THE SCIENCE *of* POSSIBILITY

VERTEX

First Quarter 2016 Financial Results

April 27, 2016

Agenda

Introduction

Michael Partridge, VP Investor Relations

CF Strategy Update

Jeff Leiden, M.D., Ph.D., Chairman and CEO

ORKAMBI Launch Update

Stuart Arbuckle, Chief Commercial Officer

First Quarter 2016 Financial Results

Ian Smith, Chief Financial Officer

Q&A

Safe Harbor Statement

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, including, without limitation, information pertaining to KALYDECO® and ORKAMBI®, the ongoing discovery, development and commercialization of Vertex's product candidates and the Company's future financial performance. 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 others, 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 April 27, 2016 press release and under Risk Factors in the Company's 10-K and other filings with the SEC.

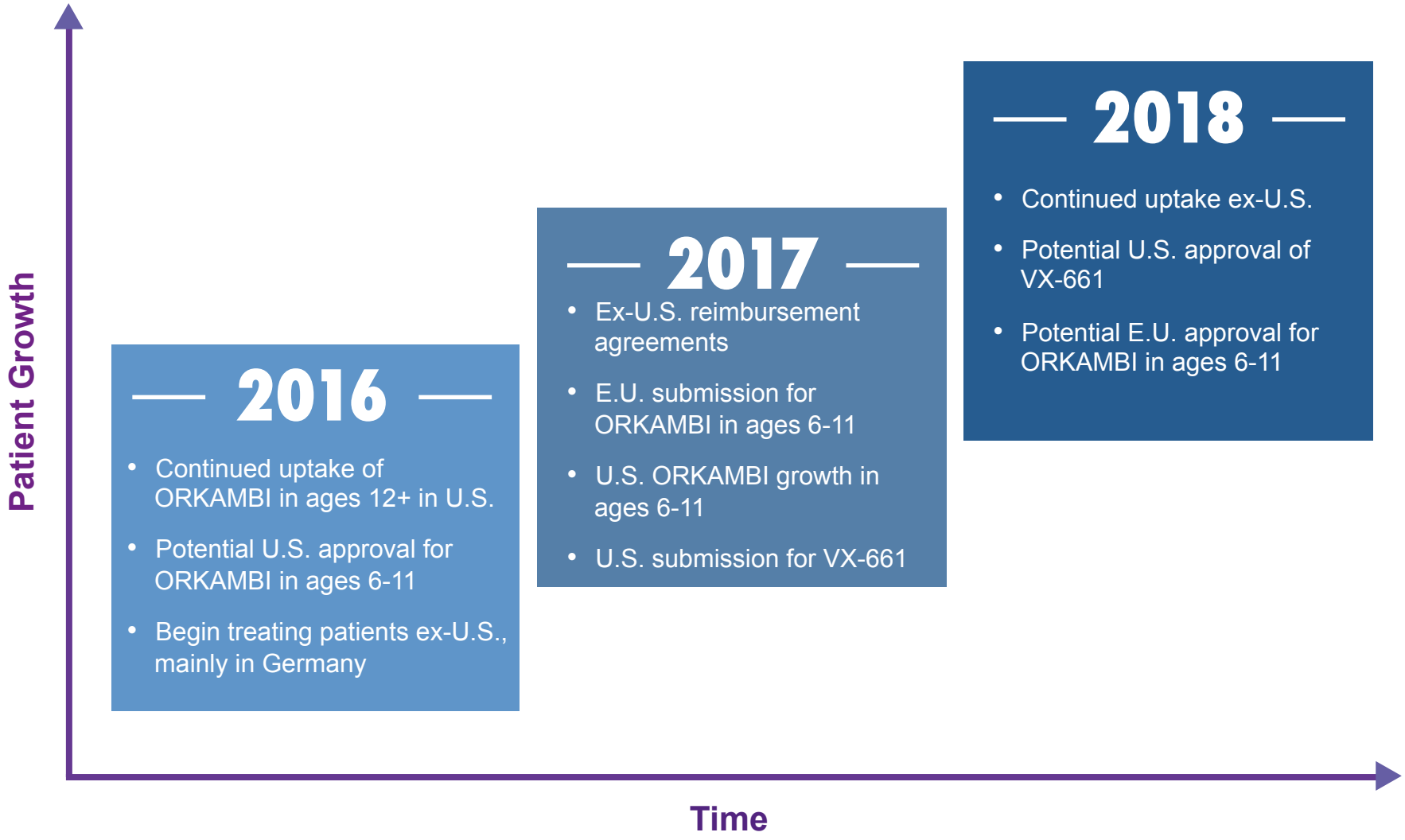
Non-GAAP Financial Measures

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 exclude stock-based compensation expense, costs and credits related to the relocation of the company's corporate headquarters and hepatitis C-related revenues and costs and 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. A reconciliation of the GAAP financial results to non-GAAP financial results is included in the attached financial information.

