Third-Quarter 2019 Financial Results

October 30, 2019

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Agenda

Introduction

Michael Partridge, Senior Vice President, Investor Relations

CEO Perspective

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

Commercial Update & TRIKAFTA Launch

Stuart Arbuckle, Executive Vice President and Chief Commercial Officer

Clinical Update

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

Financial Results

Charlie Wagner, Executive Vice President and Chief Financial Officer

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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 2019 Financial Guidance" and statements regarding (i) the timing and expected outcome of regulatory applications and reimbursement for CF medicines globally and (ii) the development plan and timelines for our product development candidates, including CTX001, VX-814, VX-864, VX-147 and VX-961. 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 2019 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) revenues and expenses related to business development transactions including collaboration agreements, asset acquisitions and consolidated variable interest entities, (iii) gains or losses related to the fair value of the company's strategic investments, (iv) acquisition-related costs and (v) 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.

2019 Key Goals and Milestones

	2018	2019
ACHIEVE OUR VISION IN CYSTIC FIBROSIS	☑ Phase 2 data for triple combinations in CF patients ☑ Initiation of pivotal development of up to two triple combination regimens ☑ Approval for tezacaftor/ivacaftor combination in the U.S. (Europe anticipated in 2H 2018) ☑ Advance additional next-generation correctors into development	☑ **Phase 3 data for VX-445 in patients ages 12+** ☑ **Submit NDA for a triple combination regimen no later than mid-2019** ☑ **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	☑ Advance one or more compounds from research into clinical development ☑ Initiate clinical development of CRISPR-Cas9 treatment in Beta Thalassemia & Sickle Cell Disease	☐ **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	☑ Significantly increase 2018 total CF product revenues ☑ Obtain reimbursement for ORKAMBI in additional countries outside the U.S. ☑ Continued management of non-GAAP combined R&D and SG&A expenses ☑ Continue to increase operating margins and cash flows	☑ **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**

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Vertex Strategy and Business Model

A Blueprint for Serial Innovation

CORPORATE STRATEGY

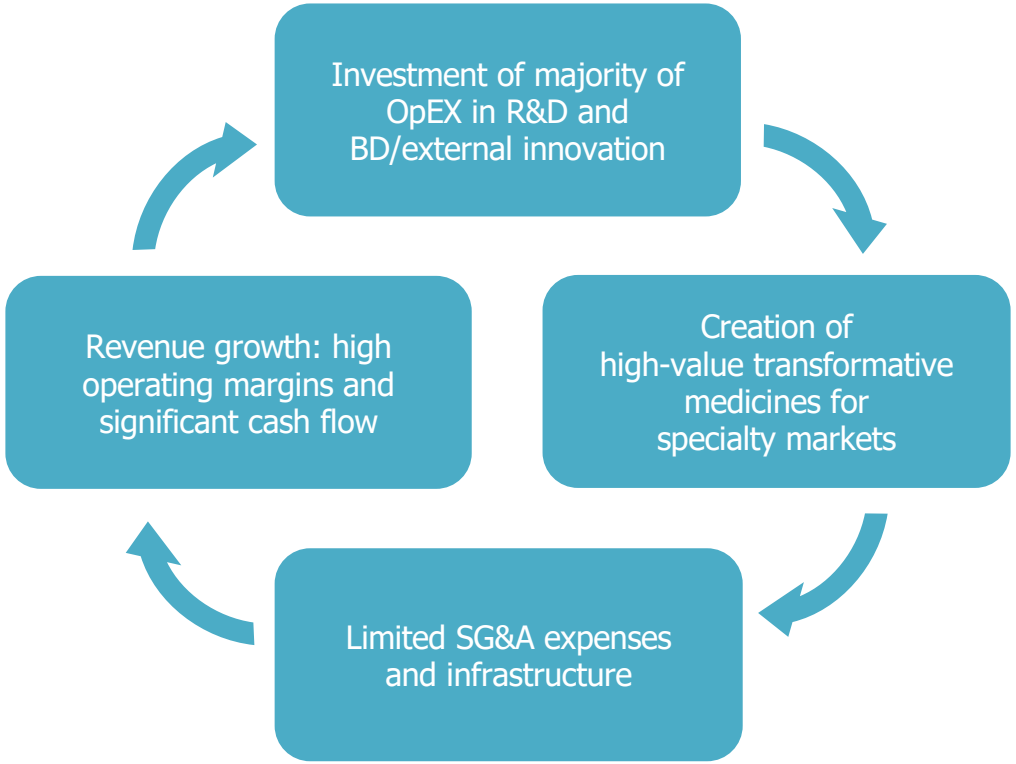
Vertex invests in **scientific innovation** to create **transformative medicines** for people with **serious diseases** with a focus on **specialty markets**

