



THE SCIENCE *of* POSSIBILITY

Full-Year and Fourth-Quarter 2016 Financial Results

January 25, 2017

Agenda

Introduction

Michael Partridge, VP Investor Relations

Business Update

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

Full Year and Fourth Quarter Financial Results

Ian Smith, Executive Vice President, COO and CFO

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, (i) information pertaining to KALYDECO and ORKAMBI and the ongoing discovery, development and commercialization of Vertex's product candidates, (ii) information regarding the Company's financial guidance for 2017 and (iii) the Company's 2017 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, 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 January 25, 2017 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 and guidance exclude stock-based compensation expense, revenues and expenses related to consolidated variable interest entities, 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. 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 business development activities. A reconciliation of the GAAP financial results to non-GAAP financial results is included in the Company's January 25, 2017 press release.

Growing Our Business in 2017 and Beyond



Treating more patients



Creating new CF medicines



Reinvesting in other serious diseases

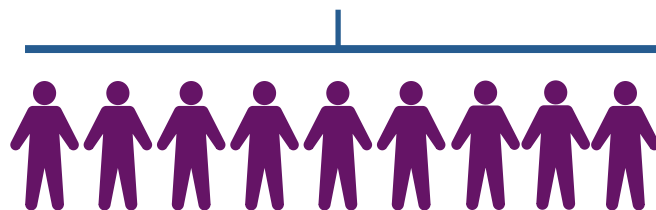
Growth for ORKAMBI

Increasing the Number of Eligible Patients Treated

*~25,000 Patients Eligible for Treatment with ORKAMBI
in US, Europe, Australia and Canada*

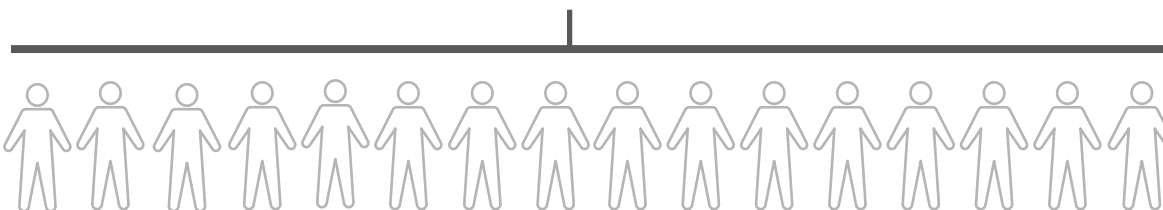
Initiated ORKAMBI

~9,000 Patients



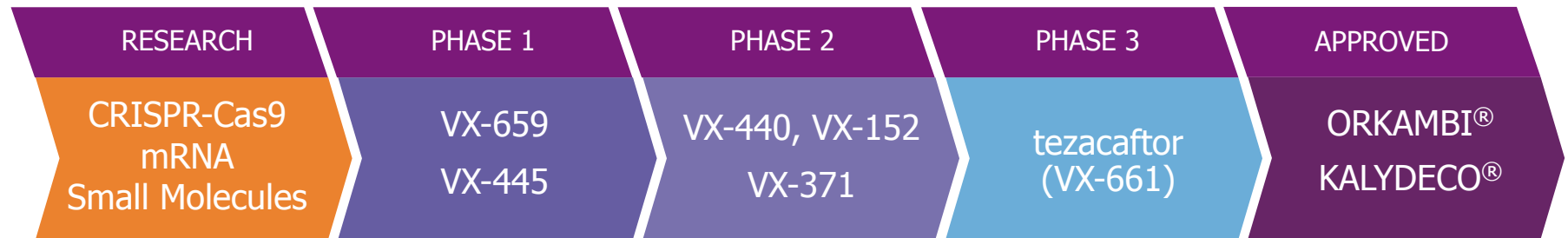
Not Initiated ORKAMBI

~16,000 Patients



*~13,000 Patients Outside the U.S.,
Primarily Those Awaiting Formal
Reimbursement Approvals*

