First-Quarter 2019 Financial Results

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April 30, 2019

Agenda

Introduction

Michael Partridge, Senior Vice President, Investor Relations

Business Highlights

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

Commercial Update

Stuart Arbuckle, Executive Vice President and Chief Commercial Officer

Financial Results

Charlie Wagner, Executive Vice President and Chief Financial Officer

Q&A

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

Paul Silva, Corporate Controller and Chief Accounting 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, (i) information pertaining to our medicines and the ongoing discovery, development and commercialization of Vertex's product candidates, (ii) 2019 financial guidance and (iii) Vertex's 2019 key milestones and goals. While the Company believes that these forward-looking statements are accurate, these statements are subject to risks and uncertainties that could cause actual outcomes to differ materially from the Company's current expectations. These risks and uncertainties include, among other things, the risk 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, the Company's expectations regarding future financial performance may be incorrect, and the risks and uncertainties listed under Risk Factors in the Company's 10-K and other filings with the SEC.

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 and (iii) other adjustments, including gains or losses related to the fair value of the company's strategic investments. 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.

Vertex Strategy and Business Model

A Blueprint for Serial Innovation

CORPORATE STRATEGY

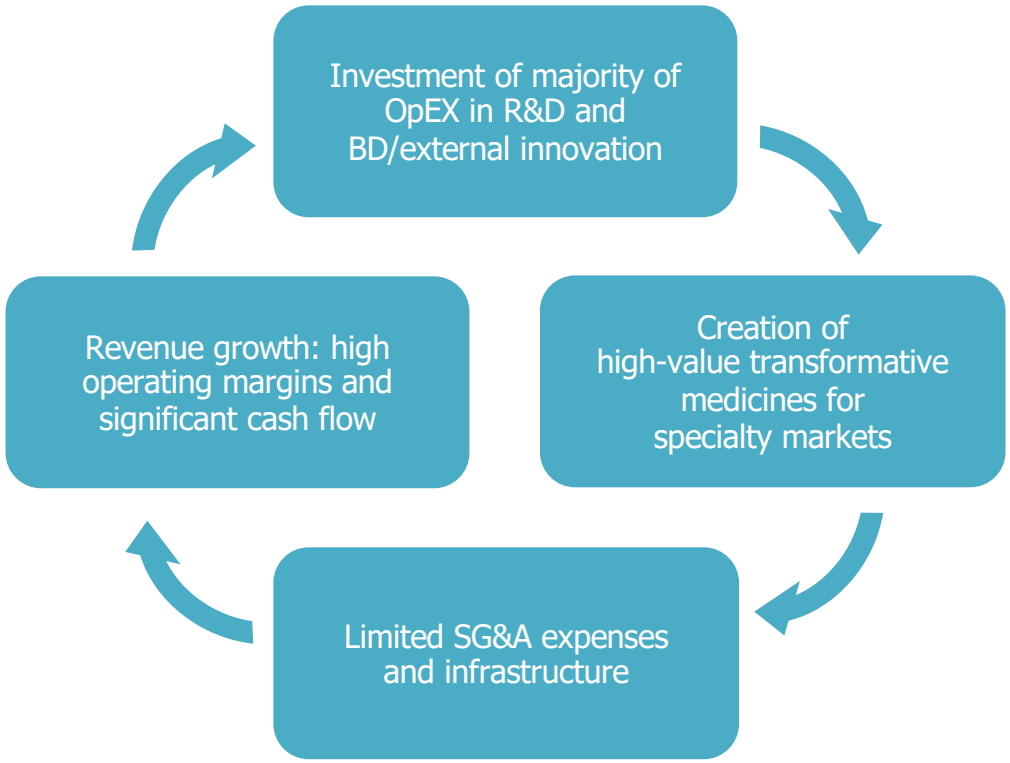
Vertex invests in **scientific innovation** to create **transformative medicines** for people with **serious diseases** with a focus on **specialty markets**

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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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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Developing Medicines for All People with CF

