VERTEX

THE SCIENCE *of* POSSIBILITY

J.P. Morgan Healthcare Conference

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Chairman, President and CEO

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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, ORKAMBI, tezacaftor in combination with ivacaftor and the ongoing discovery, development and commercialization of Vertex's product candidates, (ii) graphical representations of future financial performance and (iii) Vertex's 2018 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 references financial guidance and results that have been 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 expenses on both a GAAP and a non-GAAP basis. The most recent reconciliation of the GAAP financial results to non-GAAP financial results is included in the Company's October 25, 2017 press release.

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 in 2H 2018) ☐ Advance additional next-generation correctors into development
EXPAND PIPELINE BEYOND CF	☑ Initiate additional Phase 2 studies of VX-150 in acute and neuropathic pain ☑ Bolster the 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	☑ Increased total CF revenue guidance from $1.79 - $2.01B to $2.1 - $2.15B; >25% 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 total 2018 CF 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

Notes: Growth for 2017 reflects the midpoint of the total CF revenue and non-GAAP R&D and SG&A expenses guidance provided on 10/25/17 versus 2016; not meant as a reiteration of guidance or as financial results

2018 and Beyond

Achieving our Vision in Cystic Fibrosis

Expanding Pipeline Beyond CF

Increasing Financial Strength

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Achieving our Vision in Cystic Fibrosis

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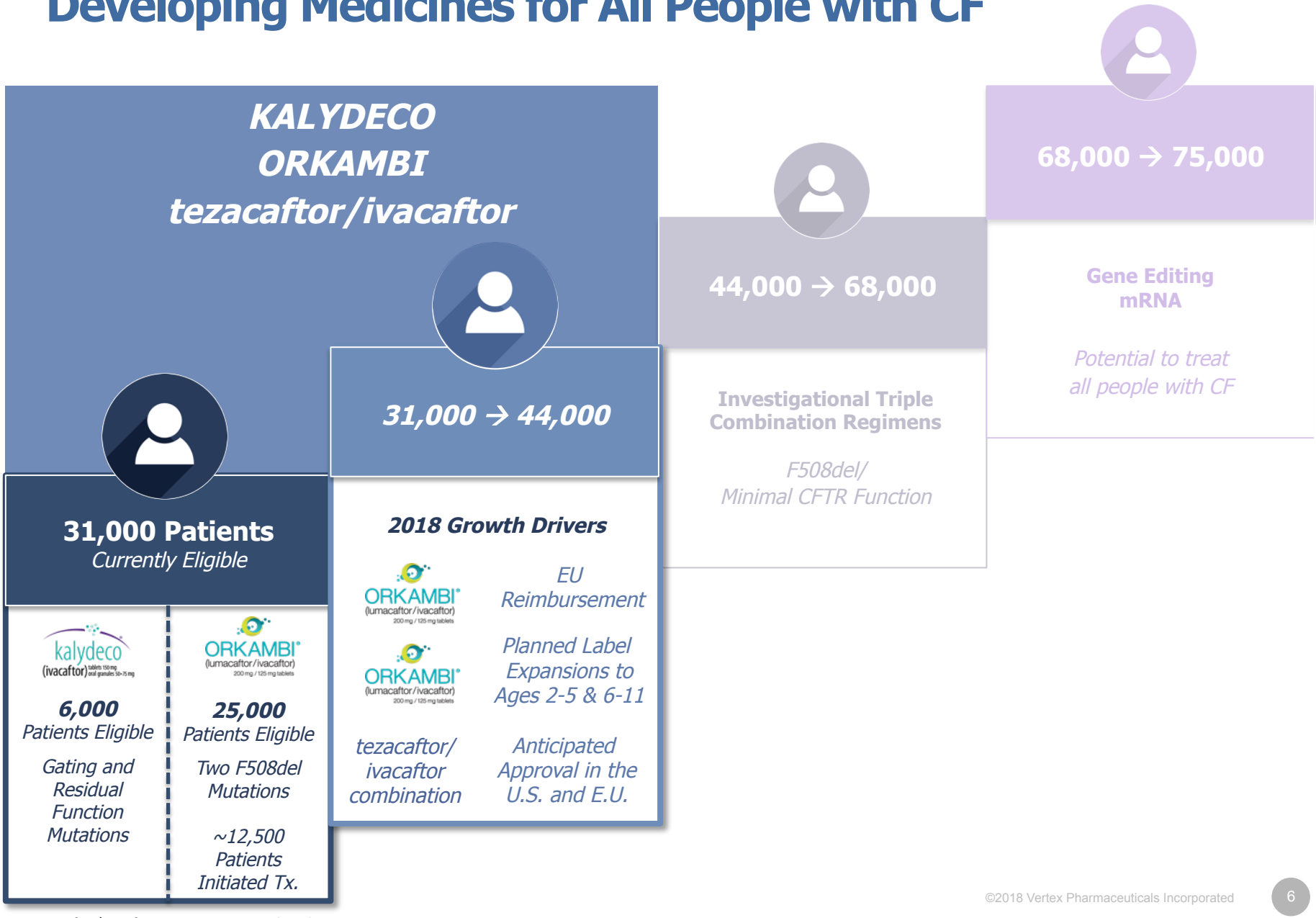
Increasing Financial Strength

