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Second Quarter 2018 Earnings Call

July 25, 2018

Agenda

Introduction

Michael Partridge, Senior Vice President, Investor Relations

Business Highlights

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

Second-Quarter 2018 Financial Results

Ian Smith, Executive Vice President and Chief Operating Officer

Q&A

Stuart Arbuckle, Executive Vice President and Chief Commercial Officer

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

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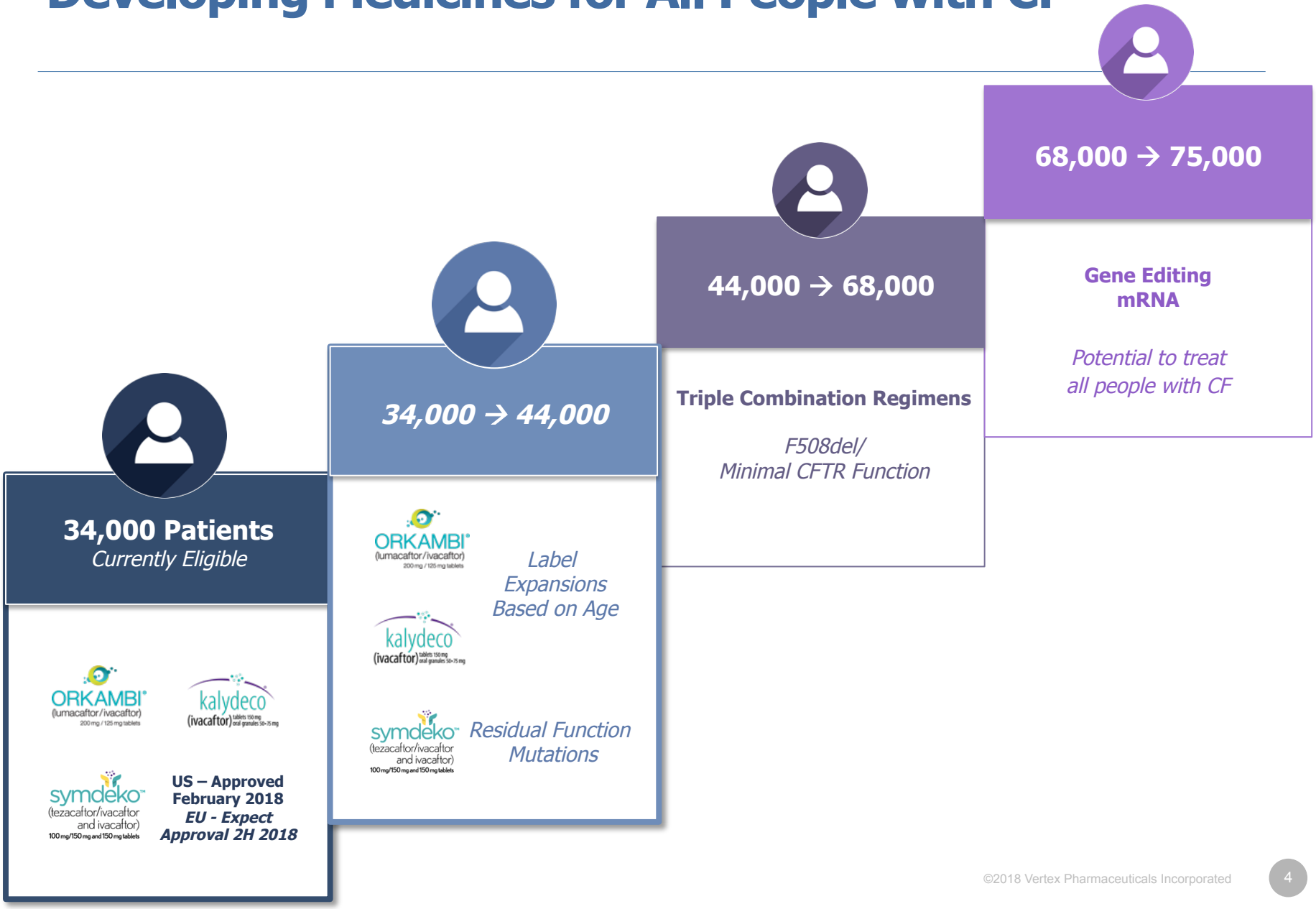
Safe Harbor Statement & Non-GAAP Financial Measures