KALYDECO
ORKAMBI
SYMDEKO

39,000 Patients
Currently Eligible

39,000 → 44,000

- *Treating younger patients*
- *Label expansions*

44,000 → 68,000

Triple Combination Regimens

F508del/ Minimal CFTR Function

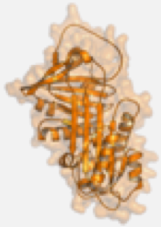
68,000 → 75,000

Gene Editing mRNA

Potential to treat all people with CF

Beyond CF

Multiple Opportunities for Transformative Medicines



Alpha-1 Antitrypsin Deficiency

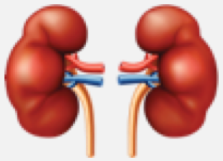
First molecule (VX-814) advanced into Phase 1 development in December 2018; Fast Track Designation granted by FDA; Expect second molecule to enter clinic in 2019; Other molecules in late preclinical development

Pain

First selective NaV1.8 inhibitor (VX-150) to demonstrate proof-of-concept in acute, musculoskeletal and neuropathic pain; Ongoing research to discover/develop additional NaV1.8 inhibitors and other potential pain molecules

Sickle Cell Disease / Beta Thalassemia

Initiated Phase 1/2 studies of gene editing therapy CTX001; First patient dosed in beta-thalassemia study; first patient enrolled in SCD study and expected to be dosed in mid-2019



Focal Segmental Glomerulosclerosis

Novel approach to underlying biology of severe kidney disease; Potential clinical candidate in 2019

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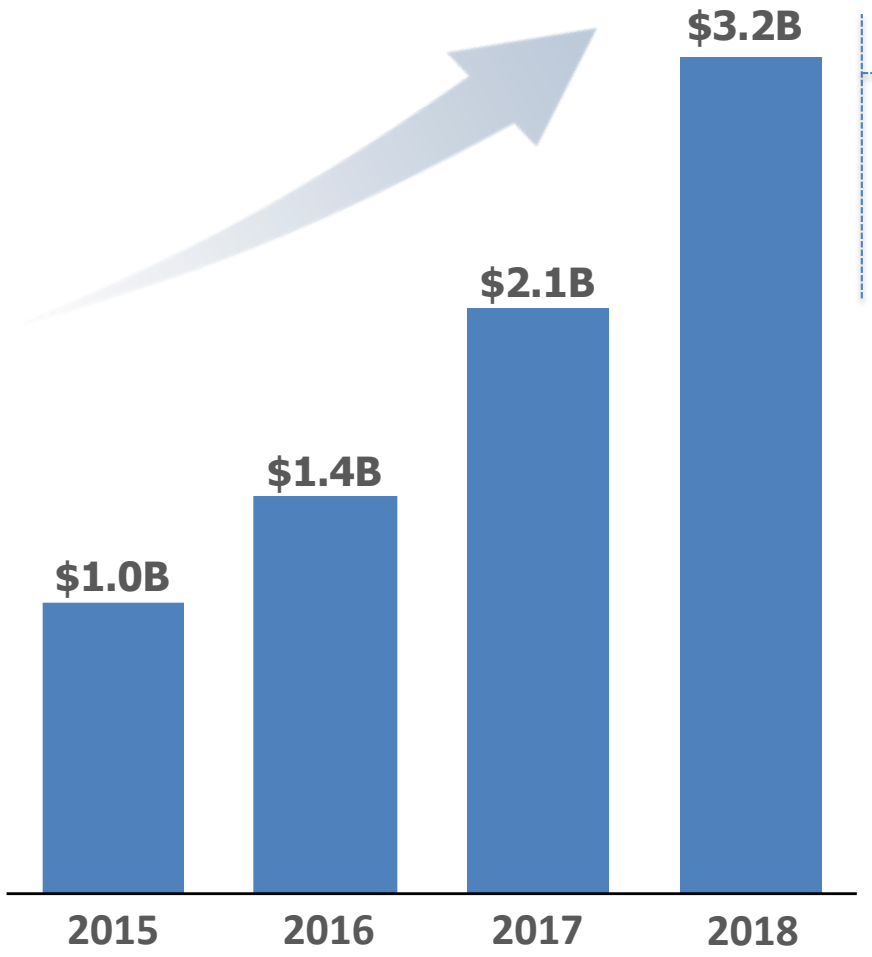
Increasing Cash Flow Enables Investment for Future Growth