Vertex CF Opportunity

Total Patients Eligible Today or Potentially Eligible in the Future	Patient Groups	Treatment
Today ~27,000	F508del/F508del ages 12+ (US, EU, CAN, AUS) G551D & gating ages 2+ (WW) R117H ages 2+ (US) R117H ages 18+ (EU, CA) R117H ages 6+ (AUS)	Currently eligible for **ORKAMBI** or **KALYDECO**
From ~27,000 to ~44,000	F508del/F508del under age 12 (WW) Residual function; under age 2 (WW)	Potential label expansions for **ORKAMBI** or **KALYDECO**
From ~44,000 to More than 60,000	F508del/Minimal Function ages 6+ (WW)	Potential to address with **next-generation corrector combinations** or other medicines

CF Strategy



VX-661 + Ivacaftor

Potential for Broad Benefit for CF Patients

Phase 3 studies ongoing to evaluate efficacy and safety in CF patients ages 12+ across 4 groups

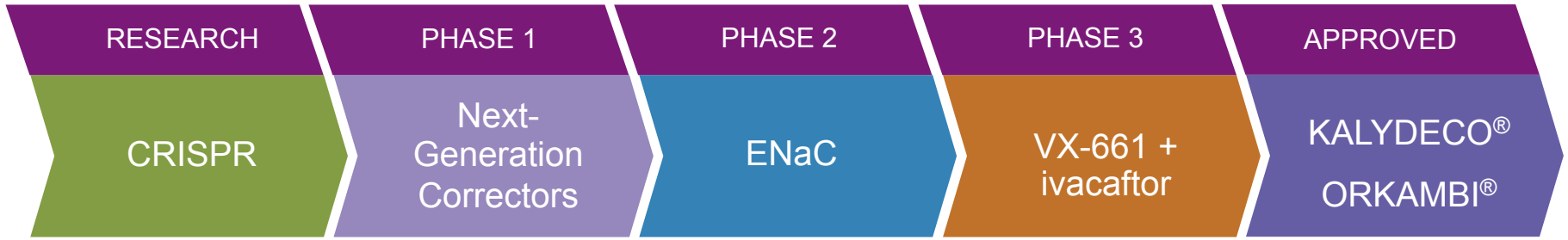
Dual combination could play an important role in treatment of CF, including:

- Improved benefit-risk profile in people with two copies of *F508del* mutation compared to ORKAMBI
- Potential to provide enhanced clinical benefit over KALYDECO for other patients with gating mutations
- Potential to play key role in development of triple combination with a next-generation corrector and KALYDECO

On track to obtain first data from study in people with two copies of F508del mutation in early 2017

Vertex Goal

Long-Term Leadership in CF



RESEARCH

- Gene editing research collaboration to evaluate potentially all CF mutations
- Initial focus in CF and Sickle Cell Disease

PHASE 1

- Phase 1 underway with Next-Gen correctors VX-152 and VX-440
- Phase 2, 28-day triple combination study in patients planned to begin 2H16

PHASE 2

- Initiated Phase 2 combination study with ORKAMBI in 1Q 2016
- Phase 2 monotherapy study completed in April 2016
- Potential complementary mechanism for current and future CF treatments