Developing Medicines for All People with CF



Notes: Tezacaftor/ivacaftor is an investigational medicine

Tezacaftor/Ivacaftor

Potential To Significantly Increase Number of Eligible Patients Treated with a CFTR Modulator

Two Groups of Patients for Tezacaftor/Ivacaftor:

Two copies of the F508del mutation

- *Patients who discontinued ORKAMBI due to respiratory adverse events*
- *Patients who never initiated ORKAMBI*

Residual function mutations

U.S. PDUFA Date of February 28, 2018

EU Approval Expected in 2H 2018

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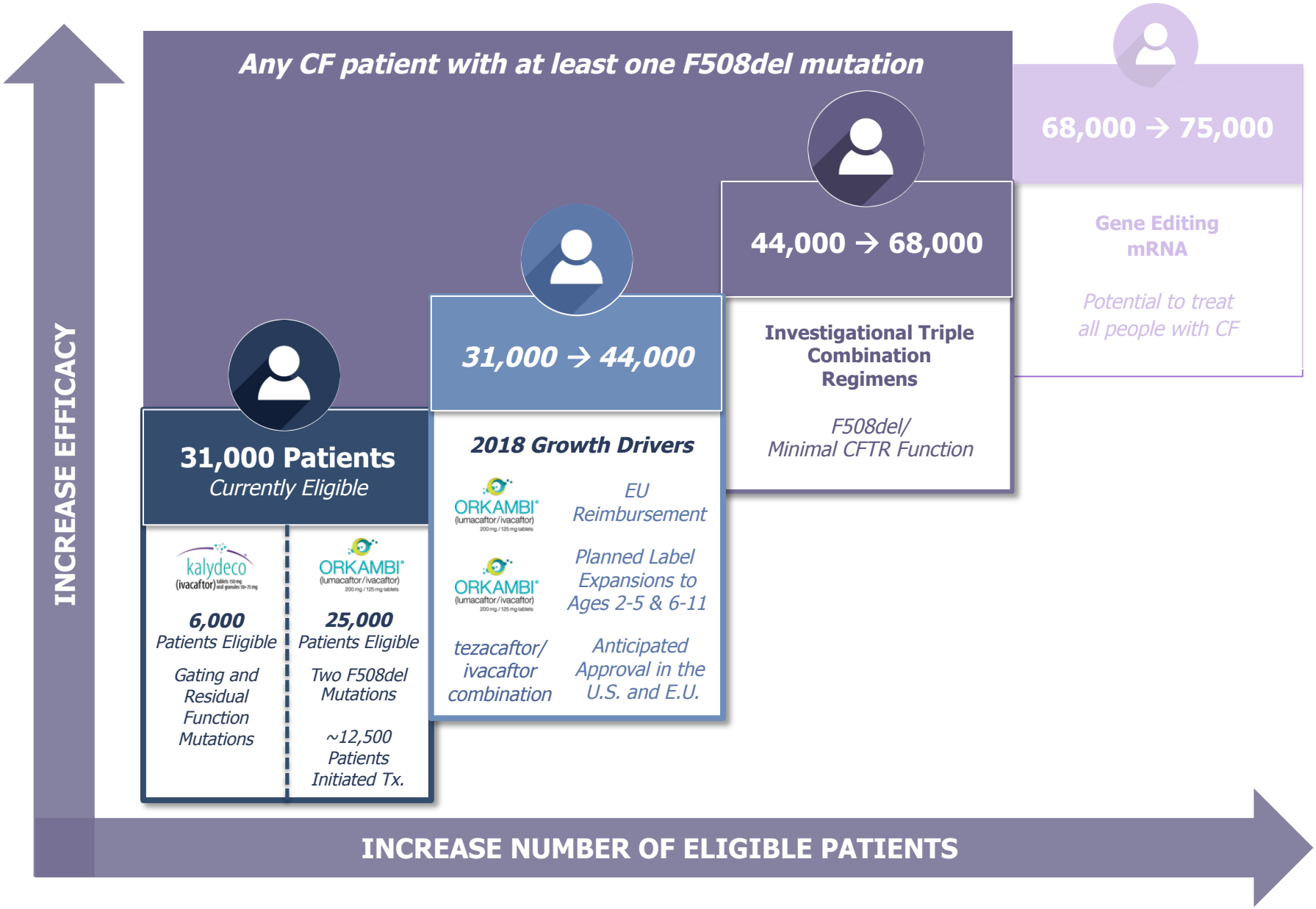
Notes: Tezacaftor/ivacaftor is an investigational medicine

