020, and the strong performance of TRIKAFTA in the U.S., including the launch of TRIKAFTA in June 2021 in children with CF 6 through 11 years of age. Decreases in revenues for our products other than TRIKAFTA/KAFTRIO were primarily the result of patients switching from these medicines to TRIKAFTA/KAFTRIO.

Our net product revenues from U.S. and ex-U.S. markets were as follows:

	Three Months Ended September 30,		Increase/(Decrease)	Nine Months Ended September 30,		Increase/(Decrease)
	2021	2020	%	2021	2020	%
	(in thousands, except percentages)					
U.S. markets	$ 1,382,892	$ 1,222,565	13%	$ 3,893,245	$ 3,620,467	8%
Ex-U.S. markets	601,272	313,706	92%	1,607,594	955,396	68%
Total product revenues, net	$ 1,984,164	$ 1,536,271	29%	$ 5,500,839	$ 4,575,863	20%

Other Revenues

Our other revenues were $1.0 million and $2.0 million related to collaborative milestones that we earned in the nine months ended September 30, 2021 and 2020, respectively. Our other revenues have historically fluctuated significantly from one period to another based on our collaborative out-license activities, and may continue to fluctuate in the future. Our future royalty revenues will be dependent on if, and when, our collaborators are able to successfully develop drug candidates that we have out-licensed to them.

Operating Costs and Expenses

	Three Months Ended September 30,		Increase/(Decrease)		Nine Months Ended September 30,		Increase/(Decrease)	
	2021	2020	$	%	2021	2020	$	%
	(in thousands, except percentages)							
Cost of sales	$ 236,512	$ 186,182	$ 50,330	27%	$ 656,813	$ 533,199	$ 123,614	23%
Research and development expenses	493,751	493,497	254	—%	2,356,814	1,362,953	993,861	73%
Selling, general and administrative expenses	198,189	184,551	13,638	7%	584,935	558,613	26,322	5%
Change in fair value of contingent consideration	1,200	1,800	(600)	(33)%	(1,100)	12,600	(13,700)	**
Total costs and expenses	$ 929,652	$ 866,030	$ 63,622	7%	$ 3,597,462	$ 2,467,365	$ 1,130,097	46%

** Not meaningful

Cost of Sales

Our cost of sales primarily consists of third-party royalties payable on our net sales of our products as well as the cost of producing inventories that corresponded to product revenues for the reporting period. Pursuant to our agreement with the Cystic Fibrosis Foundation our tiered third-party royalties on sales of TRIKAFTA/KAFTRIO, SYMDEKO/SYMKEVI, KALYDECO and ORKAMBI, calculated as a percentage of net sales, range from the single digits to the sub-teens, with royalties on sales of TRIKAFTA/KAFTRIO slightly lower than for our other products. Over the last several years, our cost of sales has been increasing due to increased net product revenues. Our cost of sales as a percentage of our net product revenues was 12% in each of the third quarter of 2021 and 2020 and nine months ended September 30, 2021 and 2020.

Research and Development Expenses

	Three Months Ended September 30,		Increase/(Decrease)		Nine Months Ended September 30,		Increase/(Decrease)	
	2021	2020	$	%	2021	2020	$	%
	(in thousands, except percentages)							
Research expenses	$ 148,620	$ 186,152	$ (37,532)	(20)%	$ 426,352	$ 477,560	$ (51,208)	(11)%
Development expenses	345,131	307,345	37,786	12%	1,930,462	885,393	1,045,069	118%
Total research and development expenses	$ 493,751	$ 493,497	$ 254	—%	$ 2,356,814	$ 1,362,953	$ 993,861	73%

Our research and development expenses include internal and external costs incurred for research and development of our drugs and drug candidates and expenses related to certain technologies that we acquire or license through business development transactions. We do not assign our internal costs, such as salary and benefits, stock-based compensation expense, laboratory supplies and other direct expenses and infrastructure costs, to individual drugs or drug candidates, because the employees within our research and development groups typically are deployed across multiple research and development programs. These internal costs are significantly greater than our external costs excluding collaborative upfront and milestone payments, such as the costs of services provided to us by clinical research organizations and other outsourced research, which we allocate by individual program. All research and development costs for our drugs and drug candidates are expensed as incurred.

Since January 2019, we have incurred approximately $5.9 billion in research and development expenses associated with drug discovery and development. The successful development of our drug candidates is highly uncertain and subject to a number of risks. In addition, the duration of clinical trials may vary substantially according to the type, complexity and novelty of the drug candidate and the disease indication being targeted. The FDA and comparable agencies in foreign countries impose substantial requirements on the introduction of therapeutic pharmaceutical products, typically requiring lengthy and detailed laboratory and clinical testing procedures, sampling activities and other costly and time-consuming procedures. Data obtained from nonclinical and clinical activities at any step in the testing process may be adverse and lead to discontinuation or redirection of development activities. 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, nonclinical

studies and clinical trials may vary significantly over the life of a project and are difficult to predict. Therefore, accurate and meaningful estimates of the ultimate costs to bring our drug candidates to market are not available.

In 2020 and the nine months ended September 30, 2021, costs related to our CF programs represented the largest portion of our development costs, excluding the $900.0 million upfront payment to CRISPR. Any estimates regarding development and regulatory timelines for our drug candidates are highly subjective and subject to change. Until we have data from Phase 3 clinical trials, we cannot make a meaningful estimate regarding when, or if, a clinical development program will generate revenues and cash flows.

Research Expenses

	Three Months Ended September 30,		Increase/(Decrease)		Nine Months Ended September 30,		Increase/(Decrease)	
	2021	2020	$	%	2021	2020	$	%
	(in thousands, except percentages)							
Research Expenses:								
Salary and benefits	$ 34,635	$ 32,145	$ 2,490	8%	$ 102,529	$ 97,513	$ 5,016	5%
Stock-based compensation expense	17,388	15,301	2,087	14%	56,361	68,206	(11,845)	(17)%
Outsourced services and other direct expenses	35,798	27,911	7,887	28%	114,920	79,837	35,083	44%
Collaborative payments	26,750	80,050	(53,300)	(67)%	54,150	143,300	(89,150)	(62)%
Infrastructure costs	34,049	30,745	3,304	11%	98,392	88,704	9,688	11%
Total research expenses	$ 148,620	$ 186,152	$ (37,532)	(20)%	$ 426,352	$ 477,560	$ (51,208)	(11)%

We expect to continue to invest in our research programs with a focus on creating transformative medicines for serious diseases. Our research expenses have historically fluctuated, and are expected to continue to fluctuate, from one period to another due to upfront and milestone payments related to our business development activities that are reflected in the preceding table as collaborative payments. Our research expenses, excluding these collaborative payments, have been increasing over the last several years as we have invested in our pipeline and expanded our cell and genetic therapy capabilities.

Development Expenses

	Three Months Ended September 30,		Increase/(Decrease)		Nine Months Ended September 30,		Increase/(Decrease)	
	2021	2020	$	%	2021	2020	$	%
	(in thousands, except percentages)							
Development Expenses:								
Salary and benefits	$ 88,568	$ 73,698	$ 14,870	20%	$ 252,173	$ 221,828	$ 30,345	14%
Stock-based compensation expense	43,607	45,469	(1,862)	(4)%	140,051	135,526	4,525	3%
Outsourced services and other direct expenses	149,627	133,595	16,032	12%	426,441	374,926	51,515	14%
Collaborative payments	—	—	—	N/A	932,650	—	932,650	**
Infrastructure costs	63,329	54,583	8,746	16%	179,147	153,113	26,034	17%
Total development expenses	$ 345,131	$ 307,345	$ 37,786	12%	$ 1,930,462	$ 885,393	$ 1,045,069	118%

** Not meaningful

Our development expenses increased by $37.8 million in the third quarter of 2021 as compared to third quarter of 2020, primarily due to increased expenses related to our diversifying pipeline, including clinical trials, headcount and infrastructure costs. Our development expenses increased by $1.05 billion in the nine months ended September 30, 2021 as compared to the nine months ended September 30, 2020, primarily due to the $900.0 million upfront payment to CRISPR in the second quarter of 2021, that is included in the preceding table under collaborative payments, and increased expenses related to our diversifying pipeline, including clinical trials, headcount and infrastructure costs.

Selling, General and Administrative Expenses

	Three Months Ended September 30,		Increase/(Decrease)		Nine Months Ended September 30,		Increase/(Decrease)	
	2021	2020	$	%	2021	2020	$	%
	(in thousands, except percentages)							
Selling, general and administrative expenses	$ 198,189	$ 184,551	$ 13,638	7%	$ 584,935	$ 558,613	$ 26,322	5%

Selling, general and administrative expenses increased by 7% in the third quarter of 2021 as compared to third quarter of 2020 and increased by 5% in the nine months ended September 30, 2021 as compared to the nine months ended September 30, 2020, primarily due to the continued investment to support the commercialization of our medicines and increased support for our CF pipeline products and other disease areas.

Contingent Consideration

The fair value of contingent consideration potentially payable to Exonics' former equity holders increased $1.2 million and decreased $1.1 million in the third quarter and nine months ended September 30, 2021, respectively. The fair value of contingent consideration increased by $1.8 million and $12.6 million in the third quarter and nine months ended September 30, 2020, respectively.

Other Non-Operating Income (Expense), Net

Interest Income

Interest income was $1.1 million and $3.7 million in the third quarter and nine months ended September 30, 2021, respectively, which was lower than our interest income of $3.1 million and $19.9 million in the third quarter and nine months ended September 30, 2020, respectively, due to a decrease in prevailing market interest rates, despite an increase in our cash equivalents and available-for-sale debt securities. Our future interest income will be dependent on the amount of, and prevailing market interest rates on, our outstanding cash equivalents and available-for-sale debt securities.

Interest Expense

Interest expense was $15.3 million and $46.4 million in the third quarter and nine months ended September 30, 2021, respectively, as compared to $13.9 million and $41.9 million in the third quarter and nine months ended September 30, 2020, respectively. The majority of our interest expense in these periods was related to imputed interest expense associated with our leased corporate headquarters in Boston. Our future interest expense will be dependent on whether, and to what extent, we borrow amounts under our credit facilities.

Other Income (Expense), Net

Other income (expense), net was income of $42.4 million and expense of $2.2 million in the third quarter and nine months ended September 30, 2021, respectively, as compared to income of $84.4 million and $139.6 million in the third quarter and nine months ended September 30, 2020, respectively. Our other income (expense), net in these periods was primarily related to changes in the fair value of our strategic investments. We expect that due to the volatility of the stock price of biotechnology companies, our other income (expense), net will fluctuate in future periods based on increases or decreases in the fair value of our strategic investments.

Income Taxes

We recorded provisions for income taxes of $230.8 million and $287.5 million in the third quarter and nine months ended September 30, 2021, respectively, as compared to provisions for income taxes of $78.4 million and $120.7 million in the third quarter and nine months ended September 30, 2020, respectively. Our effective tax rate of 15% for the nine months ended September 30, 2021 was lower than the U.S. statutory rate primarily due to a $100 million discrete tax benefit associated with an increase in the U.K.'s corporate tax rate from 19% to 25%, which was enacted in June 2021 and will become effective in April 2023. Our effective tax rate of 5% for the nine months ended September 30, 2020 was lower than the U.S. statutory rate primarily due to (i) a $209 million discrete tax benefit associated with the transfer of intellectual property rights to the U.K., (ii) a discrete tax benefit associated with the write off of a long-term intercompany receivable,

(iii) a discrete tax benefit associated with an increase in the U.K.'s corporate tax rate from 17% to 19%, which was enacted and became effective in July 2020, and (iv) excess tax benefits related to stock-based compensation.

LIQUIDITY AND CAPITAL RESOURCES

The following table summarizes the components of our financial condition as of September 30, 2021 and December 31, 2020:

	September 30, 2021	December 31, 2020	Increase/(Decrease) $	Increase/(Decrease) %
	(in thousands)			
Cash, cash equivalents and marketable securities	$ 6,960,885	$ 6,658,897	$ 301,988	5%
Working Capital:				
Total current assets	8,852,540	8,133,379	719,161	9%
Total current liabilities	(1,914,264)	(1,877,533)	36,731	2%
Total working capital	$ 6,938,276	$ 6,255,846	$ 682,430	11%

As of September 30, 2021, total working capital was $6.94 billion, which represented an increase of $682.4 million from $6.26 billion as of December 31, 2020. The increase in total working capital in the nine months ended September 30, 2021 was primarily related to $1.65 billion of cash provided by operations, which was net of our $900.0 million payment to CRISPR, partially offset by $1.06 billion of cash used to repurchase our common stock pursuant to our share repurchase programs and expenditures for property and equipment of $173.3 million.

Sources of Liquidity

As of September 30, 2021, we had cash, cash equivalents and marketable securities of $6.96 billion, which represented an increase of $302 million from $6.66 billion as of December 31, 2020. We intend to rely on our existing cash, cash equivalents and marketable securities together with cash flows from product sales as our primary source of liquidity.

We may borrow up to a total of $2.5 billion pursuant to two revolving credit facilities. We may repay and reborrow amounts under these revolving credit agreements without penalty. Subject to certain conditions, we may request that the borrowing capacity for each of the credit agreements be increased by an additional $500.0 million, for a total of $3.5 billion collectively.

Other possible sources of future liquidity include commercial debt, public and private offerings of our equity and debt securities, strategic sales of assets or businesses and financial transactions. Negative covenants in our credit agreement may prohibit or limit our ability to access these sources of liquidity. As of September 30, 2021, we were in compliance with these covenants.

Future Capital Requirements

We have significant future capital requirements, including:

- significant expected operating expenses to conduct research and development activities and to operate our organization; and
- substantial facility and finance lease obligations.

In addition:

- We have entered into certain collaboration agreements with third parties that include the funding of certain research, development and commercialization efforts. Certain of our business development transactions, including collaborations and acquisitions, include the potential for future milestone and royalty payments by us upon the achievement of pre-established developmental and regulatory targets and/or commercial targets. We may enter into additional business development transactions, including acquisitions, collaborations and equity investments, that require additional capital.

- To the extent we borrow amounts under the credit agreements we entered into in 2020 and 2019, we would be required to repay any outstanding principal amounts in 2022 or 2024, respectively.
- As of September 30, 2021, we had $857.8 million available under our 2021 Share Repurchase Program. We repurchased an additional $357.8 million of our common stock during October 2021.

We expect that cash flows from our products together with our current cash, cash equivalents and marketable securities will be sufficient to fund our operations for at least the next twelve months. The adequacy of our available funds to meet our future operating and capital requirements will depend on many factors, including the amounts of future revenues generated by our products, and the potential introduction of one or more of our other drug candidates to the market, the level of our business development activities and the number, breadth, cost and prospects of our research and development programs.

Financing Strategy

We may raise additional capital by borrowing under credit agreements, through public offerings or private placements of our securities or securing new collaborative agreements or other methods of financing. We will continue to manage our capital structure and will consider all financing opportunities, whenever they may occur, that could strengthen our long-term liquidity profile. There can be no assurance that any such financing opportunities will be available on acceptable terms, if at all.

CONTRACTUAL COMMITMENTS AND OBLIGATIONS

Our commitments and obligations were reported in our Annual Report on Form 10-K for the year ended December 31, 2020, which was filed with the Securities and Exchange Commission, or SEC, on February 11, 2021. There have been no material changes from the contractual commitments and obligations previously disclosed in that Annual Report on Form 10-K.

CRITICAL ACCOUNTING POLICIES AND ESTIMATES

Our discussion and analysis of our financial condition and results of operations are based upon our condensed consolidated financial statements prepared in accordance with generally accepted accounting principles in the U.S. 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 condensed consolidated financial statements and the reported amounts of revenues and expenses during the reported periods. These items are 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 reflected in reported results for the period in which the change occurs. 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. During the nine months ended September 30, 2021, there were no material changes to our critical accounting policies as reported in our Annual Report on Form 10-K for the year ended December 31, 2020, which was filed with the SEC on February 11, 2021.

RECENT ACCOUNTING PRONOUNCEMENTS

For a discussion of recent accounting pronouncements, please refer to Note A, “Basis of Presentation and Accounting Policies.”

Item 3. Quantitative and Qualitative Disclosures About Market Risk

Information required by this item is incorporated by reference from the discussion in Part II, Item 7A, “Quantitative and Qualitative Disclosures About Market Risk,” of our Annual Report on Form 10-K for the year ended December 31, 2020, which was filed with the SEC on February 11, 2021.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management (under the supervision and with the participation of our chief executive officer and chief financial officer), after evaluating the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended) as of the end of the period covered by this Quarterly Report on Form 10-Q, has concluded that, based on such evaluation, as of September 30, 2021 our disclosure controls and procedures were effective and designed to provide reasonable assurance that the information required to be disclosed is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. In designing and evaluating our disclosure controls and procedures, our management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and our management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Changes in Internal Controls Over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934, as amended) occurred during the three months ended September 30, 2021 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II. Other Information

Item 1. Legal Proceedings

We are not currently subject to any material legal proceedings.

Item 1A. Risk Factors

Information regarding risk factors appears in Part I, Item 1A. "Risk Factors" of our Annual Report on Form 10-K for the year ended December 31, 2020, which was filed with the SEC on February 11, 2021. There have been no material changes from the risk factors previously disclosed in the Annual Report on Form 10-K.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q and, in particular, our Management's Discussion and Analysis of Financial Condition and Results of Operations set forth in Part I, Item 2, contain a number of forward-looking statements. Forward-looking statements are not purely historical and may be accompanied by words such as "anticipates," "may," "forecasts," "expects," "intends," "plans," "potentially," "believes," "seeks," "estimates," and other words and terms of similar meaning. Such statements may relate to:

- our expectations regarding the amount of, timing of, and trends with respect to our financial performance, including revenues, costs and expenses and other gains and losses, including those related to net product revenues;
- our expectations regarding clinical trials, development timelines, regulatory authority filings, submissions and potential approvals and label expansions for our medicines, product candidates and other pipeline programs, including timing and structure of clinical trials, anticipated enrollment and dosing of patients, timing of availability of data from our ongoing and planned clinical trials, and timing of anticipated regulatory filings;
- our ability to obtain reimbursement for our medicines in the U.S. and ex-U.S. markets and our ability to launch, commercialize and market our medicines or any of our other drug candidates for which we obtain regulatory approval;
- the data that will be generated by ongoing and planned clinical trials and the ability to use that data to advance compounds, continue development or support regulatory filings;

- our beliefs regarding the support provided by clinical trials and preclinical and nonclinical studies of our drug candidates and other pipeline programs for further investigation, clinical trials or potential use as a treatment;
- our beliefs regarding the number of people with CF and those potentially eligible for our medicines, and our ability to grow our CF business by increasing the number of people with CF eligible and able to receive our medicines;
- our expectations regarding the potential benefits and commercial potential of our product candidates, including the potential approach to treating or curing specific diseases;
- our plan to continue investing in our research and development programs, including anticipated timelines for our programs, and our strategy to develop our pipeline programs, alone or with third party-collaborators;
- the potential future benefits of our acquisitions and collaborations, including our CTX001 collaboration with CRISPR, our CF mRNA therapeutics collaboration with Moderna, Inc., our collaboration with Arbor and our collaboration with Mammoth;
- the establishment, development and maintenance of collaborative relationships, including potential milestone payments or other obligations;
- potential business development activities, including the identification of potential collaborative partners or acquisition targets;
- our expectations regarding the effect of COVID-19 on, among other things, our financial performance, liquidity, business and operations, including manufacturing, supply chain, research and development activities and pipeline programs;
- potential fluctuations in foreign currency exchange rates;
- our expectations regarding our provision for or benefit from income taxes and the utilization of our deferred tax assets;
- our ability to use our research programs to identify and develop new drug candidates to address serious diseases and significant unmet medical needs; and
- our liquidity and our expectations regarding the possibility of raising additional capital.