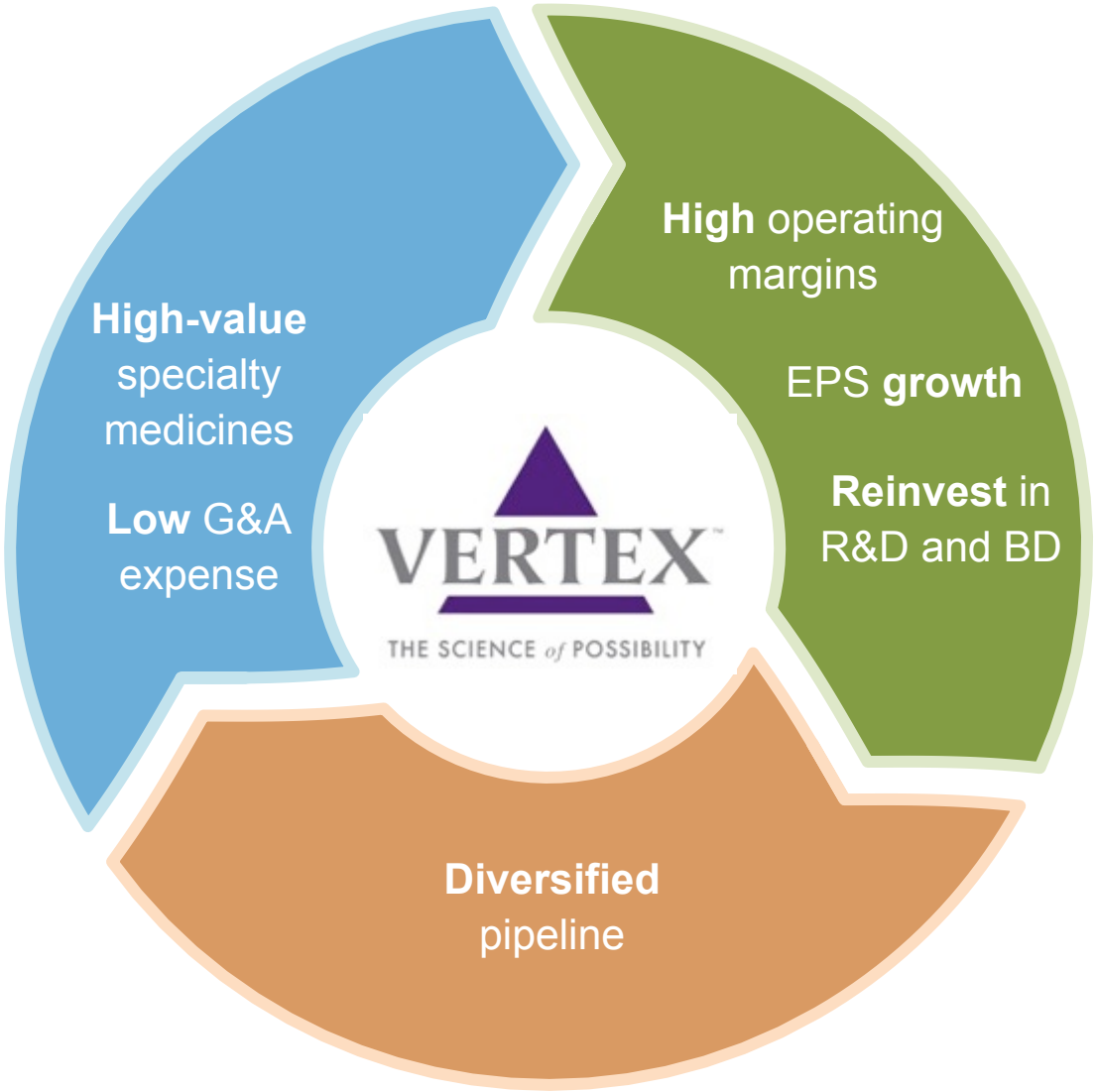
PHASE 3

- Ongoing broad Phase 3 program
- Potential opportunity to provide improved benefit-risk profile v. ORKAMBI and enhanced clinical benefit over KALYDECO
- Key role in development of triple combination regimen

APPROVED

- Approximately 27,000 patients eligible for treatment with ORKAMBI or KALYDECO in U.S., E.U., Canada and Australia

Building a Sustainable Business in CF and Beyond



Create **high-value** breakthrough medicines

Allow **significant reinvestment** in R&D

Maximize **shareholder returns**

ORKAMBI Launch Update

1Q'16 ORKAMBI net revenues of $223M

- 1Q'16 geographic breakout:
  - $214M in U.S.
  - $9M ex-U.S. (primarily Germany)
- As of March 31, 2016, approximately 5,500 patients ages 12+ with two copies of the F508del mutation have started treatment in the U.S.

- Broad access to the medicine through public and private insurance with assistance programs in place for eligible patients who need help
- sNDA submitted for treatment in ages 6-11 in the U.S. with two copies of the F508del mutation

ORKAMBI Guidance

Providing 2016 ORKAMBI guidance of $1.0 to $1.1 billion, based on:

- Continued uptake in people ages 12+ with two copies of F508del mutation in the U.S.
- Understanding of current treatment patterns, including persistence and compliance
- Anticipated approval in the U.S. for people ages 6-11 with two copies of the F508del mutation in 2H'16
- Ex-U.S. revenues, primarily from Germany

Continued KALYDECO Growth Based on Geographic and Label Expansion

1Q'16 KALYDECO net revenues of $171M, an increase of 31% v. $130M in 1Q'15

- Increased 2016 KALYDECO revenue guidance to $685 to $705 million from $670 to $690 million
- 2016 Market Dynamics:
  - Approved for approximately 4,000 patients worldwide
  - Continued uptake in eligible patients

