



Full-Year and Fourth-Quarter 2019 Financial Results



January 30, 2020

Agenda

Introduction

Michael Partridge, Senior Vice President, Investor Relations

CEO Perspective

Jeff Leiden, M.D., Ph.D., Chairman, President and Chief Executive Officer

2020 Review

Reshma Kewalramani, M.D., Executive Vice President and Chief Medical Officer

Commercial & TRIKAFTA Launch Update

Stuart Arbuckle, Executive Vice President and Chief Commercial Officer

Financial Results

Charlie Wagner, Executive Vice President and Chief Financial Officer

Safe Harbor Statement & Non-GAAP Financial Measures

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, including, without limitation, the information provided regarding future financial performance, including in the section captioned "Full-Year 2020 Financial Guidance", section captioned "2020 Key Goals and Milestones" and statements regarding the development plan and timelines for our product development candidates. While Vertex believes the forward-looking statements contained in this press release are accurate, these forward-looking statements represent the company's beliefs only as of the date of this presentation and there are a number of risks and uncertainties that could cause actual events or results to differ materially from those expressed or implied by such forward-looking statements. Those risks and uncertainties include, among other things, that the company's expectations regarding its 2020 CF net product revenues, expenses and effective tax rates may be incorrect (including because one or more of the company's assumptions underlying its expectations may not be realized), that data from the company's development programs may not support registration or further development of its compounds due to safety, efficacy or other reasons, and other risks listed under Risk Factors in Vertex's annual report and subsequent quarterly reports filed with the Securities and Exchange Commission and available through the company's website at www.vrtx.com. Vertex disclaims any obligation to update the information contained in this presentation as new information becomes available.

In this presentation, Vertex's financial results and financial guidance are provided in accordance with accounting principles generally accepted in the United States (GAAP) and using certain non-GAAP financial measures. In particular, non-GAAP financial results and guidance exclude from Vertex's pre-tax income (i) stock-based compensation expense, (ii) an adjustment to revenues and related cost of sales to reflect the conclusion of the early access program for ORKAMBI in France, (iii) revenues and expenses related to business development transactions including collaboration agreements, asset acquisitions and consolidated variable interest entities, (iv) gains or losses related to the fair value of the company's strategic investments, (v) acquisition-related costs and (vi) other adjustments. The company's non-GAAP financial results also exclude from its provision for or benefit from income taxes the estimated tax impact related to its non-GAAP adjustments to pre-tax income described above. These results are provided as a complement to results provided in accordance with GAAP because management believes these non-GAAP financial measures help indicate underlying trends in the company's business, are important in comparing current results with prior period results and provide additional information regarding the company's financial position. Management also uses these non-GAAP financial measures to establish budgets and operational goals that are communicated internally and externally and to manage the company's business and to evaluate its performance. The company adjusts, where appropriate, for both revenues and expenses in order to reflect the company's operations. The company provides guidance regarding product revenues in accordance with GAAP and provides guidance regarding combined research and development and sales, general, and administrative expenses on both a GAAP and non-GAAP basis. The company also provides guidance regarding its anticipated income taxes as a percentage of pre-tax income on a non-GAAP basis. The guidance regarding GAAP research and development expenses and sales, general and administrative expenses does not include estimates associated with any potential future business development activities. A reconciliation of the GAAP financial results to non-GAAP financial results is included in the attached financial information and in the company's Q4 2019 press release dated January 30, 2020.

2019 Milestones and Accomplishments

ACHIEVE OUR VISION IN CYSTIC FIBROSIS

- ✓ Submit NDA for a triple combination regimen no later than mid-2019
- ✓ U.S. approval for TRIKAFTA for people ages 12+
- ✓ U.S. approval for SYMDEKO for children ages 6 through 11
- ✓ Initiate POC study of additional next-generation corrector
- ✓ Phase 2 dose-ranging study of potential once-daily regimen VX-561

EXPAND PIPELINE BEYOND CF

- ✓ Complete Phase 1 studies in at least two new diseases
- ✓ Bolster pipeline with internal and external assets
- ✓ Advance one or more compounds from research into clinical development

BUILD FINANCIAL STRENGTH

- ✓ Continued CF product revenue growth
- ✓ Continued uptake and reimbursement for ORKAMBI and SYMDEKO in additional countries outside the U.S.
- ✓ Continued management of non-GAAP combined R&D and SG&A expenses
- ✓ Continued expansion of non-GAAP operating margins and cash flow

2020 Key Goals and Milestones

***ACHIEVE
OUR
VISION IN
CYSTIC
FIBROSIS***

- Successful launch of TRIKAFTA in the U.S. for ages 12+
- EU approval of triple combination regimen for ages 12+
- EU approval of SYMKEVI for ages 6 to 11
- Submit sNDA for triple combination regimen for ages 6 to 11