Forward-looking statements are subject to certain risks, uncertainties, or other factors that are difficult to predict and could cause actual events or results to differ materially from those indicated in any such statements. These risks, uncertainties, and other factors include, but are not limited to, those described in our “Risk Factors” in Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2020, which was filed with the SEC on February 11, 2021, and those described from time to time in our future reports filed with the Securities and Exchange Commission.

Any such forward-looking statements are made on the basis of our views and assumptions as of the date of the filing and are not estimates of future performance. Except as required by law, we undertake no obligation to publicly update any forward-looking statements. The reader is cautioned not to place undue reliance on any such statements.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds

Issuer Repurchases of Equity Securities

On June 23, 2021, our Board of Directors approved a share repurchase program (the "2021 Share Repurchase Program"), pursuant to which we are authorized to repurchase up to $1.5 billion of our common stock by December 31, 2022. The table set forth below shows repurchases of securities by us during the three months ended September 30, 2021 under our 2021 Share Repurchase Program.

Period	Total Number of Shares Purchased	Average Price Paid per Share	Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs (1)	Approximate Dollar Value of Shares that May Yet be Purchased Under the Plans or Programs (1)
July 1, 2021 to July 31, 2021	—	$ —	—	$ 1,500,000,000
August 1, 2021 to August 31, 2021	2,532,454	$ 197.79	2,532,454	$ 999,107,701
September 1, 2021 to September 30, 2021	760,707	$ 185.77	760,707	$ 857,793,473
Total	3,293,161	$ 195.01	3,293,161	$ 857,793,473

(1) Under our 2021 Share Repurchase Program, we are authorized to purchase shares from time to time through open market or privately negotiated transactions. Such purchases may be pursuant to Rule 10b5-1 plans or other means as determined by our management and in accordance with the requirements of the Securities and Exchange Commission.

Item 6. Exhibits

Exhibit Number	Exhibit Description
10.1	Research, Development and Commercialization Agreement, dated as of May 24, 2004, between Vertex Pharmaceuticals Incorporated and Cystic Fibrosis Foundation Therapeutics Incorporated.†
10.2	Amendment No. 1 to Research, Development and Commercialization Agreement, dated as of January 6, 2006, between Vertex Pharmaceuticals Incorporated and Cystic Fibrosis Foundation Therapeutics Incorporated.†
10.3	Amendment No. 5 to Research, Development and Commercialization Agreement, effective as of April 1, 2011, between Vertex Pharmaceuticals Incorporated and Cystic Fibrosis Foundation Therapeutics Incorporated.†
10.4	Amendment No. 7 to Research, Development and Commercialization Agreement, dated October 13, 2016, between Vertex Pharmaceuticals Incorporated and Cystic Fibrosis Foundation Therapeutics Incorporated.†
31.1	Certification of the Chief Executive Officer under Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of the Chief Financial Officer under Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certification of the Chief Executive Officer and the Chief Financial Officer under Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.
101.SCH	XBRL Taxonomy Extension Schema
101.CAL	XBRL Taxonomy Extension Calculation
101.LAB	XBRL Taxonomy Extension Labels
101.PRE	XBRL Taxonomy Extension Presentation
101.DEF	XBRL Taxonomy Extension Definition
104	Cover Page Interactive Data File—the cover page interactive data file does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.

† Confidential portions of this document have been redacted according to the applicable rules.

SIGNATURES

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

Vertex Pharmaceuticals Incorporated

November 3, 2021 By: /s/ Charles F. Wagner, Jr.

Charles F. Wagner, Jr.

Executive Vice President, Chief Financial Officer
(principal financial officer and
duly authorized officer)

Exhibit 10.1

Certain confidential information contained in this document, marked by [***], has been omitted because it is not material and would likely cause competitive harm to Vertex Pharmaceuticals Incorporated if publicly disclosed.

RESEARCH, DEVELOPMENT AND COMMERCIALIZATION AGREEMENT

between

Vertex Pharmaceuticals Incorporated

and

Cystic Fibrosis Foundation Therapeutics Incorporated

Research, Development and Commercialization Agreement

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RESEARCH, DEVELOPMENT AND COMMECIALIZATION AGREEMENT

Agreement made this 24th day of May, 2004, (the "Agreement"), between Vertex Pharmaceuticals Incorporated ("Vertex"), a Massachusetts corporation with principal offices at 130 Waverly Street, Cambridge, MA 02139-4242, and Cystic Fibrosis Foundation Therapeutics Incorporated, a Delaware corporation with principal offices at 6931 Arlington Road, Bethesda, Maryland 20814 ("CFFT").

This Agreement is a modification and continuation of a relationship originally set forth in an earlier Cystic Fibrosis Research Alliance and Commercialization Agreement dated as of May 19, 2000 (the "Original Agreement"), between the Cystic Fibrosis Foundation, which is an Affiliate of CFFT, and Aurora Biosciences Corporation, which was acquired by Vertex in 2001. Except as specifically provided herein, this Agreement supercedes in its entirety the Original Agreement which shall be of no further force and effect.

WHEREAS, Vertex has expertise in the discovery and development of small molecule compounds addressing a variety of diseases for which there are limited treatment options, including extensive expertise in the study of disease mechanisms and the design of novel chemical compounds which modulate biological targets with therapeutic effect; and

WHEREAS, Vertex has developed significant scientific expertise and capacity in the area of CFTR protein modulation; and

WHEREAS, CFFT is significantly focused on the discovery and development of methods of treatment for cystic fibrosis, to which CFFT and its Affiliates bring significant scientific and human resources and financial support; and

WHEREAS, CFFT wishes to continue support for, and expand, the CFTR project underway at Vertex.

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

ARTICLE I - DEFINITIONS

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 who 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 Cystic Fibrosis Foundation and CFFT are considered to be Affiliates.

1.2 "Agreement" means this agreement, together with all appendices, exhibits and schedules hereto, and as the same may be amended or supplemented from time to time hereafter by a written agreement duly executed by authorized representatives of each party hereto.

1.3 "Back-up Compound" shall mean, with reference to any particular Development Candidate or Drug Product Candidate, a Compound which (a) has the same principal mode of action (i.e., Potentiator or Corrector) as that Development Candidate or Drug Product Candidate; and (b) was among the group of Compounds, identified by VERTEX as potential additional lead

molecules having the same principal mode of action, from which the Development Candidate was selected.

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 "CF" means the disease known as Cystic Fibrosis.

1.6 "CF Field" means the treatment of humans diagnosed with CF.

1.7 "CFTR" shall mean a CF transmembrane conductance regulator protein which has the biological effect of transporting molecules across human cellular membranes.

1.8 "Compound" shall mean a chemical compound, including salts and prodrugs thereof, which is synthesized and/or tested by or under the direction of VERTEX or its Affiliates during the term of the Research Program under this Agreement, or which was synthesized and/or tested by and/or under the direction of Aurora or its Affiliates under the Original Agreement; which is either a Potentiator or a Corrector, or both; and which **[***]**

1.9 "Controlled" (except in the context of Section 1.1) 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.

1.10 "Corrector" shall mean a Compound which, as its principal mode of therapeutic action, modulates the biological effect of CFTR by increasing **[***]**

1.11 "Development Candidate" shall mean a Compound that meets the Development Candidate Criteria for the initiation of a Development Program for the treatment of CF, and which is the subject of a notice from Vertex to CFFT that Vertex intends to commence formal pre-clinical development of the Compound in the Field pursuant to the provisions of Section 3.1 hereof.

1.12 "Development Candidate Criteria" shall mean the criteria set forth in Schedule 1.14 hereto which shall be applicable to any Compound selected by Vertex as a Development Candidate hereunder.

1.13 "Development Candidate Information" will mean a full summary of all material information known to VERTEX about a Development Candidate, which CFFT reasonably needs in order to assess the potential of that Development Candidate as a treatment for CF and to pursue CFFT's Special Rights under Sections 10.5 and 10.6, if they are applicable. Development Candidate Information will also include comparable information known to VERTEX concerning

Compounds which are Back-up Compounds, as defined herein, to the Development Candidate which is the subject of the Development Candidate Information.

1.14 "Development Candidate Milestone" shall have the meaning ascribed to it in Section 4.4 hereof.

1.15 "Development Plan" shall have the meaning ascribed to it in Section 3.2.2 hereof.

1.16 "Development Program" shall mean activities associated with development of a Drug Product Candidate which are conducted by or at the direction of Vertex, its Affiliates, licensees or sublicensees, 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; (c) planning, implementation, evaluation and administration of human clinical trials; (d) manufacturing process development, scale-up and manufacture/analysis/QC/QA of Drug Product for clinical trials; (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.

1.17 "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.

1.18 "Drug Product Candidate" shall mean any Development Candidate for which a Development Program has commenced under Section 3.1 hereunder.

1.19 "Effective Date" shall mean April 1, 2004.

1.20 "Field" shall mean the treatment of conditions or diseases in the CF Field and the Pulmonary Field.

1.21 "First Commercial Sale" shall mean the first sale of a Drug Product by Vertex or an Affiliate, licensee or sublicensee of Vertex 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 that country.

1.22 "FTE" shall mean the equivalent of the work of one Vertex scientist or other project managerial professional, full time for one year, on or directly related to the Research Program. Work in the Research Program can include, but is not limited to the following activities that relate solely to the Research Program: (i) experimental laboratory work, (ii) project and research management, (iii) intellectual property creation, (iv) management activities directed toward evaluation of the commercial potential of a possible Drug Candidate, (v) recording and writing up results, (vi) reviewing literature and references, (vii) holding scientific

discussions, (viii) traveling to and attending appropriate seminars and symposia, (ix) and carrying out Joint Research Committee duties. Activities included in calculating FTE's shall not include negotiation of this Agreement or modifications or extensions thereof or administration activities such as accounting, invoicing, personnel related activities or the like. Moreover, activities specified in (iv) through (ix) above shall be taken into account only when performed by individuals substantially all of the activities of whom are otherwise dedicated to the Research Program. 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 not more than half of the total Research Program FTEs shall be delegated to Third Parties. FTE's which result from work delegated to and carried out by contractors, if not separately accounted for by the contractor, will be computed by dividing the total amount of the contractor's invoice by **[***]**, and the resulting FTE calculation will be separately identified by Vertex on its reports provided to CFFT under Section 4.3 hereof.

1.23 "Joint Research Committee" or "JRC" shall have the meaning ascribed to it in Section 2.6 of Agreement.

1.24 "Joint Steering Committee" or "JSC" shall have the meaning ascribed to it in Section 2.7 of Agreement.

1.25 "Net Sales" with respect to any Drug Product shall mean the gross amount invoiced by Vertex and any Vertex Affiliate, licensee or sublicensee for that Drug Product sold in bona fide, arms-length transactions to Third Parties for use in the Field, less (i) quantity and/or cash discounts from the gross invoice price which are actually allowed or taken; (ii) freight, postage and insurance included in the invoice price; (iii) amounts repaid or credited by reasons of

rejections or return of goods or because of retroactive price reductions specifically identifiable to the Drug Product; (iv) amounts payable resulting from government (or agency thereof) mandated rebate programs; (v) third-party rebates to the extent actually allowed; (vi) invoiced customs duties and sales taxes (excluding income, value-added and similar taxes), if any, actually paid and directly related to the sale that are not reimbursed by the buyer; and (vii) any other specifically identifiable amounts included in the Drug Product's gross invoice price that should be credited for reasons substantially equivalent to those listed above; all as determined in accordance with Vertex's usual and customary accounting methods, which are in accordance with generally accepted accounting principles.

1.25.1 In the case of any sale or other disposal of a Drug Product between or among Vertex 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;

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

1.25.3 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;

1.25.4 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 **[***]** The principles of this section shall also apply to a Combination Product in the event Sections 10.5.5, 10.5.6 and 10.6.2 are applicable.

1.26 "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.

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

1.28 "Positive Control" shall mean with respect to a Corrector, the Compound known as **[***]**, and with respect to a Potentiator, the Compound known as **[***]**, except as otherwise agreed by the Parties.

1.29 "Potentiator" shall mean a Compound which, as its principal mode of therapeutic action, modulates the biological effect of CFTR by enhancing the gating activity of ΔF508 CFTR present in the apical cell membrane.

1.30 "Prime Rate" shall mean the average prime rate published in the *Wall Street Journal* during the relevant period.

1.31 This section has been intentionally left blank.

1.32 "Pulmonary Field" shall mean the treatment of diseases of the human pulmonary tract or lungs, other than CF.

1.33 "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 § 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, or equivalent.

1.34 "Research Plan" shall have the meaning set forth in Section 2.4 hereof.

1.35 "Research Program" shall mean all research activities undertaken under this Agreement associated with the identification and design of Compounds and Development Candidates as provided herein; including but not limited to the identification and initial testing of Compounds; the conduct of those activities referenced in the Development Candidate Criteria with respect to Compounds; selection of Development Candidates and the presentation of those Development Candidates and related Development Candidate Information to CFFT.

1.36 "Research Termination Date" shall mean the earlier of December 31, 2005 or the date upon which the Research Program is terminated under Article X.

1.37 "Termination Know-How Package" shall mean, for the Research Program generally or for a particular Program (Primary or Alternate) within the Research Program, as the context may require, (a) all data and study results (including formulae for calculating EC50 and efficacy) from *in vitro* and *in vivo* efficacy testing and experimentation conducted with respect to Compounds under that Program, pursuant to the applicable Research Plan or Subplan, all as recorded in electronic form in Vertex's electronic database known as VERDI (Vertex Research Data Interface), and including Compound structure information; (b) standard operating procedures for the following assays: **[***]** all as conducted with commercially available instruments and equipment, and any other assay the creation of which was substantially paid for by CFFT under the Research Program or the Original Agreement and supported by medicinal

chemistry during the Research Program or the Original Agreement; and (c) any physical stocks of Compounds from the Program which are on hand on the date of Interruption, and information on chemical routes Controlled by Vertex for synthesis of additional stocks of Compounds.

1.38 "Territory" shall mean worldwide.

1.39 "Third Party" shall mean any person or entity which is not a party or an Affiliate of any party to this Agreement.

1.40 "Third Party Referral" shall mean the procedure for resolution of certain disputes hereunder which is set forth in Section 12.2(b) hereof.

1.41 "Vertex CF Technology" shall mean all data, technical information, know-how, inventions (whether or not patented) trade secrets, processes and methods discovered or developed, and Controlled by Vertex or its Affiliates, in the course of its performance of the Research Program under this Agreement, or in the course of activities undertaken by Vertex or Aurora under the Original Agreement, and related to CFTR modulation; provided, however, that the term "Vertex CF Technology" shall not apply to Vertex's general drug design technology whether in hardware or software form, tangible or intangible.

1.42 "Vertex Patents" shall mean any Patents Controlled by Vertex or its Affiliates claiming Vertex CF Technology.

ARTICLE II – RESEARCH PROGRAM

2.1 Commencement; Objective.

Research under the Original Agreement commenced on May 19, 2000 and is being continued under this Agreement pursuant to the Research Program described below. Vertex will be principally responsible for the conduct of the Research Program and CFFT will provide financial support, consultation and advice as provided herein and through its participation on the JRC and the JSC as provided below. The Research Program will be directed toward the identification of Development Candidates which are suitable for development and commercialization as human therapeutics for the treatment of CF.

2.2 Term.

The Research Program will be deemed to have commenced on the Effective Date, and will conclude on December 31, 2005, unless extended by agreement of the parties (including any such extension, the "Research Termination Date"), or unless earlier terminated in accordance with the provisions of Article X hereof. The parties may discuss at any time whether, and upon what basis, the Research Program might be extended beyond the initial Research Termination Date, and those discussions may include proposed extensions under Section 2.9 hereof.

2.3 Research Diligence.

The common objective of the parties is to identify Development Candidates as soon as practicable for worldwide development and marketing under the terms of this Agreement. Vertex will work diligently and use all reasonable efforts, consistent with prudent business judgment, to identify Development Candidates and to commence the development of those

Development Candidates as Drug Product Candidates. Vertex will dedicate to the Research Program at least that level of staffing referenced in Section 4.1 hereof, and expects to employ an optimal combination of experience and training in the CF Field.

2.4 Research Plan.

2.4.1 General. Vertex and CFFT have agreed upon an overall research plan for the Research Program, a copy of which is attached to this Agreement as Exhibit 2.4. The JRC will review and evaluate the Research Plan, taking into consideration ongoing research outcomes and other scientific and commercial developments, at each meeting of the JRC after the Effective Date, and any resulting modifications will be incorporated into the Research Plan (the original plan, and any such modifications are referred to herein as the "Research Plan"). Modifications to the Research Plan may be proposed by either Vertex or CFFT and will be reviewed by the JRC before being adopted. Any modification to the Research Plan that would (a) reduce the levels of FTE resources to be devoted by Vertex to the Research Program below the minimum provided in Section 4.1; or (b) materially alter the overall allocation of Research Program resources between the Primary and the Alternate Program, from the allocation specified in Section 4.1 hereof or (c) materially alter the goals and/or scientific focus of the Research Plan, shall not be adopted without the approval of CFFT, which will act expeditiously on any such proposal made by Vertex.