First Quarter 2016 Financial Highlights

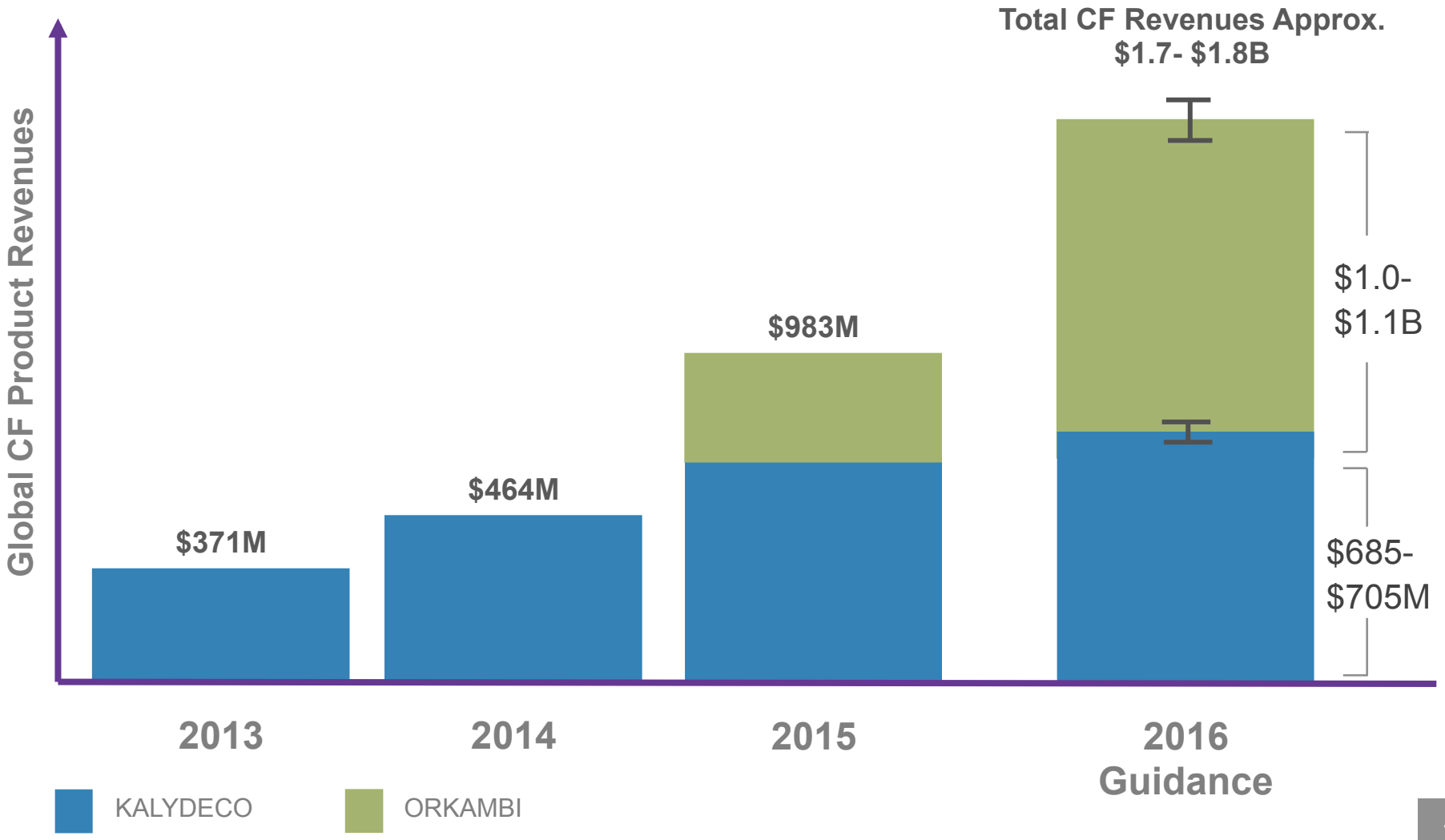
(in $M except per share data)	1Q'16	1Q'15
ORKAMBI Revenues	223	--
KALYDECO Revenues	171	130
Total CF Revenues	394	130
Combined Non-GAAP R&D and SG&A Expense*	306	246
Non-GAAP R&D Expense*	222	177
Non-GAAP SG&A Expense*	84	69
Non-GAAP Net Income (Loss)*	22	(148)
Non-GAAP Net Income (Loss) Per Share*	0.09	(0.62)
*Cash Balance at March 31, 2016**	*1.03B*	