***DEVELOP NEW
TRANSFORMATIVE
MEDICINES
FOR ADDITIONAL
SERIOUS DISEASES***

- Generate proof-of-concept data for AAT program
- Generate proof-of-concept data for both sickle cell disease and beta thalassemia
- Advance cell therapy for type 1 diabetes into clinical development in late 2020/early 2021
- Advance two new compounds into clinical development

***DELIVER
FINANCIAL
PERFORMANCE***

- Continued CF product revenue growth
- Disciplined management of non-GAAP combined R&D and SG&A expenses
- Further expansion of non-GAAP operating margins and cash flows
- Effectively deploy capital to pursue future growth opportunities

Pipeline of Transformative Therapies Across Multiple Modalities

Small Molecule Therapies



Cystic Fibrosis

Small molecule approach targeting defective CFTR proteins

- **VX-561:** Phase 2 dose-ranging study of once-daily potentiator
- **VX-121:** Phase 2 study evaluating VX-121/tezacaftor/VX-561 once-daily triple combination regimen



Alpha-1 Antitrypsin Deficiency

Small molecule to correct protein misfolding and enable secretion of functional AAT from the liver

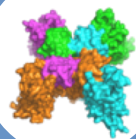
- **VX-814:** Phase 2 study started in Q4'19; Data expected in 2020
- **VX-864:** Phase 1 study ongoing



APOL1-Mediated Kidney Diseases

Small molecule inhibitor of APOL1 function, a causal genetic factor in FSGS/other proteinuric kidney diseases

- **VX-147:** Phase 1 study completed in Q4'19; Phase 2 POC study expected to begin in 2020



Pain

Small molecule inhibitors of NaV1.8 as a novel treatment for pain

- Advancing portfolio of NaV1.8 inhibitors; POC established in multiple pain types

Pipeline of Transformative Therapies Across Multiple Modalities

Cell and Genetic Therapies



Sickle Cell Disease

Ex vivo gene editing with goal of providing one-time curative therapy

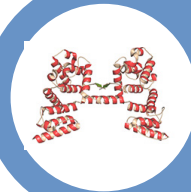
- **CTX001:** First clinical data reported in Q4'19



Beta Thalassemia

Ex vivo gene editing with goal of providing one-time curative therapy

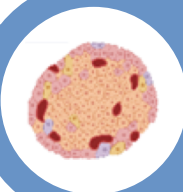
- **CTX001:** First clinical data reported in Q4'19



Duchenne Muscular Dystrophy

Novel gene editing platform to potentially restore and repair dystrophin in DMD

- Exonics Therapeutics acquisition and expanded collaboration with CRISPR Therapeutics announced June 2019



