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THE SCIENCE *of* POSSIBILITY

Third-Quarter 2017 Financial Results

October 25, 2017

Agenda

Introduction

Michael Partridge, VP Investor Relations

Business Update

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

Clinical Update

Jeff Chodakewitz, M.D., Executive Vice President and Chief Medical Officer

Third-Quarter Financial Results and 2017 Financial Guidance

Ian Smith, Executive Vice President and Chief Operating Officer

Q&A

Stuart Arbuckle, Executive Vice President, Chief Commercial 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 KALYDECO and ORKAMBI and the ongoing discovery, development and commercialization of Vertex's product candidates, and (ii) information regarding the Company's financial guidance for 2017. 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, that the Company's expectations regarding its 2017 revenues and expenses may be incorrect (including because one or more of the Company's assumptions underlying its expectations may not be realized), 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, and the risks and uncertainties listed in the Company's October 25, 2017 press release and 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 (i) stock-based compensation expense, (ii) revenues and expenses related to business development transactions including collaboration agreements and asset acquisitions, (iii) revenues and expenses related to consolidated variable interest entities, including asset impairment charges and related income tax benefits and the effects of the deconsolidation of a variable interest entity and (iv) other adjustments. 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 October 25, 2017 press release.

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Key Milestones and Goals

	2017	2018
CYSTIC FIBROSIS	✓ Phase 3 tezacaftor/ivacaftor data in multiple mutations ✓ Phase 1 and 2 proof-of-concept data for multiple triple combination regimens in CF patients ✓ Approval of KALYDECO in residual function mutations	○ Phase 2 data for VX-445 and VX-659 triple combinations in CF patients (1H18) ○ Initiation of pivotal development of up to two triple combination regimens (1H18) ○ Approval for tezacaftor/ivacaftor combination in the U.S. (1Q18) and Europe (2H18) ○ Advance additional next-generation correctors into development
FINANCIAL	○ Total 2017 CF revenues of $2.10 - $2.15B ✓ Obtain reimbursement for ORKAMBI in multiple countries outside the U.S. ○ Total 2017 non-GAAP combined R&D and SG&A expenses of $1.33 - $1.36B	○ Continued growth in product revenues ○ Management of operating expense ○ Additional reimbursement agreements for ORKAMBI outside the U.S.
PIPELINE	✓ Bolster the CF and non-CF pipeline with internal and external assets ✓ Initiate additional Phase 2 studies of VX-150 in acute and neuropathic pain	○ Advance one or more compounds from research into clinical development

Phase 3 Study of ORKAMBI in Children Ages 2 to 5

- ORKAMBI was well tolerated and led to improvements in CF-related disease measures, including sweat chloride and nutritional status
- No new safety concerns compared to prior studies of ORKAMBI in people ages 6 through 11
- First data indicating safety and benefit of ORKAMBI in young children with CF
- NDA and MAA submissions planned for Q1 2018

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Phase 3 Study of Tezacaftor/Ivacaftor Combination in Gating Mutations

- Tezacaftor/ivacaftor combination was generally well tolerated and safety profile was consistent with prior Phase 3 studies of tezacaftor/ivacaftor combination
- No change in ppFEV$_1$ when tezacaftor was added to ivacaftor compared to people who continued to receive ivacaftor monotherapy
- Decrease in sweat chloride of 5.8 mmol/L when tezacaftor was added to ivacaftor compared to people who continued to receive ivacaftor monotherapy, similar to prior Phase 2 study
- Vertex does not plan to seek regulatory approval for tezacaftor/ivacaftor combination for people with gating mutations

Vast majority of gating patients are eligible for and are receiving KALYDECO

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Phase 2 Study of VX-371 (ENaC inhibitor) in Combination with ORKAMBI

- In people already receiving ORKAMBI, no improvement in ppFEV$_1$ was observed through Day 28 with the addition of VX-371, with or without hypertonic saline
- Addition of VX-371 to ORKAMBI was generally well tolerated and safety profile was consistent with prior studies of VX-371 monotherapy

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Q3 2017 Financial Results

($ in millions)	FY 2016	Q1 17	Q2 17	Q3 17	YTD 2017
ORKAMBI	980	295	324	**336**	955
KALYDECO	703	186	190	**213**	589
Total CF product revenues	$1.68B	481	514	**550**	$1.54B
Combined non-GAAP R&D and SG&A	$1.20B	313	333	**334**	$980M
Non-GAAP operating income	288	122	112	**145**	380
Non-GAAP operating margin	17%	25%	22%	**26%**	24%
Cash, cash equivalents & marketable securities (quarter-end)	$1.43B	$1.41B	$1.67B	**$1.81B**	

(1) 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 October 25, 2017 press release.

(2) Reconciliation of non-GAAP operating income and non-GAAP operating margin to corresponding GAAP measures is included in Appendix A of this presentation

2017 Financial Guidance

	FY 2016 Actuals	Previous 2017 Guidance	Current 2017 Guidance	2017 Guidance Commentary
ORKAMBI	$980M	$1.1 - $1.3B	**$1.29 - $1.32B**	• Strong underlying demand in U.S. for ages 6+ and potential revenues from countries where OKB is currently reimbursed • Does not assume product revenues from France in 2017
KALYDECO	$703M	$770 - $800M	**$810 - $830M**	• Recent label expansions • Strong underlying demand from eligible patients
Total CF product revenues	$1.68B	$1.87 - $2.10B	**$2.10 - $2.15B**	
Combined non-GAAP R&D and SG&A	$1.20B	unchanged	**$1.33 - $1.36B**	Expected growth in remainder of 2017 from: • Progression of CF portfolio • Preparation and acceleration of triple-combination studies • Investment in development of VX-561
Combined GAAP R&D and SG&A	$1.48B	unchanged	**$1.79 - $1.92B**	• As above • Includes recognition of $160M R&D expense associated with acquisition of VX-561 • Includes stock-comp expense

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 October 25, 2017 press release.

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Appendix A

Reconciliation of GAAP to non-GAAP Financial Information

	FY 2016	Q1 2017	Q2 2017	Q3 2017	FY 2017
GAAP total revenues	$1,702	$715	$544	$578	$1,837
Non-GAAP total revenues	$1,701	$482	$517	$552	$1,551
GAAP income (loss) from operations	$10	$271	$53	$(326)	$(2)
Stock compensation expense	238	69	73	74	215
Concert upfront and transaction expenses	-	-	4	161	165
Revenues and expenses related to VIEs	10	2	(18)	(16)	(33)
Other collaborative and transaction revenue and expenses	33	(230)	(3)	252	19
Other adjustments	(2)	11	4	1	16
Non-GAAP income from operations	$288	$122	$112	$145	$380
Operating Margin %:					
GAAP	1%	38%	10%	-56%	0%
Non-GAAP	17%	25%	22%	26%	24%

All numbers in the above reconciliation table are in millions, totals may not add due to rounding.