2.4.2 Primary and Alternate Programs. Potentiators and Correctors are thought to operate through different CFTR modulator mechanisms. Based on research efforts conducted under the Original Agreement and during 2004, Vertex in consultation with CFFT will determine, on or before the end of 2004, whether in its judgment the development of

Potentiators or Correctors represents the most promising approach to disease modification in the Field, based on scientific, regulatory, medical and business considerations. Thereafter, Vertex's activities under the Research Program aimed at identifying Development Candidates which act through the mechanism deemed by Vertex to be the most promising – either Potentiator or Corrector – will be called the "Primary Program" of research, and research activity directed toward the other mechanism will be referred to as the "Alternate Program."

2.4.3 Primary and Alternate Subplans. As soon as practicable after the Primary and Alternate Programs have been designated, Vertex will prepare and submit to the JRC for its review and comment research plans for the Primary Program (a "Primary Subplan") and the Alternate Program (an "Alternate Subplan") in each case covering the balance of the time remaining until the Research Termination Date. The Plans will be accompanied by budgets for the remaining period prior to the Research Termination Date. The budgets will each specify the aggregate amounts allocated for internal FTE's and other costs and the aggregate amounts allocated for external FTE's and other costs, and will be otherwise consistent with the requirements of Section 4.1 hereof. The date upon which the Primary Subplan, the Alternate Subplan, and the related budgets have been submitted to the JRC shall be called the "Primary Program Designation Date."

2.5 CFFT Special Rights at Program Selection Point.

If CFFT shall disagree with Vertex's choice in designating the Primary Program, it may refer the matter to the JSC for review under Section 2.7.1(iii) hereof, and may in any event:

2.5.1 Accept any decision of the JSC and proceed accordingly; or

2.5.2 Terminate support of the Primary and Alternative Programs upon the terms and with the consequences specified in Section 10.5 hereof;

2.6 Joint Research Committee.

2.6.1 Composition and Purposes. Vertex and CFFT have established a Joint Research Committee ("**JRC**") consisting of at least **[***]** (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 no less frequently than once in each three (3) month period during the Research Program, and at such time and location, as may be established by the Committee, for the following purposes:

(i) To review reports prepared by Vertex, which shall be submitted to the JRC within fifteen (15) days prior to each meeting, and shall include a thorough summary in written text of progress made during the preceding three month period under the Research Plan (although chemical structures will only be disclosed to CFFT in the context of a publication referenced in Article VII hereof, or as part of the Termination Know-How Package provided to CFFT in connection with an Interruption) and to CFFT's chemistry advisors in accordance with the following sentence. Chemical Structures will be separately disclosed to CFFT's chemistry advisors serving on the JRC, who will agree to maintain the confidentiality of the structures, to allow them to fulfill their JRC

responsibilities; provided that Vertex shall not be required to disclose structures to any advisors other than CFFT's chemistry advisors who are currently working with Vertex on CFFT's behalf, and to any other chemistry advisors approved by Vertex, which approval shall not be unreasonably withheld.

(ii) To review and discuss the Research Plan, and the Primary and the Alternate Subplans prepared by Vertex as provided in Section 2.4.3 above, and evaluate any proposed revisions to any of those Plans;

(iii) To assist Vertex in determining as soon as possible whether the Potentiator or Corrector approach should be the subject of the Primary Program; and

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

Vertex shall prepare and deliver minutes of the meeting to the members of the JRC, within thirty (30) days after the date of each meeting, setting forth, *inter alia*, all decisions of the JRC, and including as an attachment the report on the progress of work performed required by Section 2.6.1(i).

2.6.2 Decision-Making.

(i) Each of Vertex and CFFT 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 or any Subplan. 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 subsections (ii) and (iii) 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 which approach – Potentiator or Corrector – should be the subject of the Primary Program, any disagreement between the parties that cannot be resolved within thirty (30) days by the JRC shall be referred to the JSC and, failing agreement, Vertex's selection shall be controlling and CFFT shall have the alternatives set forth in Sections 10.5.1 and 10.5.3 below; and

(y) as to whether or not a given Compound proposed by Vertex as a Development Candidate actually

meet the Development Candidate Criteria, any disagreement between the parties that cannot be resolved within thirty (30) days by the JRC shall be referred to the JSC for resolution and if not resolved within seven (7) business days after referral, shall be referred for resolution by the Chief Executive Officer of Vertex and the Chief Executive Officer of CFFT, and failing resolution, the matter will be referred for final decision under the provisions of Section 12.2(b) of this Agreement; and

(z) as to the nature and extent of any additional Development Candidate Criteria referenced in Section 2.6.3 hereof, if any disagreement cannot be resolved by the JRC and the JSC as provided in (x) above, then there will be no change in the Development Candidate Criteria.

(iii) Notwithstanding the provisions of Section 2.6.2(i) hereof, if Vertex and CFFT deadlock on any matters being considered by the JRC which might have a significant impact on the time or likely success of the Research Program (other than those matters addressed in Section 2.6.2(ii) hereof), the matter shall be referred to the JSC for resolution in accordance with Section 2.7.1(iii) hereof.

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

2.6.3 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 based upon the particular mode of action of that Compound as a Potentiator or Corrector. 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 a change is proposed to the JRC by either party. Any disagreements with respect to the selection of additional Development Candidate Criteria hereunder will be addressed as provided in Section 2.6.2(ii).

2.7 Joint Steering Committee.

2.7.1 Composition and Purposes. Vertex and CFFT have established and will continue to participate in a Joint Steering Committee ("JSC") which shall consist of an equal number of senior management personnel as may be agreed by the parties from time to time. The JSC shall initially have six (6) members. If the JSC chooses to designate a Committee Chair, the Chair will be appointed from among the members of the JSC designated by Vertex. The JSC

shall meet semi-annually, or with such other frequency, and at such time and location, as may be established by the Committee, for the following purposes:

(i) To provide general oversight of the Research Program ;

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

(iii) To 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 referred to it under Section 2.6.2(ii)(x) and 2.6.2 (ii)(z), which shall be resolved as provided therein.

2.8 Exchange of Information.

2.8.1 Vertex 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.

2.8.2 CFFT shall not use Vertex CF Technology (excluding information which is no longer subject to confidentiality restrictions under Article V by reason of the exceptions set forth in Section 6.2) for any purpose, including the filing of patent applications containing such information, without Vertex's consent, except as otherwise explicitly permitted in this Agreement.

2.9 Extension of Research Termination Date.

Vertex and CFFT may extend the term of the Research Program, or the term of either the Primary Program or the Alternate Program, by mutual agreement. Any party desiring such an extension shall notify the other party in writing of that fact not less than sixty (60) days prior to the initial Research Termination Date. That notice shall include a summary of the material terms upon which the extension is proposed. The general expectation of the parties is that any such extension would be undertaken on terms substantially identical to those which appear in this Agreement, except that CFFT would bear only **[***]** of Vertex's on-going research costs. Any such proposal that relates to an extension of the Research Program, generally, shall be called a "Research Extension Proposal," and proposals that relate to extensions of the Primary Program or the Alternate Program, respectively, shall be called a "Primary Extension Proposal" or an "Alternate Extension Proposal."

2.10 Third Party Testing.

At CFFT's written request (a "Testing Request") delivered as provided below, Vertex will supply to an "Agreed Lab" reasonably adequate quantities of its "Lead Compounds" as necessary to enable the Agreed Lab to conduct *in vitro* testing of the efficacy and potency of the Lead Compounds in agreed CF assay models. All such testing will be undertaken at the expense of CFFT in addition to any funding otherwise provided hereunder.

An "Agreed Lab" is a commercial testing laboratory unaffiliated with either CFFT or Vertex and reasonably acceptable to both, which (a) specializes in rendering services to the pharmaceutical industry and has nationally recognized expertise in the testing of pharmaceutical compounds; (b) has a superior reputation for integrity in dealing with the proprietary information

of others and would be free of any real or apparent conflict of interest in performing the services which are the subject of this Section 2.10; and (c) is bound by the terms of a confidentiality agreement with Vertex which is customary in form and content, which covers the testing contemplated by this Section 2.10, and which permits the Lab to report to CFFT, directly, the results which it obtains with respect to efficacy and potency of the Lead Compounds, but only those results.

A "Testing Request" is a written request relating to the testing of Lead Compounds from either or both of the Primary and the Alternate Programs, which is delivered by CFFT to Vertex during any of the following periods: (i) the ninety day period beginning on the Primary Program Designation Date; (ii) the ninety day period prior to the due date for delivery to Vertex of any Early Termination Notice under Section 10.5.2 hereof; and (iii) the sixty day period beginning with the delivery by either party to the other of a Research Extension Proposal as provided in Section 2.9 hereof.

"Lead Compounds" shall mean not more than two Compounds from each Program – Primary or Alternate - for which a Testing Request is delivered, none of which are a Development Candidate, which meet the following criteria: (i) the Compound(s) have been selected by Vertex from the Primary Program and/or the Alternate Program, as relevant to the Testing Request (assuming CFFT has not terminated the Alternate Program under the provisions of Section 10.5.3 hereof); (ii) each Compound will be representative of those Compounds in each Program which Vertex believes to be the most promising as potential Drug Products; and

(iii) each Compound shall have been previously tested by Vertex, *in vitro*, as to potential efficacy and potency in CF, and the results of that testing shall have been provided to CFFT.

Vertex and CFFT acknowledge that commercially available assays for the testing of Lead Compounds may yield results which are less robust than the results obtained by Vertex in its own proprietary assays. The parties also acknowledge that the transfer of Vertex's proprietary assays to an Agreed Lab may be difficult, and the results less than satisfactory, without a commitment of substantial time and effort by Vertex which, if undertaken, may adversely impact the progress of the Research Program. Therefore, the parties agree that Vertex's responsibility for the testing provided under this Section 2.10 shall be limited as follows: (a) Vertex will cooperate with CFFT in the selection of an Agreed Lab as soon as practicable following the Effective Date, as may be requested by CFFT, and thereafter will assist in the determination whether commercially available assays conducted by the Lab are likely to provide satisfactory results; (b) Vertex will provide the Lab with requisite amounts of each Lead Compound, in connection with formal Testing Requests from CFFT as provided above, and up to three additional Compounds from each of the Primary or Alternate Programs, out of any supplies which Vertex may have on hand, the chemical structures of which have been published by Vertex in peer-reviewed journals or through posters or presentations at scientific conferences, which the Agreed Lab may use for control purposes; (c) Vertex will provide telephone consulting to appropriate representatives of the Agreed Lab concerning applicable assay methodology; (d) if the parties conclude that conventional testing will not yield adequate results, and upon the formal written request of CFFT rendered with due regard to **[***]** to establish an assay based on proprietary protocols from Vertex, Vertex will provide its proprietary assay protocol to the Agreed Lab sufficiently in

advance of any testing provided for in this Section 2.10 to accommodate such testing, under provisions of confidentiality, restricted access and non-use (for other than testing hereunder), and will ensure that appropriate Vertex representatives are available by telephone from time to time to answer questions and otherwise assist the Agreed Lab representatives in their efforts to establish Vertex's proprietary assay. Vertex shall in no event be responsible for any failure by the Agreed Lab to establish an effective assay using Vertex's protocols, nor shall any time periods provided herein for action by CFFT be extended by reason of any such failure.

ARTICLE III- DEVELOPMENT

3.1 Commencement of Development Program.

As soon as Vertex has identified a Development Candidate which it believes meets the Development Candidate Criteria, it will so notify CFFT and the JRC and will include with that notice the Development Candidate Information with respect to that Development Candidate and its Back-up Compounds. Vertex will promptly commence and pursue a Development Program with respect to that Development Candidate, at its expense, applying diligent, commercially reasonable efforts to develop Drug Product Candidates into Drug Products, consistent with those used by Vertex for its own compounds of similar potential.

3.2 Joint Development Committee.

3.2.1 Formation and Responsibilities. As soon as practicable after the commencement by Vertex of a Development Program with respect to a Drug Product Candidate, VERTEX will establish a Joint Development Committee ("JDC") which shall include a

representative designated by CFFT. Additional JDC's, which shall also include one CFFT representative, may be established from time to time in connection with the development of additional Drug Product Candidates. The JDC (or its successor organization, as designated by Vertex) 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 VERTEX from time to time. In addition to the CFFT member, the JDC 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. VERTEX will appoint the JDC Chair. The JDC will typically meet at least quarterly, 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 JDC shall be responsible for review of the goals and strategy for development of each Drug Product Candidate and shall prepare and oversee the implementation of an 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.

3.2.3 Meeting Materials. The JDC 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 JDC Chair will ensure that minutes are prepared and distributed to each member of the JDC promptly after each meeting. Those minutes shall contain a report on the activities of the JDC during its meeting. CFFT's representative on the JDC will receive all documents and information distributed or communicated to members of the JDC, and may review copies of all other information material to the development of a Drug Product Candidate unless the JDC denies access to that information for demonstrable competitive reasons.

3.2.4 CFFT and its Affiliates will use good faith efforts to enlist the Therapeutic Development Network and its resources and expertise in support of the development efforts for each Drug Product Candidate, and will involve appropriate Vertex representatives in that effort.

3.3 Development Responsibility and Costs.

Vertex 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.

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

3.4.1 Vertex Ownership. All Regulatory Approvals shall be held by and in the name of Vertex, and Vertex shall own all submissions in connection therewith.

3.4.2 Principal Interface. All formulary or marketing approvals shall also be obtained by and in the name of Vertex, and Vertex will be the principal interface with and will otherwise handle all interactions with regulatory agencies concerning any Drug Product.

3.4.3 Regulatory Meetings. If requested by Vertex, CFFT will arrange for one or more representatives of CFFT to participate in meetings between representatives of Vertex and any of the FDA, the EMEA and Koseisho (MHW Japan), to the extent that Vertex reasonably believes that representatives from CFFT would further the regulatory approval process.

ARTICLE IV – PAYMENTS

4.1 Staffing and Research Support Payments.

CFFT will make the payments to Vertex specified below during 2004 and 2005 in support of the Research Program under this Agreement.

[***]	**[***]**
[***]	**[***]**
[***]	**[***]**
Total	**$21.281**

Vertex will dedicate a minimum average **[***]** during its term, **[***]** Unless otherwise agreed in writing by CFFT, from and after the earlier of the date upon which Vertex notifies CFFT of its selection of a Primary and an Alternate Program, Vertex will devote **[***]** to the Alternate Program, and will apply **[***]**. Subject to the foregoing requirements, the research support specified above can be allocated as Vertex may determine in good faith between in-house and outside resources, between the Primary Program and the Alternative Program, and between and among individual budget line items.

4.2 Budget.

The initial budget for the Research Program is attached hereto as Exhibit 4.2 (the "Initial Budget"). Any material revisions to the Initial Budget which would result in an increase in total funding for the Research Program, or which are specified in Section 2.4.1, will require the prior approval of CFFT. Any other adjustments to the Research Program budget may be undertaken by Vertex with prior notice to, but without prior approval from, CFFT. The Initial Budget as revised or adjusted pursuant to the foregoing and in effect at any given time, shall be called the "Current Budget." Vertex will provide CFFT with quarterly reports, within thirty (30) days after the end of each quarter, showing expenses incurred under the Research Program during the quarter just ended against budgeted expenses for that quarter.

4.3 Payments.

Payments due under the Current Budget on account of internal FTEs shall be made by CFFT **[***]**. Payments due under the Current Budget on account of external costs shall be made by CFFT **[***]** 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 CFFT. 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. On or before each of March 1, 2005 and March 1, 2006, Vertex will provide CFFT with an accounting of all internal FTE costs and outsourcing costs incurred under the Research Program during the most recently concluded calendar year. Internal FTE costs will be calculated **[***]**. Costs incurred will be compared with funds provided by CFFT on account of that year, and **[***]**.

4.4 Clinical Trial Commencement Milestone.

CFFT will pay to Vertex the sum of $1.5 million (the "Development Candidate Milestone") with respect to the first Drug Product Candidate under the Research Program to commence human clinical trials of that Drug Product Candidate in any country with a generally accepted system of Regulatory Approvals. The first human clinical trial of a Drug Product Candidate will be deemed to have commenced when that Candidate is first dosed in a human under a clinical trial protocol which has been approved by the relevant oversight authority in the country in which the trial is being conducted. Payment with respect to a Drug Product Candidate will be made within thirty (30) days after receipt by CFFT of notice from Vertex that human clinical trials of that Drug Product Candidate have commenced.

4.5 Records.

Vertex shall keep accurate records and books of accounts containing all data reasonably required for the calculation and verification of FTE's employed, and outsourcing costs incurred, by Vertex in the Research Program. CFFT, through an independent accounting firm unaffiliated with either CFFT or Vertex, shall have the right at its expense to audit Vertex's

relevant records to verify compliance with FTE and other research funding allocation requirements hereunder.

At CFFT'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 CFFT's expense, for the sole purpose of verifying the accuracy of those records in the calculation of Research Program FTEs and outsourcing costs. Vertex shall not, however, be required to retain or make available to CFFT or its accountants, any such records or books of account for either 2004 or 2005, beyond thirty-six (36) months from the termination of the Research Program. CFFT shall cause the accounting firm to retain all such information in confidence.

In the event that the aggregate costs actually chargeable to the Research Program during any year are less than the amount previously advanced to Vertex by CFFT and properly attributable to that year (a "Negative Difference"), in addition to reimbursing CFFT for the Negative Difference plus interest calculated at **[***]** if the Negative Difference is more than **[***]** then Vertex shall also pay the reasonable costs of the independent accountant employed by CFFT in the review.

4.6 Payments Due Under the Original Agreement.

Vertex acknowledges that no further milestone payments, beyond those made to Vertex prior to the Effective Date of this Agreement under the Original Agreement. Outsource costs incurred by Vertex under the Original Agreement prior to the Effective Date will be reimbursed by CFFT under the terms of the Original Agreement from available funds provided under the Original Agreement. Except as specified in the preceding sentence, neither Vertex nor

CFFT shall have any remaining obligations under the Original Agreement after the Effective Date.

ARTICLE V – COMMERCIALIZATION; ROYALTIES

5.1 Marketing and Promotion.

Vertex and/or its licensees and sublicensees shall have exclusive rights to market, sell and distribute all Drug Products in the Territory, subject to the Special CFFT Rights provided in Sections 10.5 and 10.6 below.