Total Cash at Year-End

Growing Cash Position 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 · GENOMICS PLC · arbor · MERCK · X-CHEM PHARMACEUTICALS

Note: *Year-end cash includes cash, cash equivalents and marketable securities.*

Multiple Medicines to Treat Underlying Cause of CF

Increasing Access and Reimbursement for CF Patients Globally

KALYDECO

Recent Accomplishments:

- *Approved in Canada for ages 12 - <24 months*
- *Approved in U.S. for ages 6 - <12 months*
- *Available in Ireland for ages 1+*

ORKAMBI

Recent Accomplishments:

- *Approved in EU for ages 2-5*
- *Reimbursement in Sweden for ages 2-5*
- *Pricing agreement in Germany for ages 6-11*
- *Available in Ireland for ages 2+*

SYMDEKO/SYMKEVI

Recent Accomplishments:

- *Positive recommendation in Australia for ages 12+*
- *sNDA submitted in U.S. for ages 6-11*
- *Available in Ireland for ages 12+*

- Full-year 2019 total CF product revenue guidance of $3.45 - $3.55 billion -

Note:

- *SYMKEVI EU indication is for F508del/F508del and F508del/residual function mutations*
- *SYMKEVI availability in Ireland includes people with a residual function mutation*

Q1 2019 Financial Highlights

($ in millions except per share data and percentages)	Q1 18	FY 2018	Q1 19
Total CF product revenues	$638	$3.04B	**$857**
KALYDECO	250	1.01B	**244**
ORKAMBI	354	1.26B	**293**
SYMDEKO/SYMKEVI	34	769	**320**
Combined non-GAAP R&D and SG&A	360	1.53B	**388**
Non-GAAP operating income	208	1.11B	**377**
Non-GAAP operating margin	33%	37%	**44%**
Non-GAAP net income	196	1.06B	**296**
Non-GAAP net income per share - diluted	$0.76	$4.08	**$1.14**
Cash, cash equivalents & marketable securities (period-end)		$3.2B	**$3.5B**

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 Q1 2019 press release dated April 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*

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2019 Financial Guidance

	FY 2018 Actuals	FY 2019 Guidance	FY 2019 Guidance Commentary
Total CF Product Revenues	$3.04B	**$3.45 - $3.55B**	Revenue guidance primarily based on the full year impact of: • SYMDEKO and SYMKEVI launch • Label expansions for approved CF medicines • Reimbursement agreements achieved in 2018
Combined Non-GAAP R&D and SG&A	$1.53B	**$1.65 - $1.70B**	Year-over-year increase based on: • CF development efforts, incremental investments to support potential launch of a triple combination regimen and investment to support expansion of pipeline into additional disease areas
Combined GAAP R&D and SG&A	$1.97B	**$2.0 - $2.15B**	
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 Q1 2019 press release dated April 30, 2019*

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Appendix

Reconciliation of GAAP to non-GAAP Financial Information

	Q1 2018	FY 2018	Q1 2019
GAAP total revenues	$641	$3,048	**$858**
Non-GAAP total revenues	$639	$3,043	**$858**
GAAP operating income	129	635	**277**
Stock compensation expense	78	325	**94**
Other adjustments	1	152	**6**
Non-GAAP operating income	208	1.11B	**377**
Operating Margin %:			
GAAP	20%	21%	**32%**
Non-GAAP	33%	37%	**44%**
Net income			
GAAP	210	2.10B	**269**
Non-GAAP	196	1.06B	**296**
Net income per share - diluted			
GAAP	$0.81	$8.09	**$1.03**
Non-GAAP	$0.76	$4.08	**$1.14**

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