Vertex CF Pipeline



RESEARCH

CRISPR/Cas9

- Gene editing research collaboration

mRNA

- Research collaboration and licensing agreement to develop mRNA Therapeutics™

Small Molecules

- Additional next-gen correctors potentially increasing benefit

PHASE 1

Next-Generation Correctors:

- Phase 1 study of VX-659 ongoing
- Phase 1 study of VX-445 planned for Q1 2017

PHASE 2

Next-Generation Correctors:

- Phase 2 studies of VX-440 and VX-152 ongoing

ENaC:

- Phase 2 study of VX-371 in combination with ORKAMBI ongoing

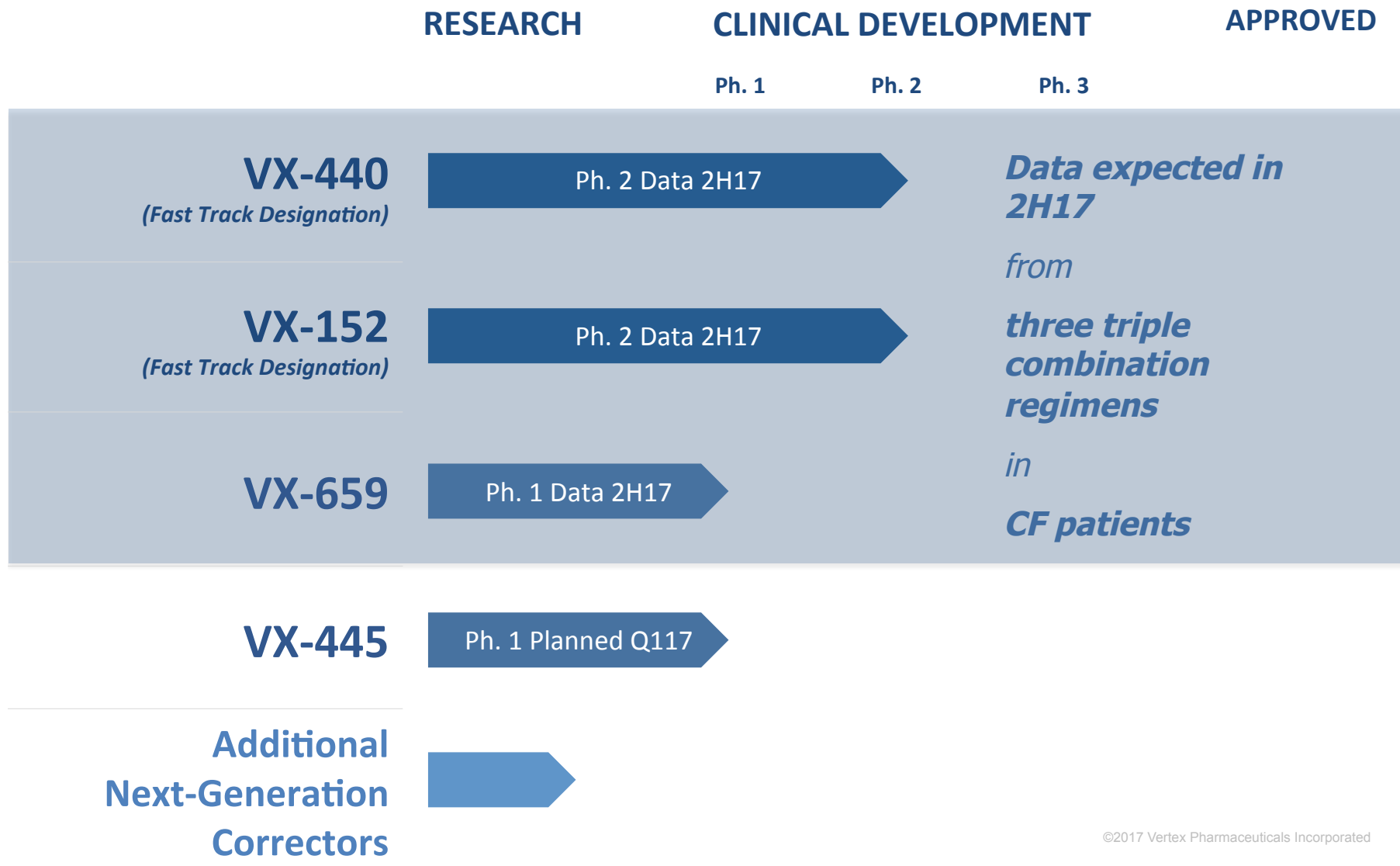
PHASE 3

- Ongoing broad Phase 3 program
- Key role in development of triple combination regimen

APPROVED

- First medicines to treat the cause of CF for people with specific mutations in the CFTR gene

Broad Portfolio of Next-Generation Correctors



Learnings in CF Have Transformed Our Investments in Early Research

Vertex invests in scientific innovation to create transformative medicines for specialty diseases.

RESEARCH PRINCIPLES

- **Focus** on validated targets that address causal human biology
- **Create** lab assays and clinical biomarkers to predict clinical response
- **Discover and develop** medicines that offer transformative benefit
- **Identify** rapid path to registration and beyond

DISEASES CURRENTLY BEING TARGETED IN VERTEX RESEARCH

Adrenoleukodystrophy (ALD)

Alpha-1 Antitrypsin Deficiency (AATD)

Sickle Cell Disease & Beta Thalassemia

Polycystic Kidney Disease

Key Q4 and Full Year 2016 Financial Metrics

<i>(in \$M except per share data)</i>	Q4 2016	FY 2016
ORKAMBI Revenues	\$277M	\$980M
KALYDECO Revenues	\$177M	\$703M
Total CF Revenues	\$454M	\$1.68B
Non-GAAP Combined R&D and SG&A Expense	\$295M	\$1.20B
Non-GAAP Net Income	\$88M	\$211M
Non-GAAP Net Income Per Share	\$0.35	\$0.85
<i>Cash Balance at December 31, 2016*</i>	\$1.43B	