5.2 Due Diligence.

Vertex 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 in North America and Europe as soon as reasonably practicable, devoting the same degree of attention and diligence to those efforts that it devotes to similar activities for its other products of comparable market potential.

5.3 Royalties.

5.3.1 Net Sales in the Field. Vertex shall pay to CFFT the following royalties on annual Net Sales of each Drug Product:

4% **[***]** Net Sales

[***] Net Sales

[***] Net Sales [***]

[***] Net Sales under this Section 5.3.1 shall not in any event include any Net Sales of Drug Products which are the subject of the royalty obligations set forth in Sections 5.3.2, 10.5.4, 10.5.5, and 10.5.6 hereof.

5.3.2 Net Sales outside the Field. Vertex shall pay CFFT a royalty of **[***]** of annual Net Sales of each Drug Product for use outside the Field.

5.4 Sales Reports.

(a) After the First Commercial Sale of a Drug Product, Vertex shall furnish or cause to be furnished to CFFT 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") within sixty days after the close of each quarter showing, for Net Sales in the Field and, separately, for Net Sales outside the Field, (i) the Net Sales of each Drug Product in each country in the world during the reporting period by Vertex and each Affiliate, licensee and sublicensee; (ii) the royalties, payable in U.S. dollars ("Dollars"), which shall have accrued under Section 5.3 hereof in respect of such sales and the basis of calculating those royalties; (iii) withholding taxes, if any, required by law to be deducted from any royalties payable 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 CFFT 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 CFFT hereunder shall be expressed in the domestic currency of the party making the sale, together with the Dollar equivalent of the amount payable to CFFT, calculated by translating foreign currency sales into U.S. dollars based on the average of the exchange rates reported in *The Wall Street Journal* or comparable publication over the period covered by the royalty report. If any licensee or 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 licensee's or sublicensee's normal accounting principles. Vertex shall furnish to CFFT appropriate evidence of payment of any tax or other amount required by applicable laws or regulations to be deducted from any royalty payment payable by Vertex to CFFT pursuant to this Agreement, 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 Vertex shall also provide CFFT with a "flash" report of Net Sales, only, within ten (10) business days after the end of each month. Vertex shall keep accurate records in sufficient detail to enable the amounts due hereunder to be determined and to be verified by CFFT.

(b) Amounts shown to have accrued by each sales report provided for under Section 5.4(a), above, shall be due and payable on the date that 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 in the Territory where Drug Products are sold, Vertex or its sublicensees shall have the right and option to make such payments by depositing the amount thereof in local currency to CFFT's account in a bank or depository in such country.

(d) Upon the written request of CFFT, at CFFT's expense and not more than once in or in respect of any calendar year, Vertex shall permit an independent accountant of national prominence selected by CFFT, to have access during normal business hours to those records of Vertex as may be reasonably necessary to verify the accuracy of the sales reports furnished by Vertex pursuant to this Section 5.4, in respect of any calendar year ending not more than thirty-six (36) months prior to the date of such notice. The report prepared by such independent accountant, a copy of which shall be sent or otherwise provided to Vertex by such independent accountant at the same time it is sent or otherwise provided to CFFT, shall contain the conclusions of such independent accountant regarding the audit and will specify that the amounts paid to CFFT pursuant thereto were correct or, if incorrect, the amount of any underpayment or overpayment. If such independent accountant's report shows any underpayment, Vertex shall remit to CFFT within thirty (30) days after Vertex's receipt of such report, (i) the amount of such underpayment plus interest at the Prime Rate plus two (2) percentage points calculated from the date such payment is due, and (ii) if such underpayment exceeds **[***]** 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. CFFT agrees that all information subject to review under this Section 5.4 or under any sublicense agreement is confidential and that CFFT shall retain and cause its accountant to retain all such information in confidence. 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 CFFT, and Vertex shall be released from any liability or accountability with respect to payments for such year.

(e) In case of any delay in payment by Vertex to CFFT not occasioned by Force Majeure, interest shall be calculated at the **[***]** from the tenth (10^{th}) day after the due date of the payment, shall be due from Vertex.

5.5 Vertex First Negotiation Right re: CFF Royalty Disposition.

If CFFT should wish to assign, sell or otherwise transfer rights in or to any of the royalty payments due or to become due from Vertex, its Affiliates, successors, assignees, licensees or sublicensees under any of the provisions of this Agreement, or to undertake any transaction which would have the same or a similar effect as any such assignment, sale or transfer, it will provide Vertex with sixty (60) days prior written notice (a "Transfer Notice"), and during that sixty day period will at Vertex's request negotiate with Vertex in good faith, with the objective of reaching an agreement under which those CFFT rights which were the subject of the Transfer Notice would be assigned, sold or transferred to Vertex, its successors or assigns in lieu of an assignment, sale, transfer or other transaction to or with a Third Party. If at the end of the sixty day period referenced above Vertex and CFFT have been unsuccessful in negotiating mutually agreeable terms of assignment, sale or transfer, then CFFT shall be under no further obligation to Vertex under this Section 5.5, unless it shall not conclude a transaction with a Third Party covering the rights which were the subject of the initial Transfer Notice within twelve (12) months after the date of delivery of that Transfer Notice, in which event any subsequent effort to assign, sell or transfer any of those rights shall be once again subject to the terms of this Section 5.5.

ARTICLE VI - CONFIDENTIALITY

6.1 Undertaking.

During the term of this Agreement, each party shall keep confidential, and other than as provided herein shall not use or disclose, directly or indirectly, any trade secrets, confidential or proprietary information, or any other knowledge, information, documents or materials, owned, developed or possessed by the other party, whether in tangible or intangible form, the confidentiality of which such other party takes reasonable measures to protect ("Confidential Information"). Neither CFFT nor Vertex will use the other party's Confidential Information except as expressly permitted in this Agreement

(a) Each party shall take any and all lawful measures to prevent the unauthorized use and disclosure of the other party's Confidential Information, and to prevent unauthorized persons or entities from obtaining or using that Information.

(b) Each party will refrain from directly or indirectly taking any action which would constitute or facilitate the unauthorized use or disclosure of the other party's Confidential Information. Each party may disclose that 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, agents, licensees, sublicensees and

subcontractors have entered into appropriate confidentiality agreements for secrecy and non-use of such Confidential 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 the other party's Confidential Information by its officers, employees and agents and any such sublicensees and subcontractors.

6.2 Exceptions.

Notwithstanding the foregoing, the provisions of Section 6.1 hereof shall not apply to Confidential Information which the receiving party can conclusively establish:

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

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

(c)has 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) is disclosed by the disclosing party to a Third Party without restrictions on its disclosure;

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

(f) is 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 CFFT 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 or time or with respect to any specific information.

6.3 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.

(a) Except to the extent already disclosed in that initial press release or other public communication, no public announcement concerning the terms of this Agreement or concerning the transactions described herein shall be made, either directly or indirectly, by Vertex or CFFT, except (i) as may be legally required by applicable laws, regulations, or judicial order, or (ii) if limited to the fact that the Research Program exists, that research is in progress, and its anticipated completion 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.

6.4 Survival.

The provisions of this Article VI shall survive the termination of this Agreement and shall extend **[***]**.

ARTICLE VII - PUBLICATION

Each of Vertex and CFFT 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 **[***]** prior to submission for publication or oral presentation. The non-publishing party shall notify the publishing party in writing **[***]** 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 VI hereof, (ii) information that if published would have an adverse effect on a patent application covering the subject matter of this 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 **[***]**, 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 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 thirty (30) days after such referral, the matter shall be referred by the JSC to the Chief Executive Officer of CFFT 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, and that appropriate credit will be acknowledged when the subject matter of a publication is derived in whole or in significant part from Vertex CF Technology or inventions licensed by CFFT pursuant to Section 9.1 of this Agreement. 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.

Notwithstanding the foregoing, Vertex intends to advance the body of general scientific knowledge of CF and its potential therapies, and to contribute to the identification of chemical

tools as optimal scientific benchmarks, all in a manner consistent with its general scientific and commercial objectives in entering into the collaboration with CFFT to which this Agreement relates. In furtherance of that objective, Vertex would expect, after giving due consideration to the appropriate protection of intellectual property, to publish information in peer-reviewed scientific journals concerning its efforts under the Research Program, including chemical structural information about at least two Compounds. Vertex will include as co-authors of any such publication contributing CFFT personnel and consultants and other persons who would customarily be considered in that regard, including members of the JRC as appropriate. CFFT's financial contribution to the Research Program also will be acknowledged.

This Article VII shall survive the termination of this Agreement for five (5) years from the date of such termination.

ARTICLE VIII- INDEMNIFICATION

8.1 Indemnification by Vertex.

Vertex will indemnify and hold CFFT 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

licensees, sublicensees or subcontractors under this Agreement, or any actual or alleged violation of law resulting therefrom; or

(b) the breach by Vertex of any of its covenants, representations or warranties set forth in this 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 CFFT or its Affiliates.

8.2 Indemnification by CFFT.

CFFT 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 CFFT or its Affiliates or their representatives, agents, authorized licensees, sublicensees or subcontractors under this Agreement, or any actual or alleged violation of law resulting therefrom; or

(b) the breach by CFFT of any of its covenants, representations or warranties set forth in this 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.

8.3 Claims Procedures.

Each Party entitled to be indemnified by the other Party (an "Indemnified Party") pursuant to Section 8.1 or 8.2 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 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.

ARTICLE IX– PATENTABLE INVENTIONS

9.1 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 Agreement relating to the Research Program 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; provided that, CFFT hereby grants to Vertex an exclusive (even as to CFFT worldwide) license

to its rights in any Joint Invention and any CFFT invention resulting from the Research Program for the purposes specified in this Agreement.

9.2 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 CFFT shall take responsibility for the preparation, filing, prosecution and maintenance of all CFFT 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.

9.3 Costs.

[***]

ARTICLE X – TERM AND TERMINATION

10.1 Term.

This Agreement will extend until the Research Termination Date as defined herein, unless earlier terminated by either party hereto in accordance with this Agreement, or unless extended by mutual agreement of the parties.

10.2 Termination of the Research Program by CFFT for Cause.

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

(a) Vertex shall materially breach any of its material obligations under this Agreement, and such material breach shall not have been remedied or material steps initiated to remedy the same to CFFT's reasonable satisfaction, within thirty (30) days after CFFT 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 events of Force Majeure.

In the event of any valid termination under this Section 10.2, CFFT shall not be required to make any payments under Section 3.2 hereof which have not accrued prior to receipt by Vertex of the notice of breach referenced under Section 10.2(a) or receipt by Vertex of the notice of termination pursuant to Section 10.2(b), as the case may be.

10.3 Termination of the Research Program by Vertex for Cause.

Vertex may at its sole discretion terminate this Agreement upon written notice to CFFT upon the occurrence of the following event:

CFFT shall materially breach any of its material obligations under this Agreement and such material breach shall not have been remedied or material steps initiated to remedy the

same to Vertex's reasonable satisfaction, within thirty (30) days after Vertex sends written notice of breach to CFFT.

10.4 General Effect of Termination.

(a) Except where explicitly provided elsewhere herein, termination of this Agreement for any reason, or expiration of this Agreement, will not affect: (i) obligations which have accrued as of the date of termination or expiration, and (ii) obligations and rights which, expressly or from the context thereof, are intended to survive termination or expiration of this Agreement. Without limitation, the following shall survive termination either indefinitely or for the period so stated: Section 2.9 (for the limited purposes of completing a Testing Request with respect to a Development Candidate after the Research Termination Date) and Articles III, V, VI, VII, VIII, IX, XI and XII.

(b) Upon termination or expiration of this Agreement, Vertex will retain exclusive rights to Vertex CF Technology and the inventions licensed to it by CFFT pursuant to Section 9.1 of this Agreement (including intellectual property), except CFFT shall hold those rights specified under Sections 10.5 and 10.6 hereof, as applicable.

10.5 CFFT Special Termination Rights.

CFFT at its sole discretion may exercise the following Special Termination Rights at or within the time period stated, before the Research Termination Date.

10.5.1 Termination after Program Designation. At any time after the Primary Program Designation Date referenced in Section 2.4 hereof, CFFT may request in writing (a "Selection Disagreement Notice") that Vertex reconsider its Primary Program choice and its primary focus on either Potentiators or Correctors. If Vertex does not elect by written notice to CFFT to amend its choice and select for the Primary Program the mode of action (i.e., Potentiator or Corrector), preferred by CFFT (the "Preferred CFFT Mode of Action"), then the Agreement will terminate effective sixty (60) days following receipt by Vertex of the Selection Disagreement Notice, unless that Notice is earlier withdrawn by CFFT by further notice in writing delivered to Vertex within sixty (60) days after receipt by Vertex of the Selection Disagreement Notice.

10.5.2 Early Termination. At its sole discretion, CFFT may terminate this Agreement effective June 30, 2005, upon not less than sixty (60) days prior written notice to Vertex, (an "Early Termination Notice").

10.5.3 Alternate Program Termination. CFFT may by written notice delivered to Vertex (the "Alternate Program Termination Notice") elect to terminate the Alternate Program and all funding which under the Current Budget would have been allocated to the Alternate Program after the effective date of termination. Termination will be effective on the 30th day following receipt by Vertex of the Alternate Program Termination Notice (the "Alternate Program Termination Date"). Notwithstanding such Termination, CFFT will reimburse Vertex during the ninety (90) days following such Termination for all outsourced costs **[***]** From and after the date the Alternate Program Termination Notice is received by Vertex, CFFT will not be obligated to fund any other outsourcing costs allocated in the Current Budget to the Alternate Program. Funding for FTEs which are allocated to the Alternate Program may at Vertex's

discretion, after consultation with CFFT, be allocated to provide additional FTE support for the Primary Program. The required minimum FTE level set forth in Section 4.1 hereof will be adjusted as appropriate to reflect termination of the Alternate Program as provided herein.

10.5.4 Upon the effective date of termination of this Agreement under Section 10.5.1 above, Vertex hereby grants to CFFT and its Affiliates an exclusive, worldwide license, with the right to sublicense, under the Vertex CF Technology to make, have made, use, have used, import, offer for sale, sell and have sold drug products in the Field for which the principal mode of action is the Preferred CFFT Mode of Action, and the license to Vertex of inventions pursuant to Section 9.1 of this Agreement regarding such Mode of Action shall terminate. In consideration of the foregoing license, CFFT will pay Vertex **[***]**.

10.5.5 In the event this Agreement is terminated by CFFT under Section 10.5.2 hereof, and in lieu of any other obligations (including royalty obligations under Section 5.3 hereof) owed by Vertex to CFFT hereunder except obligations that explicitly survive termination of this Agreement, Vertex shall pay CFFT **[***]**

10.5.6 In the event the Alternate Program is terminated by CFFT under Section 10.5.3 hereof, and Vertex thereafter sells a Drug Product in the Field which relies for its principal therapeutic effect in the Field on the mode of action which was the subject of the Alternate Program, then in lieu of the royalty obligation set forth in Section 5.3 hereof, Vertex will pay to CFFT **[***]**

10.5.7 For purposes of Section 10.5.5 and 10.5.6, a product shall constitute a Drug Product even though the notice for a Development Candidate specified in Section 1.11 has not been issued by Vertex.

10.6 Consequences of an Interruption.

10.6.1 For purposes of this Agreement, an "Interruption" shall be deemed to have occurred in any of the following circumstances:

(a) with respect to either the Primary Program or the Alternate Program, considered separately, if at any time after the Research Termination Date and before a Drug Product is achieved, Vertex or its Affiliates, licensees, sublicensees, assignees or partners (collectively, and for purposes of this Section 10.6 only, "Vertex") either, as applicable, (i) ceases reasonable research efforts directed toward identification of a Development Candidate, or (ii) ceases reasonable development efforts with respect to a Development Candidate (if one has been designated by Vertex), for a period of more than 180 consecutive days, and CFFT delivers written notice (an "Interruption Notice") to Vertex stating that an Interruption under this Section 10.6 has occurred; provided that an Interruption will not be deemed to have occurred with respect to a Development Candidate unless Vertex commences reasonable development efforts with respect to another Development Candidate from the same Program, within thirty (30) days after receipt of any such Interruption Notice and such development efforts continue uninterrupted for no less than three hundred sixty (360) days;

10.6.2 Upon the effective date of any Interruption under Section 10.6.1 above, the license granted to Vertex under Section 9.1 for any CFFT invention shall terminate with respect to the applicable Program described below, and the following license in favor of CFFT shall become effective:

(a) If the Program to which the Interruption relates involves the design of Compounds which are intended to act as Potentiators, then CFFT shall have an exclusive right **[***]** and with respect to those Compounds, CFFT shall have an irrevocable, exclusive worldwide license, with the right to sublicense, under the Vertex CF Technology to develop, manufacture, have manufactured, use, sell, offer to sell and import those Compounds in the Field.

(b) If the Program to which the Interruption relates involves the design of Compounds which are intended to act as Correctors, then CFFT shall have an exclusive right **[***]** and with respect to those Compounds, CFFT shall have an irrevocable, exclusive worldwide license, with the right to sublicense, under the Vertex CF Technology to develop, manufacture, have manufactured, use, sell, offer to sell and import those Compounds in the Field.

(c) In lieu of any other obligation owed by CFFT to Vertex pursuant to this Agreement, except obligations that explicitly survive termination of this Agreement, CFFT shall pay Vertex **[***]**

(d) In connection with either or both of the foregoing licenses, Vertex will deliver to CFFT the Termination Know-How Package associated with the Program to which the license relates expeditiously upon the occurrence of an Interruption.

(e) For purposes of CFFT's compound selection right under subsection (a) or (b) above, the classification of a particular Compound as a

Potentiator or a Corrector will be determined as specified in the respective definitions of those terms which are set forth in Article I hereof.

10.7 Refused Program Extension.

If (a) Vertex proposes a Research Program Extension under Section 2.9 hereof which is a "Qualifying Extension Proposal" as defined below: and

(b) CFFT refuses that proposal and declines to continue funding of the relevant Program (a "Refused Program") as specified in the Qualifying Extension Proposal; and

(c) Vertex continues funding of the Refused Program for the proposed term, on a funding level for the proposed term at least equal to Vertex's share of the funding provided in the Qualified Extension Proposal and a Drug Product is thereafter sold by Vertex then the royalty otherwise payable to CFFT under Section 5.3 hereof with respect to any Development Candidate selected from the Refused Program by Vertex more than twelve (12) months after the Research Termination Date, shall be reduced **[***]** An extension of any efforts by Vertex pursuant to the foregoing shall be called a "Refused Program Extension."