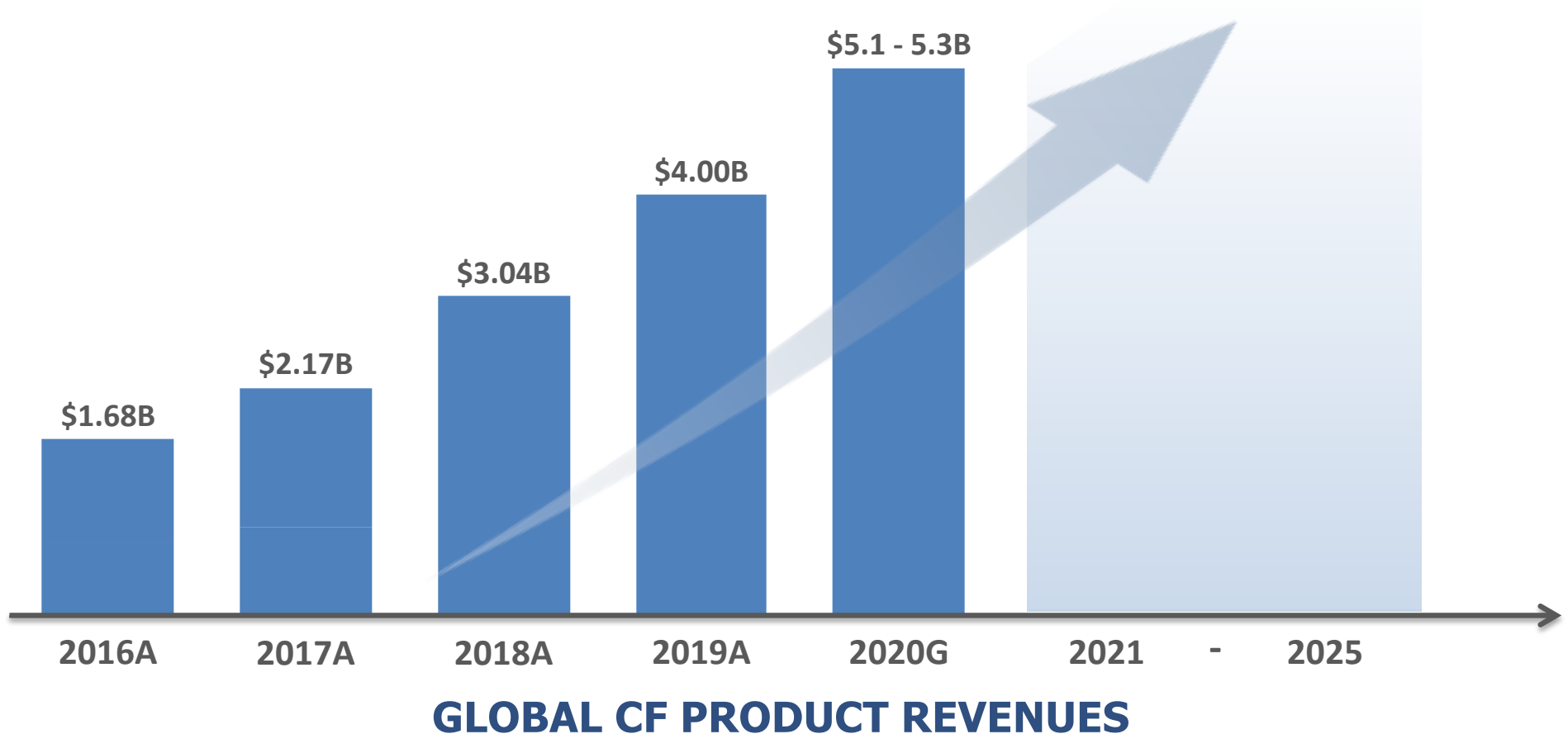
Type 1 Diabetes

Potentially curative cell-based treatment and delivery system

- Semma Therapeutics acquired October 2019
- Goal to advance cell therapy for type 1 diabetes into clinical development in late 2020/early 2021

Continued CF Revenue Growth in 2020 and Beyond

Growth to 90% of all CF patients treating younger patients and label expansions with current medicines



Notes:

- 2020 reflects the midpoint of the total CF product revenue guidance range provided on January 30, 2020
- 2021 - 2025 potential growth in CF revenues is provided as a graphical representation

U.S. TRIKAFTA Launch Underway

- Early FDA approval received on October 21, 2019 for people ages 12+ who have at least one *F508del* mutation
- ~18,000 patients in the U.S. eligible, representing largest patient population at the time of launch
 - ~6,000 newly eligible F/MF patients
- Strong interest from all eligible patients, including new initiations as well as patients transitioning from another VRTX CF medicine
- On track to obtain broad coverage and reimbursement from both commercial and government payers in the U.S.
- EMA MAA validation received on October 31, 2019



Full Year and Q4 2019 Financial Highlights

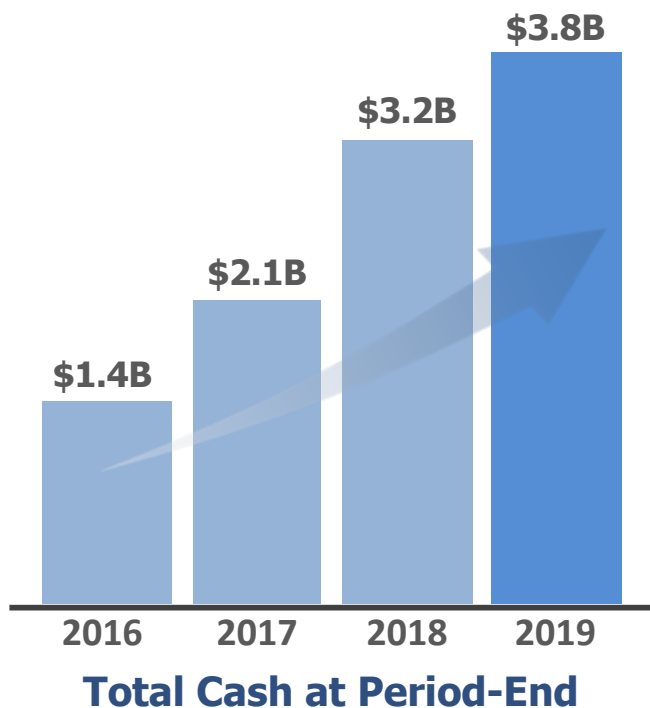
<i>(in millions except where noted)</i>	Q4 18	FY 2018	Q1 19	Q2 19	Q3 19	Q4 19	FY 2019
Total non-GAAP product revenues	<u>\$868</u>	<u>\$3.04B</u>	<u>\$857</u>	<u>\$940</u>	<u>\$950</u>	\$1.26B	\$4.00B
KALYDECO	259	1.01B	244	262	249	236	991
ORKAMBI	315	1.26B	293	316	297	270	1.18
SYMDEKO/SYMKEVI	294	769	320	362	404	332	1.42
TRIKAFTA	-	-	-	-	-	420	420
Combined non-GAAP R&D and SG&A	<u>400</u>	<u>1.53B</u>	<u>388</u>	<u>394</u>	<u>416</u>	496	1.69B
Non-GAAP operating income	348	1.11B	377	413	403	593	1.79B
Non-GAAP operating margin	40%	37%	44%	44%	42%	47%	45%
Non-GAAP net income	337	1.06B	296	327	322	444	1.39B
Non-GAAP net income per share - diluted	\$1.30	\$4.08	\$1.14	\$1.26	\$1.23	\$1.70	\$5.33
Cash, cash equivalents & marketable securities (period-end)		\$3.2B					\$3.8B