RESEARCH STRATEGY

Combine **transformative advances** in the **understanding of human disease** and in the **science of therapeutics** to dramatically advance human health

- Focus on **validated targets** that address causal human biology
- Create **predictive lab assays** and **clinical biomarkers**
- Identify **rapid path to registration** and approval
- Discover and develop medicines that offer transformative benefit, **regardless of modality**

DIFFERENTIATED BUSINESS MODEL



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Multiple Medicines to Treat Underlying Cause of CF

Increasing Access and Reimbursement for CF Patients Globally

KALYDECO

Recent Accomplishments:

- *CHMP positive opinion received in EU for ages 6 - <12mos.*
- *Reimbursement received in England for ages 18+ with R117H mutation and for ages 12mos.+ with gating mutations*

ORKAMBI

Recent Accomplishments:

- *Reimbursement received in England, Spain, Australia and Scotland for eligible patients*

SYMDEKO/SYMKEVI

Recent Accomplishments:

- *Reimbursement received in England, Spain, Australia and Scotland for eligible patients*

TRIKAFTA

Recent Accomplishments:

- *Approved in U.S. for ages 12+*
- *MAA submitted to EMA for ages 12+*

- Full-year 2019 total CF product revenue guidance of $3.70 - $3.75 billion -

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U.S. TRIKAFTA Launch Underway

- 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
- Broad coverage and reimbursement is anticipated from both commercial and government payers in the U.S.
  - First patients have already been prescribed medicine
- EU MAA submitted
- Phase 3 study in children ages 6-11 currently enrolling

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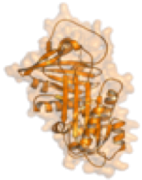
Beyond CF

Multiple Opportunities for Transformative Medicines

Alpha-1 Antitrypsin Deficiency



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

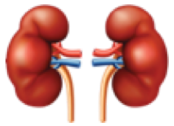
- Phase 2 study of VX-814 expected to begin in Q4 2019; clinical data from this study expected in 2020

Sickle Cell Disease & Beta Thalassemia

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

- First clinical data from Phase 1/2 study of CTX001 expected in Q4 2019

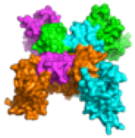
APOL1-Mediated Kidney Diseases



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

- Phase 1 study of VX-147 in healthy volunteers expected to be complete in Q4 2019
- Advancing multiple other molecules in late-stage research

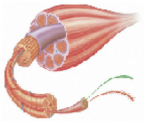
Pain



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

- Proof-of-concept established in multiple pain types
- Advancing multiple selective NaV1.8 inhibitors through late-stage research and early clinical development

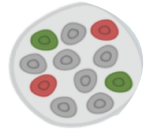
DMD and DM1



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

- Exonics Therapeutics acquisition and expanded collaboration with Crispr Therapeutics completed in Q3 2019

Type 1 Diabetes



Potentially curative cell-based treatment and delivery system

- Semma Therapeutics acquisition completed in October 2019

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Q3 2019 Financial Highlights

2019	Q3 18	FY 2018	Q1 19	Q2 19	Q3 19	YTD 2019
Total CF product revenues	$783	$3.04B	$857	$940	**$950**	$2.75B
KALYDECO	246	1.01B	244	262	**249**	755
ORKAMBI	282	1.26B	293	316	**297**	906
SYMDEKO/SYMKEVI	255	769	320	362	**404**	1.09B
Combined non-GAAP R&D and SG&A	379	1.53B	388	394	**416**	1.20B
Non-GAAP operating income	295	1.11B	377	413	**403**	1.19B
Non-GAAP operating margin	38%	37%	44%	44%	**42%**	43%
Non-GAAP net income	282	1.06B	296	327	**322**	945
Non-GAAP net income per share - diluted	$1.09	$4.08	$1.14	$1.26	**1.23**	3.63
Cash, cash equivalents & marketable securities (period-end)		$3.2B			**$4.0B**	

Notes

- *An explanation of non-GAAP financial measures and reconciliation of 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 Q3 2019 press release dated October 30, 2019*
- *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*