For purposes of this Section 10.7, a "Qualifying Extension Proposal" shall mean, with respect to any Program, a proposed extension of that Program beyond the Research Termination Date (i) at an average annualized cost not greater than the level provided under the Current Budget in effect for the six month period immediately preceding the Research Termination Date with respect to that Program; (ii) on relevant terms substantially similar to those set forth in this Agreement; but (iii) with the aggregate funding commitment divided equally between Vertex and CFFT.

ARTICLE XI – REPRESENTATIONS AND WARRANTIES

11.1 Representations and Warranties of Vertex.

Vertex represents and warrants to CFFT that 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, 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 Agreement have been duly authorized by all necessary action on the part of VERTEX, its officers and directors.:

11.2 Representations and Warranties of CFFT.

CFFT represents and warrants to Vertex that this Agreement has been duly executed and delivered by CFFT and constitutes the valid and binding obligation of CFFT, enforceable against CFFT 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 Agreement have been duly authorized by all necessary action on the part of CFFT, its officers and directors.

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 Commonwealth of Massachusetts.

12.2 Dispute Resolution Process.

(a) General. Except as set forth in (b) below or as otherwise explicitly provided herein, in the event of any controversy or claim arising out of or relating to any provision of this Agreement, or the collaborative effort contemplated hereby, the parties shall, 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 to the Chief Executive Officer of Vertex and the Chief Executive Officer of CFFT 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 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 CFFT 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 XIII – MISCELLANEOUS PROVISIONS

13.1 Waiver.

No provision of this Agreement may be waived except in writing by both parties hereto. No failure or delay by either party hereto in exercising any right or remedy hereunder or

under applicable law will operate as a waiver thereof, or a waiver of any right or remedy on any subsequent occasion.

13.2 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.

13.3 Severability.

Should one or more provisions of this Agreement be or become invalid, then the parties hereto shall attempt to agree upon valid provisions in substitution for the invalid provisions, which in their economic effect come so close to the invalid provisions that it can be reasonably assumed that the parties would have accepted this Agreement with those new provisions. If the parties are unable to agree on such valid provisions, the invalidity of such one or more provisions of this Agreement shall nevertheless not affect the validity of the Agreement as a whole, unless the invalid provisions are of such essential importance for this Agreement that it may be reasonably presumed that the parties would not have entered into this Agreement without the invalid provisions.

13.4 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 CFFT or Vertex under this Agreement, the party, if any, not so affected, shall have the right, at its option, to suspend or terminate this Agreement as to such country, if good faith negotiations between the parties to make such modifications therein as may be necessary to fairly address the impact thereof, are not successful after a reasonable period of time in producing mutually acceptable modifications to this Agreement.

13.5 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 13.5 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 assignees from either of the parties hereto.

13.6 Counterparts.

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

13.7 No Agency.

Nothing herein contained shall be deemed to create an agency, joint venture, amalgamation, partnership or similar relationship between CFFT and Vertex. Notwithstanding any of the provisions of this Agreement, neither party to this Agreement shall at any time enter into, incur, or hold itself out to third parties as having authority to enter into or incur, on behalf of the other party, any commitment, expense, or liability whatsoever, and all contracts, expenses and liabilities in connection with or relating to the obligations of each party under this Agreement shall be made, paid, and undertaken exclusively by such party on its own behalf and not as an agent or representative of the other.

13.8 Notice.

All communications between the parties with respect to any of the provisions of this Agreement will be sent to the addresses set out below, or to such other addresses as may be designated by one party to the other by notice pursuant hereto, by prepaid, certified air mail (which shall be deemed received by the other party on the seventh business day following deposit in the mails), or by 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 CFFT, at:

Cystic Fibrosis Foundation Therapeutics Incorporated
6931 Arlington Road
Bethesda, Maryland 20814
Attention: Dr. Robert J. Beall, President

with a copy to: Kenneth I. Schaner, Esq.

Swidler Berlin Shereff Friedman, LLP
3000 K Street, N.W., Suite 300
Washington, D.C. 20007

if to Vertex, at:

Vertex Pharmaceuticals Incorporated
130 Waverly Street
Cambridge, MA 02139-4211
Attention: President

with a copy to: Legal Department

Attention: General Counsel

13.9 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.

13.10 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.

13.11 Entire Agreement.

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

13.12 Notice of Pharmaceutical Side-Effects.

During the term of this 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, a Drug Product, and any other product for which royalties are payable under this Agreement.

13.13 Invoice Requirement.

Any amounts payable to Vertex hereunder shall be made within thirty days after receipt by CFFT, or its nominee designated for that purpose in advance by CFFT in writing to Vertex, of an invoice covering such payment.

VERTEX PHARMACEUTICALS INCORPORATED

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

CYSTIC FIBROSIS FOUNDATION THERAPEUTICS INCORORATED

By: /s/ Robert Beall
Title: President and CEO

EXHIBIT 2.4

RESEARCH PLAN

Research Plan

for the

CFFT – Vertex Pharmaceuticals Collaboration

May 10, 2004

[***]

[***]

• **[***]**
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EXHIBIT 4.2

INITIAL BUDGET FOR RESEARCH PROGRAM

Vertex/CFFT – CFTR Drug Discovery Budget

2004-2005

[***]

Exhibit 10.2

Certain confidential information contained in this document, marked by [***], has been omitted because it is not material and would likely cause competitive harm to Vertex Pharmaceuticals Incorporated if publicly disclosed.

AMENDMENT NO. 1
TO
RESEARCH, DEVELOPMENT AND
COMMECIALIZATION AGREEMENT (the "Existing Agreement")
DATED MAY 24, 2004 BY AND BETWEEN VERTEX PHARMACEUTICALS INCORPORATED ("Vertex") and
CYSTIC FIBROSIS FOUNDATION THERAPEUTICS INCORPORATED ("CFFT")

This Amendment No. 1 (the "Amendment") is made this 6th day of January, 2006 (the "Effective Date") between Vertex, a Massachusetts corporation with principal offices at 130 Waverly Street, Cambridge, MA 02139-4242 and CFFT, a Delaware corporation with principal offices at 6931 Arlington Road, Bethesda, Maryland 20814. Vertex and CFFT are referred to hereinafter collectively as the Parties.

INTRODUCTION

In 1998, CFFT made an award to Aurora Biosciences to do a feasibility study using high throughput screening for cf targets. On May 19, 2000, CFFT selected and provided support for Aurora Biosciences to conduct high throughput screening with respect to the CFTR target identified by CFFT. Since that time, Aurora Biosciences, and then after its merger into Vertex, Vertex, have been conducting a Research Program with CFFT's support aimed at identification and design of Potentiator and Corrector Compounds, both of which are directed as a principal mode of therapeutic action at modulation of the biological effect of CFTR in different ways and with different anticipated results. The Existing Agreement contemplated that during the course of the Research Program, Vertex, with CFFT's agreement, would select either the Potentiator or the Corrector approaches as its Primary Program, to which a majority of resources under the

Research Program would be directed, and the other approach would be designated as an Alternative Program, to which the balance of resources would be directed.

Vertex has selected the Potentiator approach as the Primary Program, with the concurrence of CFFT, and expects to designate a Potentiator Compound as a Development Candidate on or before December 31, 2005.

The Parties continue to believe that it may be possible to create Corrector Compounds of significant potential value as therapeutics in the Field. To further this effort, CFFT and Vertex agree hereinafter to provide additional funding and Vertex intends to continue its research efforts with respect to Correctors beyond the current Research Termination Date of December 31, 2005. The purpose of this Amendment is to modify the terms of the Existing Agreement to reflect the progress made in the Research Program during its current term and to set forth the terms of the extended Corrector Research Program.

Capitalized terms not otherwise defined in this Amendment shall have the meaning ascribed to them in the Existing Agreement. If specific provisions of this Amendment are inconsistent with specific provisions of the Existing Agreement, the provisions of this Amendment shall control.

In consideration of the mutual covenants set forth in this Amendment, and other good and valuable consideration, the receipt of which is hereby acknowledged, the Parties agree as follows:

1. **General.**

1.1. Vertex and CFFT acknowledge that the "Primary Program" under the Existing Agreement refers to research activities relating to Potentiator Compounds. CFFT has no further right to request under Section 2.5 of the Existing Agreement that Vertex designate Correctors as the Primary Program, or to terminate the Existing Agreement under Section 10.5.1 thereof.

1.2. After December 31, 2005, the "Research Program" will refer to research undertaken under the Existing Agreement, as amended hereby, with respect only to Corrector Compounds (except for the Potentiator research funded during 2006 as specified in the attached Research Plan). The "Research Plan" under Section 2.4 of the Existing Agreement will mean, after December 31, 2005, the initial plan for conduct of the Research Program focused on Correctors (and to a limited extent, Potentiators, as provided in the Research Plan), subject to applicable provisions of Section 2.4.1 of the Existing Agreement regarding modifications to that Research Plan. A copy of the initial Research Plan for continuing Corrector research (the "Initial Corrector Research Plan") is attached to this Amendment as Exhibit 1.2. The concepts of Primary Subplan and Alternative Subplan as referenced in Section 2.4.3 of the Existing Agreement will no longer apply to activities undertaken under the Research Program after December 31, 2005. The terms of the Existing Agreement that provide for the allocation of resources between the Primary and the Alternative Programs will not be applicable to the Research Program after December 31, 2005.

1.3. The budget for the Research Program under the Existing Agreement for the one year period ending December 31, 2005 (the "Current Budget") is attached hereto as Exhibit 1.3, has been approved by both Parties hereto and represents an agreed allocation of funding between the Primary and the Alternative Programs for the period ending December 31, 2005. The Parties have agreed on a separate budget (the "Initial Corrector Budget") representing an agreed allocation of additional Corrector research funding to be provided under this Amendment, as referenced in Section 4.1 below, for the period commencing on the Effective Date of this Amendment and ending on the Research Termination Date referenced in Section 1.4 below.

1.4. The Research Termination Date shall mean the end of the revised Research Program directed at the identification and design of Corrector Drug Product Candidates (the "Corrector Research Program") which shall be March 31, 2008, unless the Research Program under the Existing Agreement as amended hereby is otherwise extended or terminated in accordance with its terms.

1.5. The term "Drug Product[s]" is amended to mean a finished dosage form that is prepared from Bulk Drug Substance covered by Vertex CF Technology and is ready for administration to the ultimate consumer as a pharmaceutical.

1.6. The term "Vertex CF Technology" as defined in the Existing Agreement shall also be deemed to refer to data, technical information, know-how, inventions (whether or not patented), trade secrets, processes and methods discovered or developed, and Controlled by Vertex or its Affiliates, in the course of the performance of the Research Program

under this Amendment, but shall not refer to Vertex's general drug design technology whether in hardware or software form, tangible or intangible.

1.7. The provisions of Section 6.3 of the Existing Agreement shall apply to this Amendment as if it were being entered into as part of the Existing Agreement. The Parties will agree on the timing and content of a press release relating to this Amendment.

2. Termination Provisions.

2.1. On the Effective Date of this Amendment, CFFT shall no longer have the right to terminate the Existing Agreement under Section 10.5.1 (relating to a disagreement over the choice of Primary and Alternative Programs) or Section 10.6.3 (relating to termination of the Alternative Program). Therefore, those sections of the Existing Agreement are hereby deleted.

2.2. Section 10.5.2 of the Existing Agreement is hereby amended to read as follows:

> "At its sole discretion, CFFT may terminate the Research Program effective June 30, 2006 or June 30, 2007, upon not less than sixty (60) days prior written notice to Vertex (an "Early Termination Notice")."

2.3. Sections 10.5.4, 10.5.6 and 10.7 of the Existing Agreement are hereby deleted.

2.4. Section 10.6.1 of the Existing Agreement is hereby amended by substituting the word "if" for the word "unless" in the fourth-to-last line of that section.

3. Other CFTR Research.

During the period for which funding is provided to Vertex by CFFT under the Existing Agreement (as amended herein or subsequently from time to time), and under a separate agreement

providing for continued Potentiator funding (the “Potentiator Funding Agreement”), if such funding is provided in other than in the Existing Agreement, all of Vertex’s research efforts directed at the identification, development and commercialization of pharmaceutical products that have as their principal mode of action the modulation of CFTR shall be conducted under the Existing Agreement (as amended herein or subsequently from time to time) and under the Potentiator Funding Agreement. During the [***] period following the later of the last date upon which CFFT provides funding to Vertex under the Existing Agreement (as amended herein or subsequently from time to time), or the last date upon which CFFT provides continuing Potentiator funding under the Potentiator Funding Agreement, if such funding is provided for other than in the Existing Agreement, Vertex shall not enter into any research, development or commercialization agreement (a “Third Party Agreement”) with a third party directed toward the eventual commercialization (including the acquisition and sale of a marketed product) of a pharmaceutical product that has as its principal mode of action the modulation of CFTR and is not a Drug Product (the “New Product”), unless CFFT will receive the same royalty rate from Vertex or the third party under the Third Party Agreement as is provided under Section 5.3.1 of the Existing Agreement (as it may be subsequently amended), on account of any Net Sales of the New Product. An agreement between Vertex and a third party for the conduct of research activities, under which that third party does not then (or by subsequent agreement with such third party) receive any license rights to, or compensation with respect to the development or sale of, any pharmaceutical product that has CFTR modulation as its principal mode of action, shall not be deemed a Third Party Agreement for the purposes of the foregoing restriction. The foregoing provisions of this Section 3 shall not apply to any Third Party Agreement relating to a New Product that is a Corrector from and after the date upon which CFFT exercises its termination rights under section 10.5.2 of the Existing Agreement (as amended pursuant to this Amendment No. 1). In the event of an Interruption under Section 10.6.2 of the Existing Agreement with respect to either Potentiator or Corrector research programs, Vertex shall not enter into any agreement

with a third party for commercial purposes, for a period of [***] after such Interruption, relating to the program to which the Interruption related.

4. Budget and Funding.

From and after the Effective Date of this Amendment, the following provisions shall apply to any incremental funding for Corrector research in 2005, and to the budget and funding for all Corrector research thereafter under the Research Plan, in lieu of the provisions in Sections 4.1, 4.2 and 4.3 of the Existing Agreement.

4.1. The initial budget for incremental funding of the Corrector Research Program, relating to discovery, optimization and IND-enabling activities for Corrector Compounds, is attached hereto as Exhibit 4.1 (the "Initial Corrector Budget"). The Initial Corrector Budget includes only amounts that are incremental to the funding currently provided for Corrector research in the "Alternative Program" under the Current Budget. Any material revisions to the Initial Corrector Budget which would result in an increase in total funding for the Corrector Research Program beyond the amount provided under this Amendment will require the prior approval of CFFT. Any other adjustments to the Initial Corrector Budget may be undertaken by Vertex with prior notice to, but without prior approval from, CFFT. Vertex will provide CFFT with [***] reports within [***] showing expenses incurred under the Corrector Research Program during the quarter just ended against budgeted expenses for that quarter. For [***], the report will cover the period from the Effective Date of this Amendment through the end of that quarter.

4.2. CFFT will fund [***] of the Initial Corrector Budget and Vertex will fund [***] of the Initial Corrector Budget. Based on the approved Initial Corrector Budget of [***], CFFT will make the payments to Vertex specified below during the specified periods.

	INITIAL CORRECTOR BUDGET (millions $)	
Research Period	***Aggregate Budget Amount***	***CFFT Financial Commitment***
January 1, 2006 – December 31, 2006	[***]	[***]
January 1, 2007 – March 31, 2008	[***]	[***]

Payments due under the Initial Corrector Budget on account of internal FTEs shall be made by CFFT [***]. Payments due under the Initial Corrector Budget on account of external costs shall be made by CFFT to Vertex [***] within [***] following [***]. All payments shall be made without deduction for withholding or similar taxes in United States dollars to the credit of such bank account as may be designated in writing to CFFT. Any payments which fall due on a date that is a legal holiday in The Commonwealth of Massachusetts may be made on the next following day that is not a legal holiday in The Commonwealth. On or before January 31 of 2006, 2007, 2008 and 2009, Vertex will provide CFFT with an accounting of all internal FTE costs and external Research costs (including documentary evidence of such external costs) incurred under the Research Program during the most recently concluded calendar year. Internal FTE costs will be calculated at an annual rate of [***] per FTE.

4.3. If CFFT's contribution for any reporting period is in excess of its agreed portion of the total expense incurred by Vertex (internal and external) for the Corrector Research Program for that period, the excess amount will be carried over and applied as a credit

against CFFT's required contribution in future periods, except that any aggregate excess contributions provided by CFFT as of the end of the Research Program Term will be refunded to CFFT within [***] thereafter. To the extent not inconsistent with the provisions of this Amendment, the provisions of Section 4.5 will apply to the Corrector Research Program.

4.4. Vertex will dedicate a minimum average of [***] FTE scientists (on an annualized basis) to the Corrector Research Program during its term, [***].

5. Royalties Outside the Field

Section 5.3.2 of the Existing Agreement is amended as follows:

"5.3.2 Net Sales outside the Field. Vertex shall pay CFFT a royalty of [***]."

[Signature Page Follows]

IN WITNESS WHEREOF, the Parties hereto have executed this Agreement the day and year first above written.

VERTEX PHARMACEUTICALS INCORPORATED	CYSTIC FIBROSIS FOUNDATION THERAPEUTICS, INCORPORATED
By: /s/ Kenneth S. Boger	By: /s/ Robert J. Beall, Ph.D.
Title: Senior Vice President and General Counsel	Title: President and Chief Executive Officer

Exhibit 1.2
Corrector Research Plan

[***]

Exhibit 1.3
Current Budget

[***]

Exhibit 4.1
Initial Corrector Budget

[***]

Exhibit 10.3

Execution Copy

Certain confidential information contained in this document, marked by [***], has been omitted because it is not material and would likely cause competitive harm to Vertex Pharmaceuticals Incorporated if publicly disclosed.

AMENDMENT NO. 5 to
RESEARCH, DEVELOPMENT AND COMMERCIALIZATION AGREEMENT,
DATED MAY 24, 2004, by and between VERTEX PHARMACEUTICALS INCORPORATED and CYSTIC FIBROSIS FOUNDATION THERAPEUTICS INCORPORATED

This Amendment No. 5 (the "Fifth Amendment") is made effective as of April 1, 2011 (the "Effective Date") by and between Vertex Pharmaceuticals Incorporated, a Massachusetts corporation with its principal offices at 130 Waverly Street, Cambridge, Massachusetts 02139-4242 ("Vertex"), and Cystic Fibrosis Foundation Therapeutics Incorporated, a Delaware corporation with its principal offices at 6931 Arlington Road, Bethesda, Maryland 20814 ("CFFT").