Notes

- An explanation of non-GAAP financial measures and reconciliation of non-GAAP product revenues, combined non-GAAP R&D and SG&A expense, non-GAAP net income and non-GAAP net income per share is included in the company's Q4 2019 press release dated January 30, 2020
- Reconciliation of non-GAAP operating income and non-GAAP operating margin to corresponding GAAP measures is included in the appendix of this presentation; totals may not add due to rounding



Increasing Cash Flow Enables Investment for Future Growth



Increasing Cash Flow Enables Continued Investment in Internal R&D and Execution of Business Development Strategy

Business Development and Capital Allocation Strategy

- Complement ongoing R&D in CF
- Access novel platform technologies and targets
- In-license or acquire pipeline assets

~\$1.2B invested in internal R&D in 2019
~\$1.6B invested in external innovation in 2019



Note:

- Period-end cash includes cash, cash equivalents and marketable securities

Full-Year 2020 Financial Guidance

	FY 2019 Actuals	FY 2020 Guidance	FY 2020 Guidance Commentary
Total Non-GAAP Product Revenues	\$4.00B	\$5.1 - \$5.3B	Guidance reflects anticipated revenues from TRIKAFTA and reimbursement agreements from outside the U.S.
Combined Non-GAAP R&D and SG&A	\$1.69B	\$1.95 - \$2.0B	Increase over 2019 reflects the increased investment to support the launch of TRIKAFTA and expansion of the R&D pipeline into additional diseases
Combined GAAP R&D and SG&A	\$2.41B	\$2.4 - \$2.55B	
Non-GAAP Effective Tax Rate	22%	21% - 22%	The vast majority of the company's tax provision will be a non-cash expense until NOLs are fully utilized



Note: An explanation of non-GAAP financial measures and reconciliation of non-GAAP product revenues and non-GAAP combined R&D and SG&A expense is included in the company's Q4 2019 press release dated January 30, 2020



Full-Year and Fourth-Quarter 2019 Financial Results



January 30, 2020

Appendix

Reconciliation of GAAP to non-GAAP Financial Information

	Q4 2018	FY 2018	Q1 2019	Q2 2019	Q3 2019	Q4 2019	FY 2019
GAAP total revenues	\$870	\$3.05B	\$858	\$941	\$950	\$1.41B	\$4.16B
Non-GAAP total revenues	\$869	\$3.04B	\$858	\$941	\$950	\$1.26B	\$4.01B
GAAP operating income	128	635	277	270	99	551	1.20B
Stock compensation expense	79	325	94	90	85	92	360
Other adjustments	142	152	6	53	218	(50)	228
Non-GAAP operating income	348	1.11B	377	413	403	593	1.79B
Operating Margin %:							
GAAP	15%	21%	32%	29%	10%	39%	29%
Non-GAAP	40%	37%	44%	44%	42%	47%	45%
Net income							
GAAP	1.55B	2.10B	269	267	58	583	1.18B
Non-GAAP	337	1.06B	296	327	322	444	1.39B
Net income per share - diluted							
GAAP	\$5.97	\$8.09	\$1.03	\$1.03	\$0.22	\$2.23	\$4.51
Non-GAAP	\$1.30	\$4.08	\$1.14	\$1.26	\$1.23	\$1.70	\$5.33

Notes:

- Non-GAAP total revenues exclude \$155.8M related to ORKAMBI product revenues in the FY and Q4 of 2019; please refer to Note 4 in the company's Q4'19 press release dated January 30, 2020 for further information
- All numbers in the above reconciliation table are in millions except per share data and percentages; totals may not add due to rounding