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, including, without limitation, the information provided in the slide captioned "2018 Financial Guidance" and statements regarding (i) the timing and expected outcome of regulatory applications, including NDAs and MAAs and (ii) the development plan and timelines for our product development candidates, including tezacaftor in combination with ivacaftor and our next-generation triple combination regimens. While Vertex believes the forward-looking statements contained in this presentation 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 factors that could cause actual events or results to differ materially from those indicated by such forward-looking statements. Those risks and uncertainties include, among other things, that the company's expectations regarding its 2018 CF net product revenues and expenses 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 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 (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) non-operating tax adjustments and (iv) other adjustments, including gains or losses related to the fair value of the company's strategic investments in CRISPR and Moderna Therapeutics, Inc. 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 a non-GAAP basis. The guidance regarding GAAP research and development expenses and sales, general and administrative expenses does not include estimates regarding expenses associated with any potential future business development activities. A reconciliation of the GAAP financial results to non-GAAP financial results is included in the Company’s July 25, 2018 press release.

Developing Medicines for All People with CF



First-Half 2018 Progress

SYMDEKO U.S. Approval and Launch:

- Strong demand from wide range of eligible patients
- Broad access from private and public payers; similar to U.S. launches for KALYDECO and ORKAMBI

Treating Younger Patients with our CF Medicines:

- FDA approvals pending for KALYDECO in ages 12 to <24 months and ORKAMBI in ages 2 to 5; PDUFA dates in August 2018
- Data expected in 2H 2018 from Phase 3 studies evaluating ivacaftor in infants ages 6 to <12 months and tezacaftor/ivacaftor in children ages 6 to 11

Rapid Enrollment of Phase 3 Programs for Triple Combination Regimens:

- VX-659 and VX-445 Phase 3 programs expected to complete enrollment in 2H 2018
- NDA submission anticipated no later than mid-2019

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Vertex Strategy and Business Model

CORPORATE STRATEGY

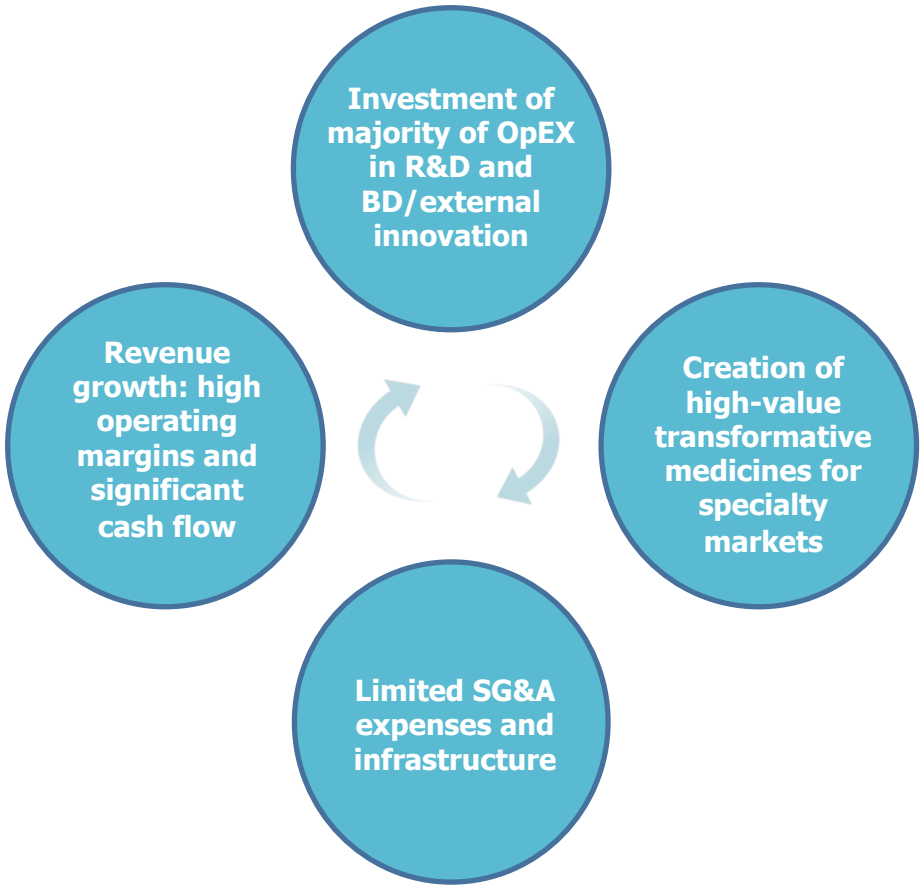
Vertex invests in **scientific innovation** to create **transformative medicines** for people with **serious diseases** with a focus on **specialty markets**