This Fifth Amendment amends the Research, Development and Commercialization Agreement, dated May 24, 2004, by and between Vertex and CFFT (the "Original Agreement"), as amended by Amendment No. 1 to the Original Agreement, dated January 6, 2006 (the "First Amendment"), Amendment No. 2 dated January 1, 2006 (the "Second Amendment"), Amendment No. 3 dated November 20, 2006 (the "Third Amendment"), and Amendment No. 4 dated August 20, 2007 (the "Fourth Amendment"). Any reference herein to the "Original Agreement, as amended", refers to the Original Agreement and all amendments, excluding this Fifth Amendment, unless the context otherwise requires. Vertex and CFFT are referred to herein individually as a "Party" and collectively as the "Parties."

Background

In 1998, CFFT made an award to Aurora Biosciences Corporation ("Aurora") to conduct a feasibility study using high throughput screening for cystic fibrosis targets. On May 19, 2000, CFFT selected and provided support for Aurora to conduct high throughput screening with

respect to the cystic fibrosis transmembrane conductance regulator ("CFTR") target identified by CFFT. From that time until March 31, 2008 (the "Original Research Term"), Aurora, and then after its merger into Vertex, Vertex, conducted a research program with CFFT's support aimed at identification and design of "Potentiator" and "Corrector" compounds, both of which are directed as a principal mode of therapeutic action at modulation of the biological effect of CFTR in different ways and with different anticipated results.

On May 24, 2004, the Parties executed the Original Agreement. The Original Agreement contemplated that during the course of the research program, Vertex, with CFFT's agreement, would select either the Potentiator or the Corrector approach as its Primary Program (as defined in the Original Agreement, as amended), to which a majority of resources under the research program would be directed, and the other approach would be designated as an Alternative Program (as defined in the Original Agreement, as amended), to which the balance of resources would be directed.

In 2005, with the concurrence of CFFT, Vertex selected the Potentiator approach as the Primary Program, and designated a certain Potentiator, VX-770, as a Development Candidate under the terms of the Original Agreement, as amended. On March 16, 2006, the Parties executed the Second Amendment, which provided for funding for the accelerated development of Potentiator Compounds. On November 20, 2006, the Parties executed the Third Amendment, which allocated on-going CFFT funding to the Vertex Potentiator Back-up Program.

To further the discovery of Corrector Compounds of significant potential value as therapeutics, on January 6, 2006, the Parties executed the First Amendment, which provided, among other things, for continued funding for research relating to Corrector Compounds. On

August 20, 2007, the Parties executed the Fourth Amendment, which re-allocated certain of the Corrector Research Program funding in order to support accelerated preclinical development of the Corrector Development Candidate VX-809. Upon termination of the Original Research Term, the Original Agreement, as amended, expired pursuant to Section 10.1, and certain provisions, set forth in Section 10.4 of the Original Agreement, as amended, survived.

As of the date of this Fifth Amendment, Vertex is continuing the clinical development of the Potentiator VX-770, the Corrector VX-809, and a combination regimen of both VX-770 and VX-809. Vertex also is developing the Corrector VX-661, which was discovered during the Original Research Term, and intends to identify VX-661 as a Development Candidate in accordance with Section 3.1 of the Original Agreement, as amended. VX-809 and VX-661, together with any additional Correctors discovered by Vertex during the Original Research Term are referred to in this Fifth Amendment as "First Generation Correctors."

In furtherance of its charitable purpose to cure and/or mitigate the effects of cystic fibrosis, CFFT intends to provide the additional funding specified in this Fifth Amendment for the research and development of Correctors for cystic fibrosis. This Fifth Amendment sets forth the Parties' agreement with respect to such (a) additional funding from CFFT to support clinical development of VX-661, (b) additional funding from CFFT for a new research term to conduct further research relating to discovery of additional Corrector Compounds, such newly-discovered compounds to be referred to herein as "Second Generation Correctors," and (c) clinical development of Second Generation Corrector(s), in accordance with the Original Agreement, as amended, together with this Fifth Amendment; and to amend the Original Agreement, as amended, accordingly.

Capitalized terms not otherwise defined in this Fifth Amendment shall have the meaning ascribed to them in the Original Agreement, as amended. Terms used in this Fifth Amendment to refer to a Drug Product which is prepared from a specific Drug Product Candidate or Category of Drug Candidate, for example, Drug Product prepared from VX-770 or Second Generation Correctors, shall be referred to herein by identifying the Drug Product Candidate or category, such as VX-770 Drug Product or Second Generation Corrector Drug Product. If specific provisions of this Fifth Amendment are inconsistent with specific provisions of the Original Agreement, as amended, the provisions of this Fifth Amendment, with respect to the subject matter of this Fifth Amendment, shall control. Otherwise the Original Agreement, as amended, to the extent its provisions have survived the termination of the Original Research Term, shall continue to be applicable.

Amendment

In consideration of the mutual covenants set forth in this Fifth Amendment, and other good and valuable consideration, the receipt of which is hereby acknowledged, the Parties agree as follows:

Section 1. <u>First Generation Corrector Development and Development Funding</u>.

1.1 VX-661 as Drug Product Candidate. The Parties agree that VX-661 will be designated as a Development Candidate, and that Vertex has commenced a Development Program with respect thereto. The Corrector JDC in place for VX-809 development shall serve as the JDC for VX-661.

1.2 Development Plan. The Corrector JDC shall review implementation of the overall development plan for VX-661. The development plan shall describe the proposed

clinical trial activities, non-clinical development activities, and supply and manufacturing activities for VX-661. Any change in the development plan for VX-661 will be reviewed [***].

1.3 Budget and Funding. Exhibit 1.3(a) contains a summary that sets forth certain estimated costs of the proposed VX-661 development activities for the period through the completion of the [***]. CFFT agrees to fund up to [***]. The proposed activities and budget[***] for the VX-661 development program may be revised by the Corrector JDC from time to time, provided that the amount of [***] to be reimbursed by CFFT shall not be increased without the written consent of CFFT.

[***]. On the Effective Date CFFT shall pay Vertex [***] (of the total [***] to be funded) [***]. For purposes of this Fifth Amendment, Vertex will provide CFFT with [***] reports within [***] (commencing with the second calendar quarter of 2011) showing expenses incurred and invoices received under the VX-661 development program during the quarter just ended against budgeted expenses for that quarter (which, for the second calendar quarter of 2011, shall include any expenses for activities undertaken during the first calendar quarter of 2011 that were invoiced [***]). Payments due for [***] shall be made by CFFT to Vertex [***] within [***] following receipt by CFFT of an invoice for such VX-661 External Development Costs accompanied by usual and customary documentation of such costs, including copies of Third Party invoices supporting such costs and evidence that the costs relate to the VX-661 development program. All payments shall be made without deduction for withholding or similar taxes in United States dollars to the credit of such bank account as may be designated in writing to CFFT. Any payments that fall due on a date that is a legal holiday in The Commonwealth of

Massachusetts may be made on the next following day that is not a legal holiday in The Commonwealth.

If the development program for VX-661 is discontinued or the VX-661 External Development Costs incurred to advance VX-661 through completion of the [***] are less than [***], CFFT agrees, subject to termination rights by CFFT in accordance with this Fifth Amendment, that any funds remaining from the original [***] funding commitment hereunder will be available to reimburse Vertex for the actual external development costs related to continued development of First Generation Correctors, on the invoicing and payment terms set forth in this Section 1.3 as if it were with respect to VX-661 External Development Costs.

At its sole discretion, CFFT shall have the right to terminate its funding obligation under this Section 1.3, effective upon written notice provided to Vertex [***]. Upon any such funding termination: (a) CFFT shall be responsible to fund only those costs incurred for activities initiated by Vertex and for which Vertex has incurred non-terminable obligations to a Third Party prior to the funding termination; (b) the royalty rates for Net Sales of VX-661 Drug Product and VX-809 Drug Product set forth in Section 5.3.1(b), [***], as illustrated by the examples set forth in Exhibit 1.3(c); and (c) Section 10.6 of the Original Agreement, as amended by this Fifth Amendment, shall terminate and CFFT shall have none of the rights set forth in such Section 10.6.

Section 2. Second Generation Corrector Research and Development Program Funding.

2.1 Research Plan and Program. Beginning on the Effective Date, the "Research Program" will refer to research undertaken under the terms of this Fifth Amendment pursuant to the research plan for Second Generation Corrector Research (which shall be the "Research Plan"

referred to in Section 2.4 of the Original Agreement, as amended, and the research conducted under the Research Plan shall be the "Research Program" under the Original Agreement, as amended, and under this Fifth Amendment), an initial version of which is attached hereto as Exhibit 2.1 (the "Second Generation Corrector Research Plan"). The "Research Term" shall begin on the Effective Date and end on the Research Termination Date (as defined in this Fifth Amendment).

2.2 Budget; Funding Obligation; Payments. The budget for the Research Program [***] (as defined in this Fifth Amendment) is attached hereto as Exhibit 2.2(a) (as revised during the term of the Research Program, the "Second Generation Corrector Research Budget"). CFFT agrees to fund up to [***] of the costs of the Research Program for Second Generation Correctors as set forth herein and in the Second Generation Corrector Research Budget, including Vertex internal costs and external costs, for research and development activities, which for purposes of this Fifth Amendment, shall include all research and development activities undertaken with respect to a Second Generation Corrector or Correctors from [***].

For purposes of this Fifth Amendment, Vertex will provide CFFT with [***] reports within [***] (commencing with the second calendar quarter of 2011) showing expenses incurred and invoices received under the Research Program during the quarter just ended against budgeted expenses for that quarter. The first such report shall be due after completion of the second calendar quarter of 2011, and will cover the period from [***] through the end of that quarter.

Payments due under the Second Generation Corrector Research Budget on account of internal FTEs shall be made by CFFT [***]. Internal FTE costs will be calculated at an annual

rate of $[***] per FTE. On the Effective Date CFFT shall pay [***] (of the total [***] to be funded), [***].

Payments due on account of external costs of the Research Program shall be made by CFFT to Vertex [***] within [***] days following receipt by CFFT of an invoice for such external costs accompanied by usual and customary documentation of such costs, including copies of Third Party invoices supporting such costs and evidence that the costs relate to the Research Program. For all non-United States Dollar expenditures, documentation of the currency conversion rate shall be provided. Each invoice shall also include a quarterly “true-up” of internal FTEs. Accounting and invoicing for expenditures for the Research Program shall be maintained and provided separately from those for the VX-661 development program.

On or before January 31 of each year during the Research Term, Vertex will provide CFFT with an accounting of all internal FTE costs and external research costs (including documentary evidence of external FTEs and other costs, which shall include a yearly FTE true-up) incurred under the Research Program during the most recently concluded calendar year. If CFFT’s funding for any reporting period is in excess of the amount set forth in the Second Generation Corrector Research Budget for that period, the excess amount will be carried over and applied as a credit against CFFT’s required funding in future periods, subject to the limit of CFFT’s funding obligation set forth above. If CFFT’s funding for any reporting period is less than the amount set forth in the Second Generation Corrector Research Budget for that period, the balance remaining will be carried over and added to the budgeted amount for the next reporting period. If there is any unexpended funding provided by CFFT at the termination of the Research Program, it shall be promptly returned to CFFT. To the extent not inconsistent with the

provisions of this Amendment, the provisions of Section 4.5 of the Original Agreement, as amended, will apply to the Research Program.

CFFT agrees to fund up to [***] of external development costs for Second Generation Correctors, as set forth in the estimated development budget in Exhibit 2.2(b), which for purposes of this Fifth Amendment shall include all costs and expenses invoiced by Third Parties, whether for goods or services, associated with the development of a Second Generation Corrector or Correctors at any time after an IND is opened for such Second Generation Corrector or Correctors. Vertex will provide CFFT with [***] reports within [***] showing external expenses incurred in development of Second Generation Corrector(s) during the quarter just ended against budgeted expenses for that quarter. Payments due for such expenses shall be made by CFFT to Vertex [***] within [***] days following receipt by CFFT of an invoice for such expenses accompanied by usual and customary documentation of such costs.

For illustrative purposes, Exhibit 2.2(c) shows the total combined costs to be funded by CFFT for (i) the Second Generation Corrector Research Program (as set forth in greater detail in Exhibit 2.2(a)) and (ii) the estimated external development costs for the clinical development of Second Generation Correctors (as set forth in greater detail in Exhibit 2.2(b)).

All payments made by CFFT under this Section 2.2 shall be made without deduction for withholding or similar taxes in United States dollars to the credit of such bank account as may be designated in writing to CFFT. Any payments that fall due on a date that is a legal holiday in The Commonwealth of Massachusetts may be made on the next following day that is not a legal holiday in The Commonwealth.

2.3 Conduct of Research. Vertex will dedicate a minimum average of [***] FTE scientists (on an annualized basis) to the Research Program during its term[***].

2.4 Termination of Research and/or Development Funding. The Research Term shall end on [***], unless the Research Program is otherwise extended or terminated in accordance with this Fifth Amendment (the "Research Termination Date"). After the Research Termination Date, CFFT shall be responsible to fund only those expenses that do not exceed the Second Generation Corrector Research Budget for activities initiated by Vertex prior to the Research Termination Date and for which Vertex has either incurred non-terminable obligations to a Third Party, or which require a minimal amount of time and/or resources to complete after the Research Termination Date.

CFFT may in its sole discretion upon [***] notice provided any time after the first anniversary of the Effective Date terminate its funding obligation for the Research Program. In addition, at its sole discretion, CFFT shall have the right to terminate its funding obligations for external development costs for Second Generation Correctors [***]. Upon any such funding termination: (a) CFFT shall be responsible to fund those internal costs incurred for research activities, if any, initiated by Vertex prior to the termination and/or external costs for activities initiated by Vertex and for which Vertex has incurred non-terminable obligations to a Third Party prior to the funding termination; (b) the royalty rates set forth in Sections 5.3.1(c)[***] shall be reduced [***]; and (c) Section 10.6 of the Original Agreement, as amended by this Fifth Amendment, shall terminate and CFFT shall have none of the rights set forth in such Section 10.6.

Section 3. Amendments to Royalty Rates.

3.1 Royalty Rates. Section 5.3.1 of the Original Agreement, as amended, is deleted, and in its place the following shall be inserted:

"**5.3.1 Net Sales in the Field**

(a) Vertex shall pay to CFFT the following royalties on Net Sales [***]:

- [***]
- [***]
- [***];

[***].

(b) [***]:

- [***]
- [***].

[***].

(c) [***]:

- [***]
- [***].

[***].

3.2 Section 5.3.2 of the Original Agreement, as amended, is amended by designating the original language as subparagraph (a), and adding the following as subparagraph (b):

(b) "Vertex also shall pay [***] in two equal installments, as set forth below. [***] which would be payable in the following amounts, in each case

within [***] after the [***] in which cumulative Net Sales of Drug Products containing VX-661 or VX-809 have reached the following levels:

[***]		[***]
[***]		[***]
[***]		[***]
	[***]	[***]”

Section 4. Miscellaneous Provisions.

Section 4.1 Interruption. Section 10.6 of the Original Agreement, as amended, shall be deleted in its entirety, and the following substituted therefore:

10.6 Interruption.

10.6.1 Definitions. For purposes of this Agreement, the terms defined in this Section 10.6.1 shall have the following meanings:

10.6.1.1 “Ceased”, with respect to the development of a Development Candidate, will mean that Vertex has ceased commercially reasonable development activity, in accordance with the standards of commercial reasonableness set forth in Section 3.1 of the Original Agreement, as amended, with respect to that Development Candidate for a period of twelve consecutive months.

10.6.1.2 “Follow-on” [***].

10.6.1.3 “Lead” [***].

10.6.1.4 “Permitted Reason” shall mean, with respect to any Second Generation Corrector:

(a) Vertex has not completed a clinical study of such Second Generation Corrector designed to establish so-called "proof-of-concept ("POC"), but either (i) Vertex obtained evidence that such compound is unlikely to achieve Successful POC; or (ii) such compound failed to demonstrate Successful Pre-Clinical CFTR Correction Activity; or

(b) Vertex completed clinical studies designed to establish POC for the compound and the compound failed to achieve Successful POC.

10.6.1.5 "Successful Pre-Clinical CFTR Correction Activity" shall mean, with respect to any compound, demonstration that the compound [***]; and (b) [***]. [***].

10.6.1.6 "Successful POC" shall mean demonstration by a compound [***] of [***].

10.6.1.7 "Vertex" for the purpose of this Section 10.6 only shall mean Vertex or any of its Affiliates, licensees, sublicensees, assignees or partners.

10.6.2 Interruption; License to CFFT. If, prior to commercialization by Vertex of a Second Generation Corrector, Vertex has ceased development with respect to all Correctors (first generation and second generation), there shall be deemed to be an "Interruption." In the event of an Interruption, the following license in favor of CFFT shall become effective:

(a) if Vertex is not commercializing any First Generation Corrector at the time of the Interruption, then CFFT shall have an

irrevocable, exclusive worldwide license [***], with the right to sublicense, under the Vertex CF Technology, to develop, manufacture, have manufactured, use, sell, offer to sell and import those Compounds in the Field; or

(b) if Vertex is commercializing a First Generation Corrector at the time of the Interruption, then CFFT shall have an irrevocable, exclusive worldwide license [***], with the right to sublicense, under the Vertex CF Technology, to develop, manufacture, have manufactured, use, sell, offer to sell and import those Compounds in the Field;

provided, however, the license under this Section 10.6.2(b) shall not encompass any Corrector for which Vertex ceased Development for a Permitted Reason.

[***].

10.6.3. Termination of Interruption Rights. This Section 10.6 shall terminate, and CFFT shall have no further rights hereunder, immediately upon the First Commercial Sale of a Second Generation Corrector Drug Product, and as otherwise provided in this Fifth Amendment.