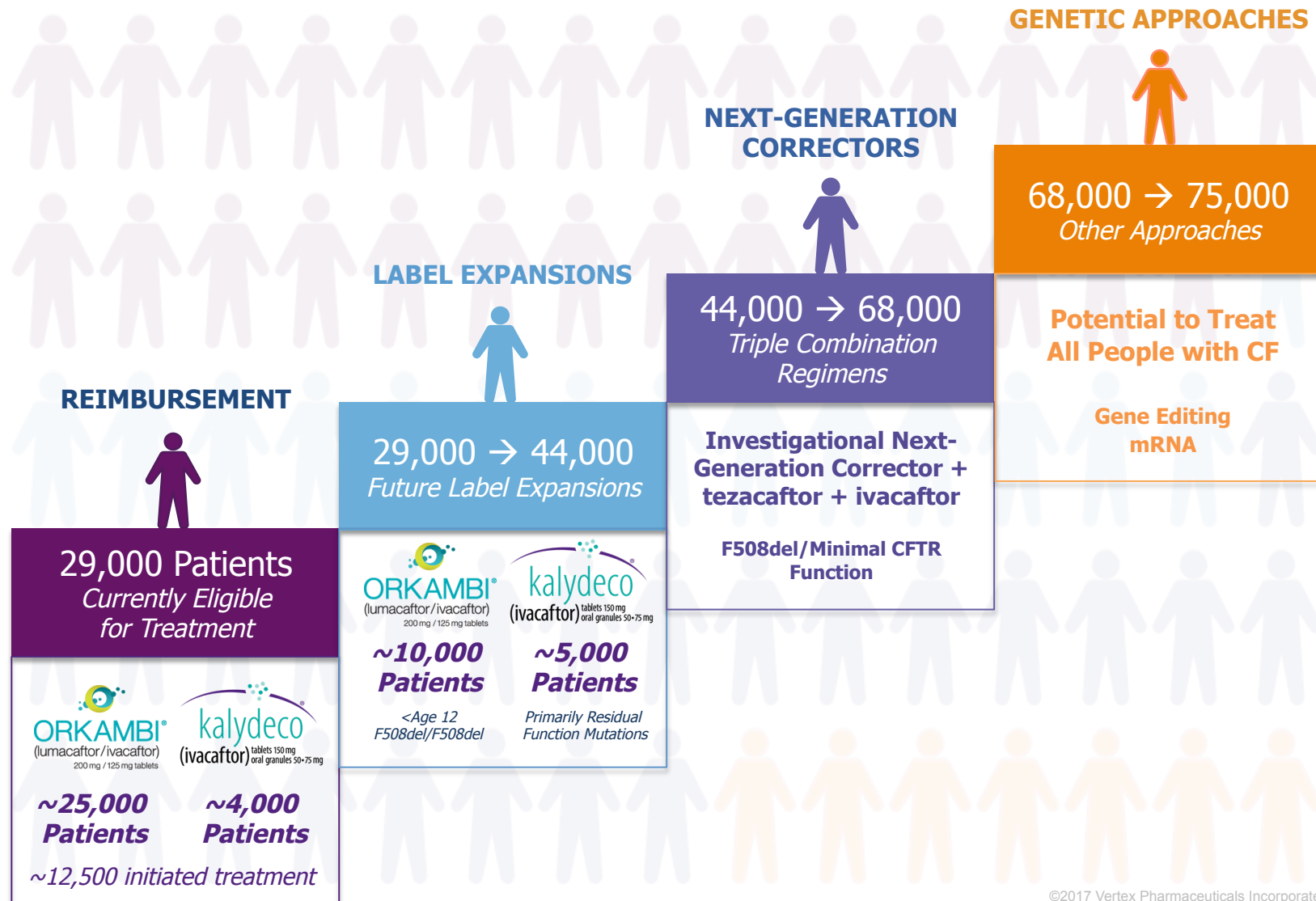
* Cash includes cash, cash equivalents and marketable securities. As of December 31, 2016, the company had \$300M of term debt. An explanation of our Non-GAAP financial measures and reconciliation of Non-GAAP combined R&D and SG&A expense is included in our January 25, 2017 press release.

2017 Financial Guidance

FY2017 Guidance	
ORKAMBI Revenues	\$1.1 – \$1.3B
KALYDECO Revenues	\$690 - \$710M
Total CF Revenues	\$1.79 - \$2.01B
GAAP Combined R&D and SG&A Expense	\$1.55 - \$1.70B
Non-GAAP Combined R&D and SG&A Expense	\$1.25 - \$1.30B

An explanation of our Non-GAAP financial measures is included in our January 25, 2017 press release.

Path to Treating All Patients



Key 2017 Milestones and Goals

CYSTIC FIBROSIS

- ☐ Phase 3 tezacaftor/ivacaftor data in multiple mutations (1H 17)
- ☐ Phase 2 proof-of-concept data for two triple combination regimens in CF patients (2H17)
- ☐ Phase 1 data for VX-659 triple combination in CF patients (2H 17)
- ☐ Clinical development of a 4th next-generation corrector (Q1 17)

FINANCIAL

- ☐ Total CF revenues of \$1.79 - \$2.01B
- ☐ Obtain reimbursement for ORKAMBI in multiple countries outside the U.S.
- ☐ Non-GAAP combined R&D and SG&A expenses of \$1.25 - \$1.3B

PIPELINE

- ☐ Bolster the CF and non-CF pipeline with internal and external assets
- ☐ Advance one or more compounds from research into clinical development