RESEARCH STRATEGY

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

- ✓ **Life-threatening, unmet need**
- ✓ **Insights into human biology; novel therapeutic approach**
- ✓ **Predictive assays and biomarkers**
- ✓ **Efficient clinical trial path**
- ✓ **Specialty sales and G&A model**

DIFFERENTIATED BUSINESS MODEL



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Key Milestones and Goals

	2017	2018
ACHIEVE OUR VISION IN CYSTIC FIBROSIS	☑ Approval of KALYDECO in residual function mutations ☑ Phase 3 tezacaftor/ivacaftor data in multiple mutations ☑ Phase 1 and 2 proof-of-concept data for multiple triple combination regimens in CF patients	☑ 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
EXPAND PIPELINE BEYOND CF	☑ Initiated additional Phase 2 studies of VX-150 in acute and neuropathic pain ☑ Bolstered CF and non-CF pipeline with internal and external assets	☐ Advance one or more compounds from research into clinical development ☐ Initiate clinical development of CRISPR-Cas9 treatment in Beta Thalassemia & Sickle Cell Disease
BUILD FINANCIAL STRENGTH	☑ Achieved total 2017 CF product revenues of $2.17B; 29% growth vs. 2016 ☑ Disciplined management of expenses (combined non-GAAP R&D and SG&A); <12% percent growth vs. 2016 ☑ Significant increase in operating margins	☑ 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

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Q2 2018 Financial Highlights

($ in millions except per share data and percentages)	Q2 17	FY 2017	Q1 18	Q2 18	1H 2018
Total CF product revenues	$514	$2.17B	$638	**$750**	$1.39
Combined non-GAAP R&D and SG&A	333	1.33B	360	**388**	748
Non-GAAP operating income	112	564	208	**260**	468
Non-GAAP operating margin	22%	26%	33%	**35%**	34%
Non-GAAP net income	99	495	196	**244**	440
Non-GAAP net income per share - diluted	$0.39	$1.95	$0.76	**$0.94**	$1.70
Cash, cash equivalents & marketable securities (quarter-end)		$2.1B		**$2.8B**	