Section 4.2 Termination upon Vertex Change-in-Control. CFFT shall have the right, exercisable in its sole discretion, to terminate all of its funding obligations under this Fifth Amendment upon a Change-in-Control of Vertex, subject to CFFT's obligations to fund previously committed amounts in accordance with the provisions of this Fifth Amendment. In the event of any such termination prior to an Interruption (as defined above), the provisions of Section 10.6 shall be terminated and have no further force or effect. For purposes of this Section

4.2, a “Change-in-Control” shall mean that any “person” or “group,” as such terms are used in Sections 13(d) and 14(d)(2) of the Securities Exchange Act of 1934 (the “Act”), becomes a beneficial owner, as such term is used in Rule 13d-3 promulgated under the Act, of securities of Vertex representing more than [***] of the combined voting power of the outstanding securities of Vertex having the right to vote in the election of directors; or (b) all or substantially all the business or assets of Vertex are sold or disposed of, or Vertex or a subsidiary of Vertex combines with another company pursuant to a merger, consolidation, or other similar transaction, other than (i) a transaction solely for the purpose of reincorporating Vertex or one of its subsidiaries in a different jurisdiction or recapitalizing or reclassifying Vertex’s stock; or (ii) a merger or consolidation in which the shareholders of Vertex immediately prior to such merger or consolidation continue to own at least a majority of the outstanding voting securities of Vertex or the surviving entity immediately after the merger or consolidation.

Section 4.3 Publicity. The provisions of Section 6.3 of the Original Agreement shall apply to this Fifth Amendment as if it were being entered into as part of the Original Agreement, as amended. The Parties will agree on the timing and content of a press release relating to this Fifth Amendment.

Section 4.4 Third Party Testing.

Upon receipt of a Testing Request (as defined below) from CFFT, Vertex will supply to an Agreed Lab (as defined below) reasonably adequate quantities of the Lead and/or the Follow-on (as such terms are defined in Section 10.6.1, as revised by this Fifth Amendment), as necessary to enable the Agreed Lab to conduct in vitro testing of the efficacy and potency of either or both of such Compounds [***] (for purposes of this Section 4.4, the “Vertex Assay”).

All such testing will be undertaken at the expense of CFFT in addition to any funding otherwise provided hereunder.

An "Agreed Lab" is a commercial testing laboratory unaffiliated with either CFFT or Vertex and reasonably acceptable to both, which (a) specializes in rendering services to the pharmaceutical industry and has nationally recognized expertise in the testing of pharmaceutical compounds; (b) has a superior reputation for integrity in dealing with the proprietary information of others and would be free of any real or apparent conflict of interest in performing the services which are the subject of this Section 4.4; and (c) is bound by the terms of a confidentiality agreement with Vertex which is customary in form and content, which covers the testing contemplated by this Section 4.4, and which permits the Agreed Lab to report directly to CFFT and Vertex the results which it obtains with respect to efficacy and potency of the Lead and/or Follow-on. The Agreed Lab will adhere strictly to testing protocol approved by Vertex and shall be required to report all testing results directly to both CFFT and Vertex. [***].

A "Testing Request" is a written request relating to the testing of either the Lead or Follow-on, which is delivered by CFFT to Vertex within the [***] period beginning upon receipt by CFFT of notification from Vertex of its identification of such Compound as Development Candidate.

Vertex and CFFT acknowledge that the use of a commercially available assay equivalent to the Vertex Assay for the testing of the Lead and Follow-on may yield results which are less robust than the results obtained by use of the Vertex Assay. The Parties also acknowledge that the transfer of the Vertex Assay to an Agreed Lab may be difficult, and the results less than satisfactory, without a commitment of substantial time and effort by Vertex which, if undertaken,

may adversely impact the progress of the Research Program. Therefore, the parties agree that Vertex's responsibility for the testing provided under this Section 4.4 shall be limited as follows: (a) Vertex will cooperate with CFFT in the selection of an Agreed Lab , as may be requested by CFFT, and thereafter will assist in the determination whether commercially available assays conducted by the Agreed Lab are likely to provide satisfactory results; (b) Vertex will provide the Agreed Lab with requisite amounts of each Compound, in connection with Testing Requests from CFFT as provided above, out of any supplies which Vertex may have on hand; (c) Vertex will provide telephone consulting to appropriate representatives of the Agreed Lab concerning applicable assay methodology; (d) if the parties conclude that conventional testing will not yield adequate results, and upon the written request of CFFT rendered with due regard to the [***] to establish an assay based on proprietary protocols from Vertex, Vertex will provide the Vertex Assay to the Agreed Lab sufficiently in advance of any testing provided for in this Section 4.4 to accommodate such testing, under provisions of confidentiality, restricted access and non-use (for other than testing hereunder), and will ensure that appropriate Vertex representatives are available by telephone from time to time to answer questions and otherwise assist the Agreed Lab representatives in their efforts to establish the Vertex Assay. Vertex shall in no event be responsible for any failure by the Agreed Lab to establish an effective assay using Vertex's protocols, nor shall any time periods provided herein for action by CFFT be extended by reason of any such failure.

Section 5. Original Agreement Ratified; Certain Expired Provisions Reinstated.

In all other respects, the Original Agreement, as amended, to the extent unexpired, is hereby ratified and confirmed. The following provisions, which expired under the Original Agreement, as amended, as a result of the conclusion of the Original Research Term, are hereby reinstated effective on the Effective Date solely for the purposes and to the extent applicable to the subjects addressed in this Fifth Amendment: 2.4.1, 2.6, 2.7, 2.8, 10.1, 10.4, and Article XIII, and all other provisions that have expired as of the Effective Date, whether set forth in the Original Agreement or any amendment to the Original Agreement, shall have no force or effect as a result of the execution of this Fifth Amendment.

[Signature Page Follows]

In witness whereof, the Parties hereto have executed this Agreement as of the day and year first above written.

VERTEX PHARMACEUTICALS, INCORPORATED	**CYSTIC FIBROSIS FOUNDATION THERAPEUTICS, INCORPORATED**
By: /s/ Matthew W. Emmens	By: /s/ Robert J. Beall
Title: Chairman, CEO & President	Title: President & CEO
Date: April 4, 2011	Date: April 4, 2011

Exhibit 1.3(a)

[***]

Exhibit 1.3(b)

[***]

Exhibit 1.3(c)

[***]

Exhibit 2.1

Second Generation Corrector Research Plan

[***]

Exhibit 2.2(a)

[***]

Exhibit 2.2(b)

[***]

Exhibit 2.2(c)

[***]

Exhibit 2.4

[***]

Exhibit 10.4

Certain confidential information contained in this document, marked by [***], has been omitted because it is not material and would likely cause competitive harm to Vertex Pharmaceuticals Incorporated if publicly disclosed.

Amendment No. 7

Research, Development and Commercialization Agreement,

Dated May 24, 2004 by and between

Vertex Pharmaceuticals Incorporated

And

Cystic Fibrosis Foundation Therapeutics Incorporated

Whereas, Cystic Fibrosis Foundation Therapeutics Incorporated, a Delaware corporation ("CFFT"), and Vertex Pharmaceuticals Incorporated, a Massachusetts corporation ("Vertex"), are parties to that certain Research, Development and Commercialization Agreement dated May 24, 2004, as previously amended by Amendment No. 1 thereto dated January 6, 2006, Amendment No. 2 thereto dated as of January 1, 2006, Amendment No. 3 thereto dated November 20, 2006, Amendment No. 4 thereto dated August 20, 2007, Amendment No. 5 thereto dated as of April 1, 2011, and Amendment No. 6 thereto dated March 29, 2012 (collectively, the "Agreement"). Capitalized terms used herein without specific definition shall have the meanings set forth in the Agreement.

Whereas, CFFT and Vertex have been engaged in discussions relating to several aspects of the Agreement, including (a) the appropriate means for allocating Net Sales of Combination Products among the components thereof for purposes of determining royalties under the Agreement, (b) the application of certain royalty provisions of the Agreement to Net Sales of certain Drug Products, and (c) the rights and obligations of the parties with respect to certain chemical compounds that Vertex represented were first synthesized and/or tested after February 28, 2014. The parties have reached agreement on the matters under discussion, and wish to memorialize such agreement pursuant to this Amendment No. 7 executed on October 13, 2016 (the "Execution Date").

Whereas, CFFT entered into an agreement with RPI Finance Trust ("RP") pursuant to which it has assigned and transferred to RP certain of its rights under the Agreement, including its right to receive certain royalty payments from Vertex under the Agreement. Solely for purposes of Sections 6, 8, 9, 10, 11, 12.1 and 13 of this Amendment No. 7, and as a material inducement for Vertex to enter into this Amendment No. 7, RP is a signatory to this Amendment No. 7.

Whereas, nothing in this Amendment No. 7. is intended to alter CFFT's original charitable purpose for entering into the Agreement.

Whereas, in connection with this Amendment No. 7, on or about the date hereof, the Cystic Fibrosis Foundation and Vertex are entering into a Data License Agreement.

Now, therefore, in consideration of the mutual covenants set forth in this Amendment No. 7, and other good and valuable consideration, the receipt and sufficiency of which are hereby

acknowledged, effective as of September 1, 2016 (the "Amendment No. 7 Effective Date"), the parties agree as follows:

1. Definitions.

1.1 Additional Definitions. The following defined terms shall be added to Section 1 of the Agreement in alphabetical order:

(a) "Additional Compound" means each chemical compound listed on Exhibit 2016-A and [***]. Vertex represents that each such compound was first synthesized and/or tested by or under the direction of Vertex on or after March 1, 2014 and on or prior to August 31, 2016 (the "Additional Term") in connection with Vertex's research and development of Correctors for the treatment of cystic fibrosis. A list of the Additional Compounds (other than [***]) is set forth in Exhibit 2016-A. Each such compound is listed by its VRT number, a designation given to each unique chemical structure by Vertex. Any compound first synthesized and/or tested by Vertex after the Additional Term that is assigned its own VRT number consistent with Vertex's historical practices, including any such compound derived from any Additional Compound, shall not be an Additional Compound for purposes of this Agreement unless such compound is [***] of a compound set forth in Exhibit 2016-A.

(b) "Additional Product" means a pharmaceutical product or formulation comprising, in whole or in part, an Additional Compound. For clarity, in no event will an Additional Product be deemed to be a Drug Product.

(c) "Corrector" means any compound which as its principal mode of therapeutic action, modulates the biological effect of CFTR by increasing the amount of functional del508 CFTR present at the apical cell membrane.

(d) "CF Spend" means, with respect to a given period, the aggregate (i) [***] (ii) [***] in each case incurred by [***]during such period in connection with [***], including, without limitation, [***].

(e) "FTE Rate" means [***]; *provided* that such rate will increase or decrease on [***]. The FTE Rate includes (i) all wages and salaries, employee benefits, bonus, travel and entertainment, supplies and other direct expenses and (ii) indirect allocations, including all general and administrative expenses, human resources, finance, occupancy and depreciation.

(f) A [***] of an Additional Compound shall mean a compound that (A) is [***]such Additional Compound as evidenced by [***], and (B) at [***], such Additional Compound represents in [***] of the compound and its [***].

1.2 Net Sales. Section 1.25 of the Agreement is deleted in its entirety and replaced with the following:

1.25 "Net Sales" with respect to any Drug Product or Additional Product shall mean the gross amount invoiced by Vertex and any Vertex Affiliate, licensee, sublicensee, assignee or transferee for that Drug Product or Additional Product sold in bona fide, arms-length transactions to Third Parties for use in the Field, less (i) quantity and/or cash discounts from the gross invoice price which are actually allowed or taken; (ii) freight, postage and insurance included in the invoice price; (iii) amounts repaid or credited by reasons of rejections or return of goods or

because of retroactive price reductions specifically identifiable to the Drug Product or Additional Product; (iv) amounts payable resulting from government (or agency thereof) mandated rebate programs; (v) third-party rebates to the extent actually allowed; (vi) invoiced customs duties and sales taxes (excluding income, value-added and similar taxes), if any, actually paid and directly related to the sale that are not reimbursed by the buyer; and (vii) any other specifically identifiable amounts included in the Drug Product's or Additional Product's gross invoice price that should be credited for reasons substantially equivalent to those listed above; all as determined in accordance with Vertex's usual and customary accounting methods, which are in accordance with generally accepted accounting principles.

1.25.1 In the case of any sale or other disposal of a Drug Product or Additional Product between or among Vertex and its Affiliates, licensees, sublicensees, assignees or transferees 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;

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

1.25.3 In the case of any sale or other disposal for value, such as barter or counter-trade, of any Drug Product or Additional 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 [***] or the [***] of the Drug Product or Additional Product in the country of sale or disposal;

1.25.4. If the Drug Product or Additional Product is sold in finished dosage form with one or more other active pharmaceutical ingredients ("Combination Product"), which may include Drug Product(s), Additional Product(s) and other active pharmaceutical ingredients that are not Drug Product(s) or Additional Product(s) (each such other ingredient, a "Non-royalty Bearing Component"), the Net Sales of each Drug Product or Additional Product, for the purposes of determining royalty payments under this Agreement, shall be determined by multiplying the Net Sales of the Combination Product by the fraction 1/n, where "n" is the total number of active ingredients (including the Drug Product(s), Additional Product(s) and Non-royalty Bearing Component(s)) in such Combination Product. For example, if a Combination Product consists of one Drug Product, one Additional Product and one Non-royalty Bearing Component, then Net Sales of the Combination Product shall be allocated one-third to each of the three (3) active pharmaceutical ingredients in such Combination Product (*i.e.* 1/3rd to the Drug Product, 1/3rd to the Additional Product and 1/3rd to the Non-royalty Bearing Component). For the avoidance of doubt, no royalty will be paid to CFFT under this Agreement with respect to any portion of Net Sales allocated to a Non-royalty Bearing Component as provided above.

2. Royalties. Section 5.3.1 of the Agreement is deleted in its entirety and replaced with the following:

5.3.1 Net Sales in the Field.

(a) Original Drug Products. Vertex shall pay to CFFT the following royalties on aggregate Net Sales of [***] Drug Product, First [***]) and Second Generation Corrector Drug Products (together, the "Original Drug Products") in the Field:

i. [***]Net Sales of Original Drug Products in the Field that are [***];

ii. [***]Net Sales of Original Drug Products in the Field [***].

The foregoing rates shall be effective as of [***]. All royalties payable on the Original Drug Products for the period from [***] through [***] shall be payable in accordance with the methodology for calculating royalties on Original Drug Products contained in the royalty reports delivered by Vertex to CFFT for the first and second calendar quarters of 2016.

(b) [Intentionally Omitted].

(c) [Intentionally Omitted].

(d) Additional Products. Vertex shall pay to CFFT the following royalties on Net Sales of Additional Products in the Field:

i. For Additional Products containing Additional Compounds first synthesized and/or tested by or under the direction of Vertex during the period commencing on [***]and ending on and including [***]: [***] of annual Net Sales of such Additional Product in the Field;

ii. For Additional Products containing Additional Compounds first synthesized and/or tested by or under the direction of Vertex during the period commencing on [***] and ending on and including [***]: [***] of annual Net Sales of such Additional Products in the Field; and

iii. For Additional Products containing Additional Compounds first synthesized and/or tested by or under the direction of Vertex during the period commencing on [***]and ending on and including [***]: [***] of annual Net Sales of such Additional Products in the Field.

(e) Royalties Payable Once. Royalties on Net Sales of any Drug Product and Additional Product will be payable only once and if there are Drug Products and/or Additional Products in a Combination Product, royalties shall only be paid once for each Drug Product or Additional Product, as applicable, with respect to the portion of the Net Sales of the Combination Product that is allocated to such Drug Product or Additional Product as provided in Section 1.25.4.

(f) Application of Royalty Provisions to ORKAMBI Net Sales. For purposes of clarity, (1) ORKAMBI is a Combination Product consisting of two Original Drug Products, VX-770 Drug Product and VX-809 Drug Product, and (2) accordingly, royalties on Net Sales of ORKAMBI shall be payable as follows: under the Combination Product principles set forth in Section 1.25.4, 1/n, where n=2, or fifty percent (50%) of Net Sales of ORKAMBI shall be allocated to each of the VX-770 Drug Product and the VX-809 Drug Product. An illustrative example of the calculation of royalties on Net Sales of ORKAMBI and KALYDECO (*i.e.*, VX-770 Drug Product sold not as a Combination Product) is attached hereto as Exhibit 2016-B.

(g) Additional Example. For purposes of clarity, if Vertex were to sell a Combination Product consisting of VX-770 Drug Product, an Additional Product described in Section 5.3.1(d)(i) and an Additional Product described in Section 5.3.1(d)(ii), royalties on Net Sales of such Combination Product shall be payable as follows: under the Combination Product principles

set forth in Section 1.25.4, one third (1/3) of Net Sales of such Combination Product shall be allocated to each of the VX-770 Drug Product and the first and second Additional Products, and royalties on the portion of Net Sales allocated to the VX-770 Drug Product would be payable under Section 5.3.1(a), royalties on the portion of Net Sales allocated to the Additional Product described in Section 5.3.1(d)(i) would be payable under Section 5.3.1(d)(i) and royalties on the portion of Net Sales allocated to the Additional Product described in Section 5.3.1(d)(ii) would be payable under Section 5.3.1(d)(ii). An illustrative example of such calculation is attached hereto as Exhibit 2016-C.

(h) Calendar Year. For the avoidance of doubt, each calculation of annual Net Sales shall be calculated on the basis of a calendar year from January 1 of such calendar year through December 31 of such calendar year.

(i) Third Party Compounds. For purposes of this Agreement, Compounds and Additional Compounds shall not include any chemical compound as to which rights are or were acquired by Vertex or any of its Affiliates from *bona fide* Third Party entities after [***], whether by merger, acquisition of shares, asset acquisition, license or other means of conveyance whether or not Vertex or its Affiliates or any third party acting under Vertex's or its Affiliate's direction evaluated such compound prior to [***]. For example, [***].

(j) Reporting on Additional Product. The reporting and payment provisions set forth in Section 5.4 of the Agreement shall apply to Additional Products (substituting "Additional Product" for "Drug Product" therein).

3. Dispute Resolution. Section 12.2 of the Agreement is deleted in its entirety and replaced with the following:

12.2 Dispute Resolution Process.

(a) In the event of any dispute, controversy or claim arising out of or relating to this Agreement, or the rights and obligations of Vertex, CFFT and RP in relation thereto, Vertex, CFFT and RP, each on its own behalf and on behalf of its predecessors, successors, assigns, officers, directors, employees, trustees, parents, subsidiaries and Affiliates, shall, before initiating any action under Section 12.2(b), refer the relevant dispute, controversy or claim to the Chief Executive Officers of Vertex, CFFT and (in the event RP has an interest in such dispute, controversy or claim) RP, who shall, as soon as practicable, attempt in good faith to resolve the dispute, controversy or claim. If such dispute, controversy or claim is not resolved within [***] after the referral of the matter to the Chief Executive Officers, Vertex or CFFT (jointly with RP, if applicable) may initiate proceedings pursuant to Section 12.2(b) below.