**An explanation of the company's non-GAAP financial measures and a full reconciliation of GAAP to non-GAAP financial results is included in the company's press release dated April 27, 2016.*

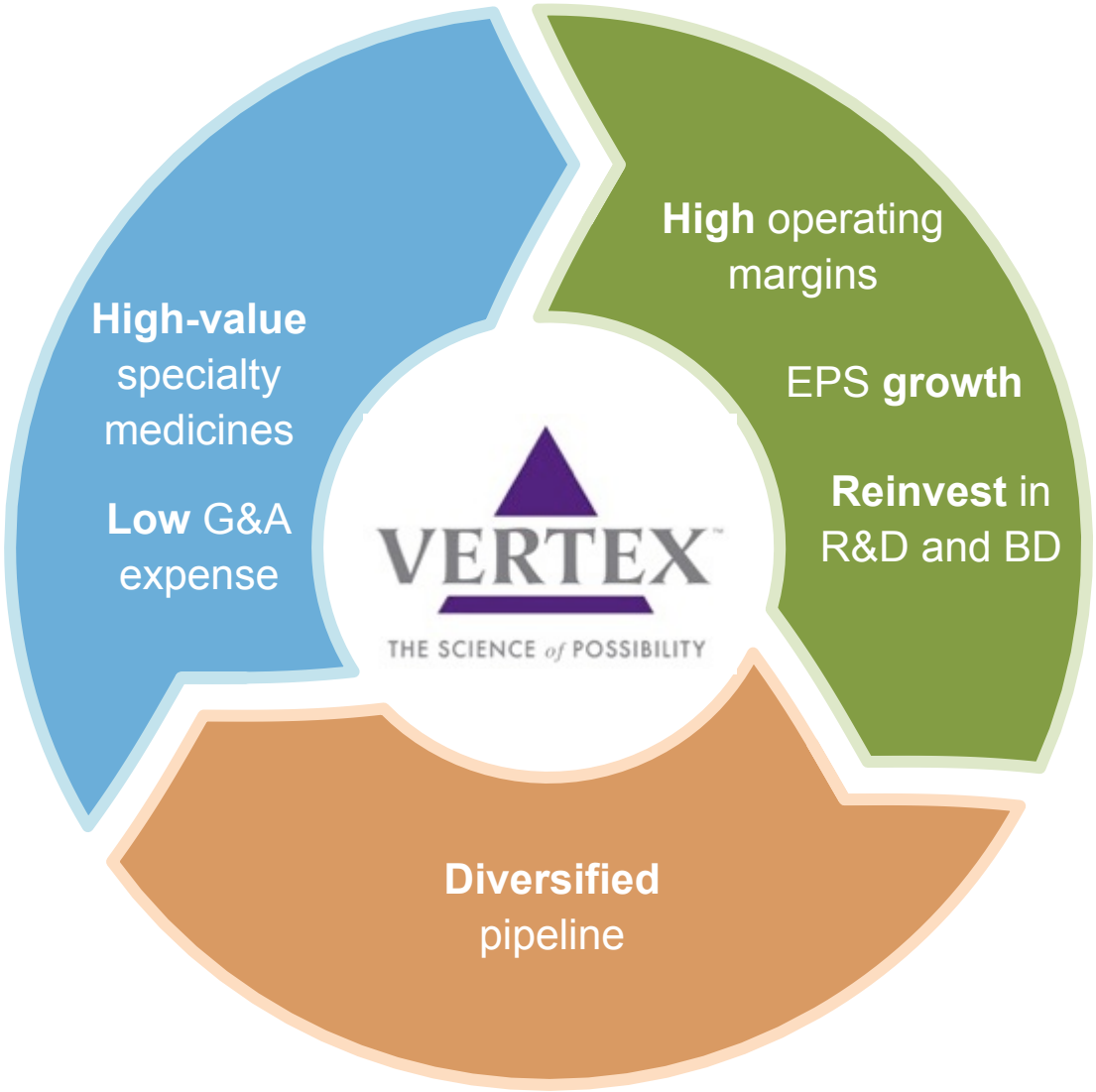
** Cash includes cash, cash equivalents and marketable securities. As of March 31, 2016 the company had $300M of term debt.*

**The company's GAAP net loss was $42M and $199M, respectively, GAAP R&D expense was $256M and $216M, respectively, and GAAP SG&A expense was $105M and $86M, respectively, in 1Q'16 and 1Q'15.*

Improving Financial Profile Through Continued KALYDECO and ORKAMBI Growth



Building a Sustainable Business in CF and Beyond



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