- *An explanation of non-GAAP financial measures and reconciliation of non-GAAP combined R&D and SG&A expense, non-GAAP net income and non-GAAP net income per share is included in the company's Q2 2018 press release dated July 25, 2018*
- *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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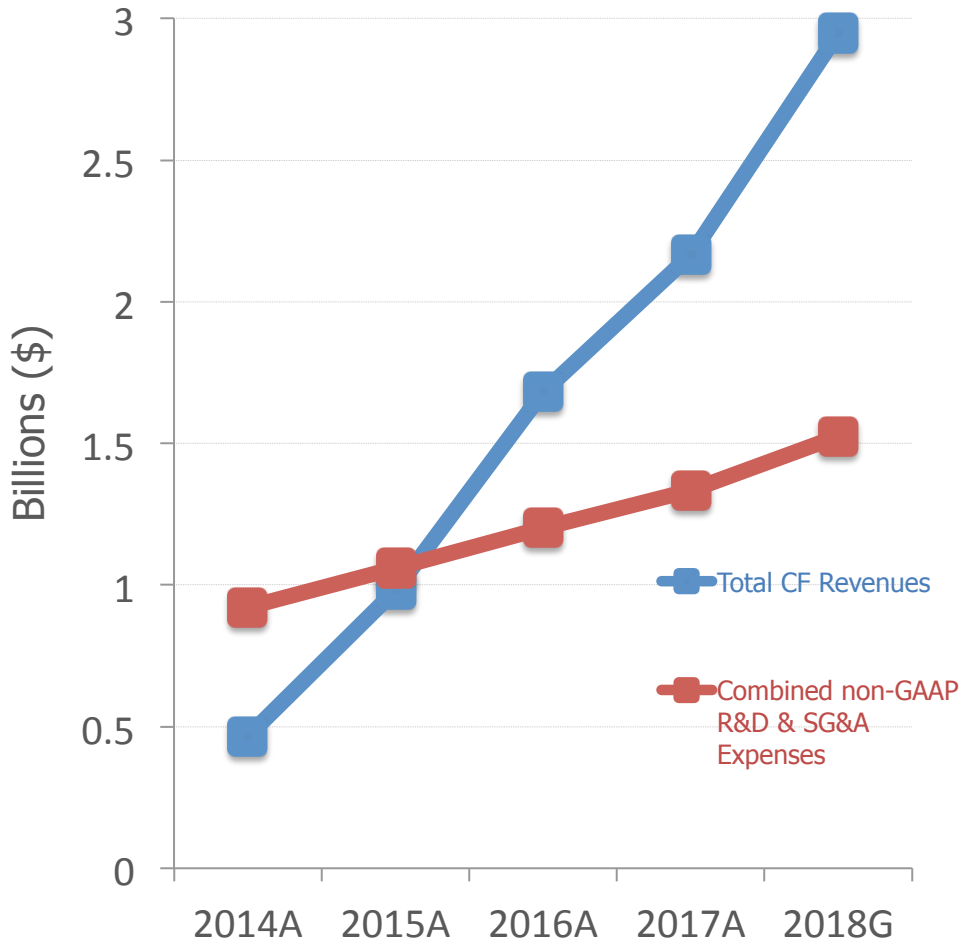
2018 Financial Guidance

	FY 2017 Actuals	2018 Guidance	2018 Guidance Commentary
Total CF Product Revenues	$2.17B	**$2.9 - $3.0B**	Increased guidance from $2.65-$2.80B based on: • Continued rapid uptake and strong demand for SYMDEKO in U.S. among ages 12+
Combined non-GAAP R&D and SG&A	$1.33B	**$1.50 - $1.55B**	Guidance unchanged and based on: • Execution of Phase 3 studies for two separate triple combination regimens • Supply chain investment for triple combination regimens • Incremental investment to support SYMDEKO launch
Combined GAAP R&D and SG&A	$1.82B	**$1.80 - $1.95B**	

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 Q2 2018 press release dated July 25, 2018

Significant Growth in Revenue Driving Operating Margin Expansion



- *2018 Total CF Revenues (guidance: $2.9– $3.0B) and combined non-GAAP R&D and SG&A expenses (guidance: $1.50 - $1.55B) graphed to reflect the midpoint of guidance ranges.*
- *Operating margins reflect total CF revenues, combined non-GAAP R&D and SG&A expenses and cost of sales.*
- *2018 projected operating margin based on the midpoint of guidance ranges and assumes a ~13.5% cost of sales; not intended as financial guidance.*

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Reconciliation of GAAP to non-GAAP Financial Information

($ in millions except per share data and percentages)	Q2 2017	FY 2017	Q1 2018	Q2 2018
GAAP total revenues	$544	$2,489	$641	$752
Non-GAAP total revenues	$517	$2,174	$639	$751
GAAP income from operations	53	123	129	173
Stock compensation expense	73	291	78	82
Collaborative and transaction revenues and expenses	(17)	133	1	4
Other adjustments	4	17	0	2
Non-GAAP income from operations	$112	$564	$208	$260
Operating Margin %:				
GAAP	10%	5%	20%	23%
Non-GAAP	22%	26%	33%	35%
Net income				
GAAP	18	263	210	207
Non-GAAP	99	495	196	244
Net income per share - diluted				
GAAP	$0.07	$1.04	$0.81	$0.80
Non-GAAP	$0.39	$1.95	$0.76	$0.94

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