(b) (i) Any dispute, controversy or claim arising out of or relating to this Agreement, or the breach thereof, shall be adjudicated by confidential arbitration administered by the American Arbitration Association in accordance with its Commercial Arbitration Rules (including Procedures for Large Complex Cases) and judgment on the award rendered by the arbitrators shall be final, not subject to appeal and may be entered in any court having jurisdiction thereof. The place of arbitration shall be New York, New York.

(ii) Claims shall be heard by a panel of three arbitrators. Each party shall select (or, if RP is a party to such claim, CFFT and RP shall jointly select) one

arbitrator and shall provide notice of such selection with its initial pleading. The two arbitrators selected by the parties (and RP, if applicable) shall select a third arbitrator within thirty days after the notice of the second arbitrator's selection. If the arbitrators selected by the parties (and RP, if applicable) are unable or fail to agree upon the third arbitrator, the third arbitrator shall be selected by the American Arbitration Association from its Large, Complex Commercial Case Panel. Each party (and RP, if applicable) shall bear its own costs and expenses and an equal share (with CFFT and RP jointly bearing [***], if applicable) of the arbitrators' fees and administrative fees of arbitration. The award of the arbitrators shall be accompanied by a reasoned opinion. Except as may be required by law, neither a party nor RP nor an arbitrator may disclose the existence, content, or results of any arbitration hereunder without the prior written consent of both parties (and RP, if applicable).

4. Confidentiality.

4.1 Undertaking. The phrase "During the term of this Agreement" shall be deleted from the first sentence of Section 6.1 of the Agreement.

4.2 Survival. Section 6.4 of the Agreement is deleted in its entirety and replaced with the following:

The provisions of this Article VI shall survive until the [***] of the date of expiration of all payment obligations under this Agreement.

5. Additional Exhibits. The new Exhibits 2016-A, Exhibit 2016-B and Exhibit 2016-C shall be added to and become part of the Agreement.

6. Acknowledgement Regarding Past Royalties and Drug Products and Additional Products.

6.1 CFFT and RP acknowledge and agree that no royalties in excess of the royalties already paid by Vertex to CFFT (and its assignees) are due to CFFT (or its assignees) based on Net Sales of Drug Products occurring prior to June 30, 2016.

6.2 CFFT and RP agree that subject to the definitions of Compound and Additional Compound, no chemical compound that is first synthesized and/or tested by or under the direction of Vertex after August 31, 2016 shall be considered a Compound or Additional Compound under the Agreement regardless of any such chemical compound's structural, chemical or other similarity to a chemical compound first synthesized and/or tested by or under the direction of Vertex prior to August 31, 2016.

7. Program Awards by CFFT to Vertex.

7.1 CFFT shall award Vertex a one-time, non-refundable, non-creditable sum of $75.0 million payable [***] after the Execution Date by wire transfer of immediately available funds to an account designated by Vertex for expenditures in connection with research and development efforts regarding Original Drug Products and Additional Products.

7.2 For so long as Vertex is conducting (or has a bona fide intention of conducting in the future) at least [***] to evaluate an Original Drug Product or an Additional Product, CFFT shall provide [***] awards to Vertex of [***], with the first payment due on [***], to support research and development efforts regarding Original Drug Products and

Additional Products; *provided*, *that* if Vertex and its Affiliates have collectively incurred [***] in CF Spend during the [***] period ending on the [***] (the "[***] Period"), the amount to be paid by CFFT on the applicable payment date will be reduced to an amount equal to [***] less the amount by which the aggregate amount of CFFT's awards under this Section 7.2 during such [***] Period exceed [***] of the applicable CF Spend during such [***] Period. Any negative amount will be carried forward and used to reduce any awards otherwise due hereunder. For so long as CFFT is obligated to provide Vertex with funding under this Section 7.2, at least [***] prior to the date on which each such payment is due, Vertex will provide CFFT with a high-level summary of the CF Spend during the applicable [***] Period (including the total number of FTEs and a break-out of the total amount of internal costs and out-of-pocket costs incurred), together with a certificate of an officer of Vertex certifying the accuracy of such high-level summary.

8. Release.

8.1 CFFT and RP and each of their predecessors, successors, assigns, officers, directors, employees, trustees, parents, subsidiaries and Affiliates fully, finally and forever release, relinquish, acquit and discharge Vertex and each of its predecessors, successors, assigns, officers, directors, employees, trustees, parents, subsidiaries, Affiliates, customers, suppliers and distributors (each individually a "Vertex Releasee") of and from, and covenant not to sue, not to assign to any other entity a right to sue, and not to authorize any other entity to sue any Vertex Releasee for any and all Losses (as defined below) of every name and nature, both at law and in equity, known or unknown, suspected or unsuspected, accrued or unaccrued that (a) arise out of or relate to the Agreement and (b) existed as of the Execution Date. This release shall not prevent or impair the right of CFFT or RP to bring a claim for any breach of the Agreement, as amended, arising on or after the Execution Date or for breach of a representation, warranty, or covenant made in this Amendment No. 7.

8.2 Vertex and each of its predecessors, successors, assigns, officers, directors, employees, trustees, parents, subsidiaries and Affiliates fully, finally and forever release, relinquish, acquit and discharge CFFT and RP and each of their predecessors, successors, assigns, officers, directors, employees, trustees, parents, subsidiaries, Affiliates, customers, suppliers and distributors (each individually a "CFFT Releasee" or "RP Releasee"), of and from, and covenant not to sue, not to assign to any other entity a right to sue and not to authorize any other entity to sue, any CFFT Releasee or RP Releasee for any and all Losses of every name and nature, both at law and in equity, known or unknown, suspected or unsuspected, accrued or unaccrued that (a) arise out of and relate to the Agreement and (b) existed as of the Execution Date. This release shall not prevent or impair Vertex from making a claim for any breach of the Agreement, as amended, arising on or after the Execution Date or for breach of a representation, warranty, or covenant made in this Amendment No. 7.

8.3 Each party waives to the fullest extent permitted by law the provisions and benefits of Section 1542 of the California Civil code, which provides that:

> "A general release does not extend to claims which the creditor does not know or suspect to exist in his or her favor at the time of executing the release, which if known by him or her must have materially affected his or her settlement to the debtor."

8.4 "Losses" shall mean claims, actions, causes of actions, suits, defenses, judgments, debts, offsets, accounts, covenants, contracts, agreements, torts, damages and any and all demands and liabilities whatsoever, including costs, expenses and attorneys' fees.

8.5 Each party represents, warrants and covenants that it has not heretofore assigned or transferred to any person or entity any matters released by such party in this Section 8, and such party agrees to indemnify and hold harmless the other party and its Releasees from and against any Losses arising from any such alleged or actual assignment or transfer.

9. Agreement to be Bound. RP (on its own behalf and on behalf of its predecessors, successors, assigns, officers, directors, employees, trustees, parents, subsidiaries and Affiliates) agrees to be bound by (a) the dispute resolution procedures set forth in Section 12.2 of the Agreement (as amended by Section 3 of this Amendment No. 7) and (ii) Sections 6, 8, 9, 10, 11, 12.1 and 13 of this Amendment No. 7.

10. Communications. Notwithstanding Section 6.3 of the Agreement, Vertex, CFFT and RP (and their respective predecessors, successors, assigns, officers, directors, employees, trustees, parents, subsidiaries and Affiliates) agree that any public or private communication regarding the terms of this Amendment No. 7, shall be made in the form of, or in a manner consistent with, Schedule 1 to this Amendment No. 7; *provided that* (a) Vertex, CFFT and RP may disclose the terms of this Amendment No. 7 to the extent required by applicable law and/or in connection with arbitration under this Agreement, (b) RP and CFFT may disclose the terms of this Amendment No. 7 in their audited financial statements to the extent so required by their independent accountants, and include comparable disclosure in its unaudited quarterly financial statements, (c) RP may disclose the terms of this Amendment No. 7 to its existing and prospective lenders and equity investors so long as such parties are subject to reasonable restrictions of confidentiality and (d) CFFT may disclose the terms of this Amendment No. 7 to Canada Pension Plan Investment Board.

11. [***]. Vertex agrees that it shall not at any time [***] regarding [***] current or former directors, officers, stockholders, employees, agents, attorneys or representatives, any of the other CFFT Releasees or RP Releasees under Section 8, or regarding CFFT's or RP's [***]. CFFT [***] each agree that neither of them shall at any time [***] regarding Vertex or Vertex's current or former directors, officers, stockholders, employees, agents, attorneys or representatives, any of the other Vertex Releasees under Section 8, or regarding Vertex's [***].

12. Representations and Warranties; Covenants.

12.1 Mutual Representations**.** Each party represents and warrants to the other party that (a) such party is duly organized, validly existing, and in good standing under the laws of the jurisdiction of its establishment or incorporation, (b) such party has taken all action necessary to authorize it to enter into this Agreement and perform its obligations under this Amendment No. 7, (c) this Amendment No. 7 has been duly executed and delivered on behalf of such party and constitutes a legal, valid and binding obligation of such party and (d) neither the execution of this Amendment No. 7 nor the performance of such party's obligations hereunder will conflict with, result in a breach of, or constitute a default under any provision of such party's organizational documents, or of any law, rule, regulation, authorization or approval of any government entity, or of any agreement to which it is a party or by which it is bound.

12.2 Vertex Representation. Vertex represents and warrants to CFFT that Exhibit 2016-A was prepared in good faith by Vertex based on its business records and includes all compounds first synthesized and/or tested by Vertex in connection with its research and development of Correctors during the Additional Term, [***]. If the parties agree (or the arbitrators acting under Section 12.2 of the Agreement determine) that any compound that was first synthesized and/or tested by Vertex in connection with its research and development of Correctors during the Additional Term is not included in Exhibit 2016-A, such compound shall be added to Exhibit 2016-A, will be an Additional Compound, and shall be treated as having been included in Exhibit 2016-A as of the Amendment No. 7 Effective Date. The addition of such compound to Exhibit 2016-A and the application of the terms of this Agreement to such compound will be CFFT's sole and exclusive remedies for any good-faith failure to include such compound on Exhibit 2016-A. Vertex represents and warrants as of the Amendment No. 7 Effective Date that no Correctors other than [***]have been advanced into clinical trials and that Vertex has a bona fide intention to advance one or more Additional Products other than [***],[***] into clinical trials in the [***] following the Amendment No. 7 Effective Date, subject to further assessment of efficacy and safety.

12.3 Vertex Covenant. If, at any time following the Amendment No. 7 Effective Date, Vertex files a new drug application with the United States Food and Drug Administration for marketing approval pursuant to 21 C.F.R. § 314.3 or submits a similar application to any regulatory authority in any other country or jurisdiction, in each case, with respect to any product containing a Corrector, if requested by CFFT in writing, Vertex will provide CFFT with reasonably detailed information regarding the date on which each such compound was first synthesized and/or tested by or at the direction of Vertex as part of its research and development of Correctors. Except as set forth in this Section 12.3, and subject to CFFT's right to enforce representations and obligation herein, Vertex will not be obligated to provide CFFT with any information regarding the date on which any compound was first synthesized and/or tested by or at the direction of Vertex as part of its research and development of Correctors.

13. Assignment. None of the Agreement, nor any Compound, any Original Drug Product or Additional Compound, or any rights to any Compound or Additional Compound, may be transferred or assigned by Vertex without the prior written consent of CFFT, except that, Vertex may transfer all of its rights in the Agreement and all Compounds, Original Drug Products, and Additional Compounds, but only if the transferee or assignee executes and delivers to CFFT an agreement to assume all of Vertex's obligations under the Agreement. CFFT may transfer or assign its rights under the Agreement solely as provided in the Agreement. RP may not assign or transfer its rights under this Amendment No. 7.

14. Existing Agreement Ratified. As amended and supplemented hereby, all terms and provisions of the Agreement in effect immediately prior to the Amendment No. 7 Effective Date shall remain in full force and effect. For the avoidance of doubt, the following sections from the Agreement remain in effect, as amended by this Amendment No. 7 and prior amendments: Articles V, VI (for the period of time specified therein), VII (for the period of time

specified therein), VIII, IX, XI, XII, XIII and any other provision of the Agreement that, by its terms, survives the termination of the Agreement. If specific provisions of this Amendment No. 7 are inconsistent with specific provisions of the Agreement, the provisions of this Amendment No. 7 shall control. This Amendment No. 7 may be executed in any number of counterparts, each of which shall be deemed an original, and all of which, taken together, shall constitutes one and the same agreement. Vertex, CFFT and RP may execute this Amendment No. 7 by electronically transmitted signature and such electronically transmitted signature will be as effective as an original executed signature page.

[Signature Page Follows]

In WITNESS WHEREOF, the undersigned have executed this Amendment No. 7 on the Execution Date effective as of the Amendment No. 7 Effective Date.

CYSTIC FIBROSIS FOUNDATION THERAPEUTICS INCORPORATED		VERTEX PHARMACEUTICALS INCORPORATED	
By:	/s/ Preston Campbell	By:	/s/ Ian Smith
Name:	Preston Campbell	Name:	Ian Smith
Title:	President & CEO	Title:	EVP& CFO

SOLELY FOR PURPOSES OF SECTIONS 6, 8, 9, 10, 11, 12.1 AND 13 OF THIS AMENDMENT NO. 7, RP HAS EXECUTED THIS AMENDMENT NO. 7 ON THE EXECUTION DATE EFFECTIVE AS OF THE AMENDMENT NO. 7 EFFECTIVE DATE.

RPI FINANCE TRUST

By: Wilmington Trust Company, not
in its individual capacity but
solely in its capacity as owner trustee

RPI FINANCE TRUST

By: Wilmington Trust Company, not
in its individual capacity but
solely in its capacity as owner trustee

By: s/ Eric A Kardash

Name: Eric A Kardash

Title: Assistant Vice President

It is expressly understood and agreed by the parties hereto that (i) this Agreement is executed and delivered by Wilmington Trust Company, not individually or personally, but solely as owner trustee of RPI Finance Trust, (ii) nothing herein contained shall be construed as creating any liability on Wilmington Trust Company, individually or personally, any such liability, if any, being expressly waived by the parties hereto and by any person claiming by, through or under the parties hereto, and (iii) under no circumstances shall Wilmington Trust Company be personally liable for the payment of any indebtedness or expenses of RPI Finance Trust.

Exhibit 2016-A

Additional Compounds

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of 99 page were omitted. [***]

Exhibit 2016-B

KALYDECO & ORKAMBI Example

If annual Net Sales of KALYDECO are equal to [***] and annual Net Sales of ORKAMBI are equal to [***], and no other products containing VX-770 Drug Product or VX-809 Drug Product or any other Original Drug Product are sold in the applicable calendar year, the royalty payable to CFFT by Vertex would be calculated as follows:

[***]	$[***]
[***]	$[***]

[***]	$[***]
[***]	$[***]
[***]	
	$[***]

Royalty Paid on Original Drug Products:	
[***]	$[***]
[***]	$[***]
Total Royalty:	$[***]

Exhibit 2016-C

Additional Example

If annual Net Sales of the Combination Product described in Section 5.3.1(g) are equal to [***] and no other products containing any of the components of such Combination Product or any Original Drug Product or Additional Product either separately or as part of another unrelated Combination Product, are sold in the applicable year, the royalty payable to CFFT by Vertex would be calculated as follows:

[***]	$[***]

[***]	$[***]
[***]	$[***]
[***]	$[***]

[***]:	
[***]	$[***]
[***]	$[***]
Royalty Paid on Additional Product under Section 5.3.1(d)(i):	
Total Annual Net Sales [***]	$[***]
Royalty Paid on Additional Product under Section 5.3.1(d)(ii):	
Total Annual Net Sales [***]	$[***]
Total Royalty:	$[***]

Schedule 1

Publicity

Item 1.01. Entry into a Material Definitive Agreement

The information contained in Item 8.01 regarding the Amendment is incorporated herein by reference.

Item 8.01 Other Events

On October 13, 2016, we amended and expanded our Research, Development and Commercialization Agreement (the "Collaboration Agreement"), dated May 24, 2004, by and between Cystic Fibrosis Foundation Therapeutics Incorporated ("CFFT") and Vertex Pharmaceuticals Incorporated (the "Amendment"), in order to update and clarify the terms of our relationship. The Amendment provides for an upfront program award from CFFT to us of $75.0 million and development funding from CFFT to us of up to $6.0 million annually. Pursuant to the Amendment, we have agreed to pay royalties ranging from low single digits to mid-single digits on certain compounds first synthesized and/or tested between March 1, 2014 and August 31, 2016. We will continue to pay royalties ranging from single digits to sub-teens on any approved drugs first synthesized and/or tested on or before February 28, 2014. The parties also clarified that net sales on combination products will be allocated equally to each of the active pharmaceutical ingredients in the combination product consistent with the allocation of net sales for ORKAMBI and provided further clarification with respect to the calculation of royalties on products covered by the Collaboration Agreement.

Independently, we entered into a data license agreement with the Cystic Fibrosis Foundation pursuant to which we will pay for continuing access to data from the CFF's patient registry, which we believe will be important for research, development and approval of future CF medicines.

Exhibit 31.1

CERTIFICATION

I, Reshma Kewalramani, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q 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;

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;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 3, 2021

/s/ Reshma Kewalramani

Reshma Kewalramani
Chief Executive Officer and President

Exhibit 31.2

CERTIFICATION

I, Charles F. Wagner, Jr., certify that:

1. I have reviewed this Quarterly Report on Form 10-Q 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;

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;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 3, 2021

/s/ Charles F. Wagner, Jr.

Charles F. Wagner, Jr.
Executive Vice President and Chief Financial Officer

Exhibit 32.1

SECTION 906 CEO/CFO CERTIFICATION

Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (Subsections (a) and (b) of Section 1350, Chapter 63 of Title 18, United States Code) each of the undersigned officers of Vertex Pharmaceuticals Incorporated, a Massachusetts corporation (the "Company"), does hereby certify, to such officer's knowledge, that the Quarterly Report on Form 10-Q for the quarter ended September 30, 2021 (the "Form 10-Q") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-Q fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: November 3, 2021

/s/ Reshma Kewalramani

Reshma Kewalramani
Chief Executive Officer and President

Date: November 3, 2021

/s/ Charles F. Wagner, Jr.

Charles F. Wagner, Jr.
Executive Vice President and Chief Financial Officer