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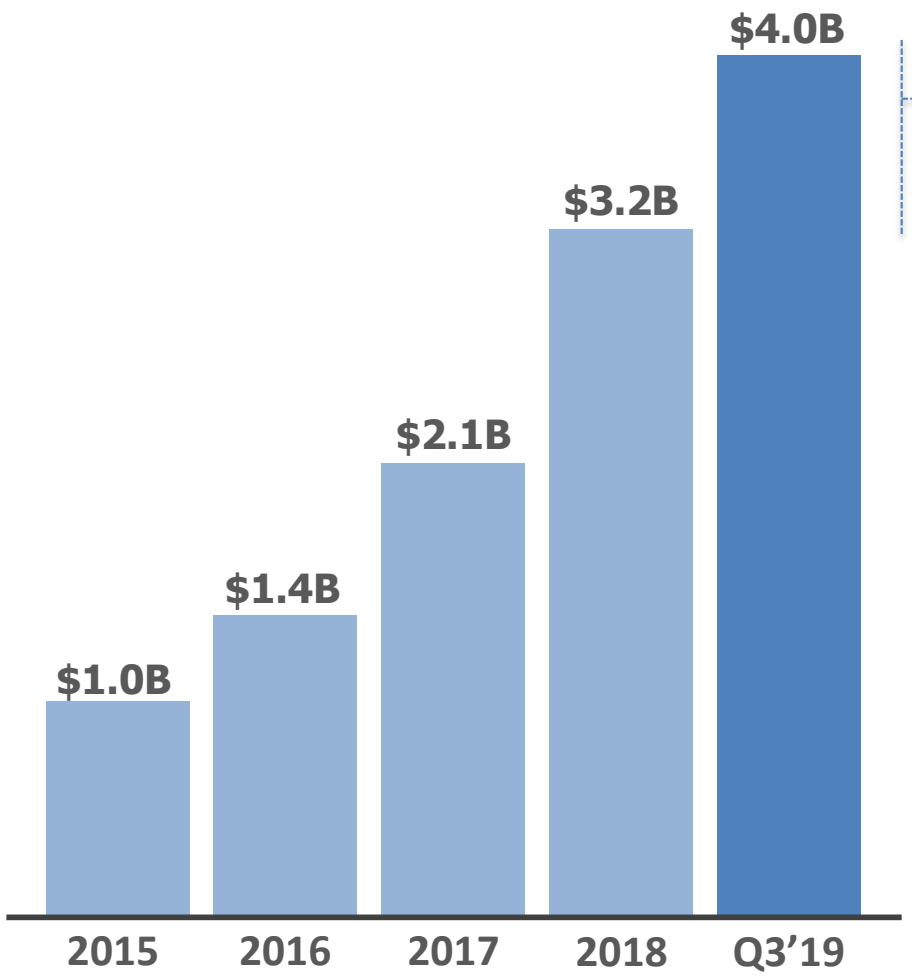
Increasing Cash Flow Enables Investment for Future Growth



Total Cash at Period-End

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

CRISPR THERAPEUTICS · semma THERAPEUTICS · exonics THERAPEUTICS · ribometrix · X-CHEM · arbor · KYMERA · MERCK · GENOMICS PLC

Notes:

- *Period-end cash includes cash, cash equivalents and marketable securities*
- *$950M payment for the acquisition of Semma Therapeutics will be reflected in the period-end December 31, 2019 cash balance*

2019 Financial Guidance

	FY 2018 Actuals	FY 2019 Guidance	FY 2019 Guidance Commentary
Total CF Product Revenues	$3.04B	**$3.70 - $3.75B**	Guidance reflects early approval of TRIKAFTA
Combined Non-GAAP R&D and SG&A	$1.53B	**$1.65 - $1.70B**	Non-GAAP guidance unchanged
Combined GAAP R&D and SG&A	$1.97B	**$2.35 - $2.45B**	
Non-GAAP Effective Tax Rate		**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 combined R&D and SG&A expense is included in the company's Q3 2019 press release dated October 30, 2019*

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Appendix

Reconciliation of GAAP to non-GAAP Financial Information

	Q3 2018	FY 2018	Q1 2019	Q2 2019	Q3 2019	YTD 2019
GAAP total revenues	$785	$3,048	$858	$941	$950	$2.75B
Non-GAAP total revenues	784	$3,043	$858	$941	950	2.75B
GAAP operating income	206	635	277	270	99	646
Stock compensation expense	86	325	94	90	85	269
Other adjustments	4	152	6	53	218	278
Non-GAAP operating income	295	1.11B	377	413	403	1.19B
Operating Margin %:						
GAAP	26%	21%	32%	29%	10%	23%
Non-GAAP	38%	37%	44%	44%	42%	43%
Net income						
GAAP	129	2.10B	269	267	58	594
Non-GAAP	282	1.06B	296	327	322	945
Net income per share - diluted						
GAAP	$0.50	$8.09	$1.03	$1.03	$0.22	$2.28
Non-GAAP	$1.09	$4.08	$1.14	$1.26	$1.23	$3.63

Note: *All numbers in the above reconciliation table are in millions except per share data and percentages; totals may not add due to rounding*