Treating More Patients with Approved Medicines Drives Revenue Growth

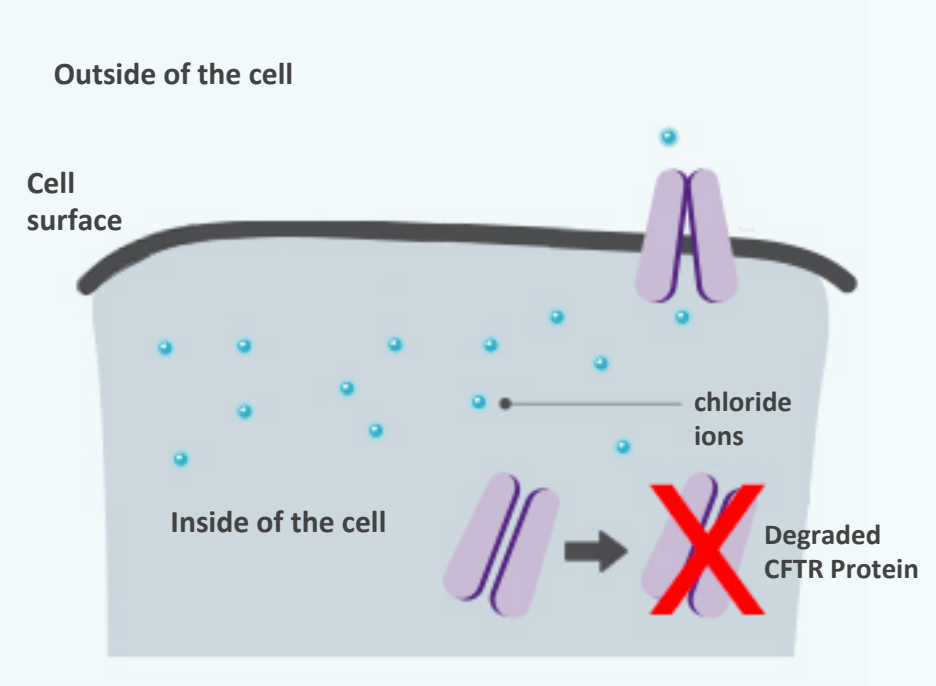
Notes: 2017 reflects the midpoint of the total CF revenue guidance provided on 10/25/17; not meant as a reiteration of guidance; 2018 potential growth in CF revenues provided as a graphical representation and not intended as financial guidance.

Triple Combination Regimens Have the Potential to Provide Additional Benefit for up to 90% of All Patients with CF

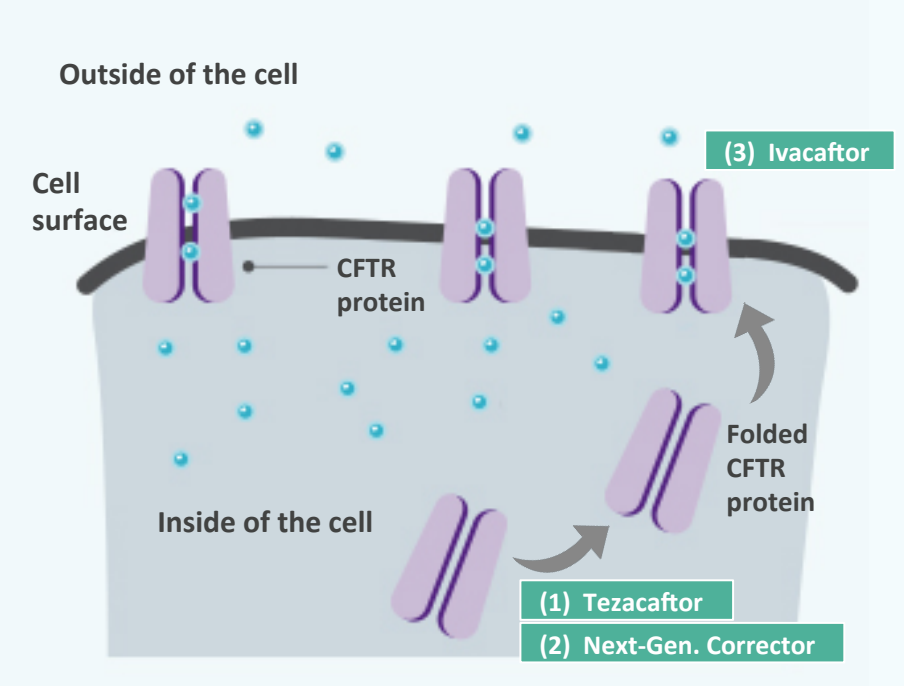


Triple Combinations to Enhance CFTR Function Via Three Additive Mechanisms

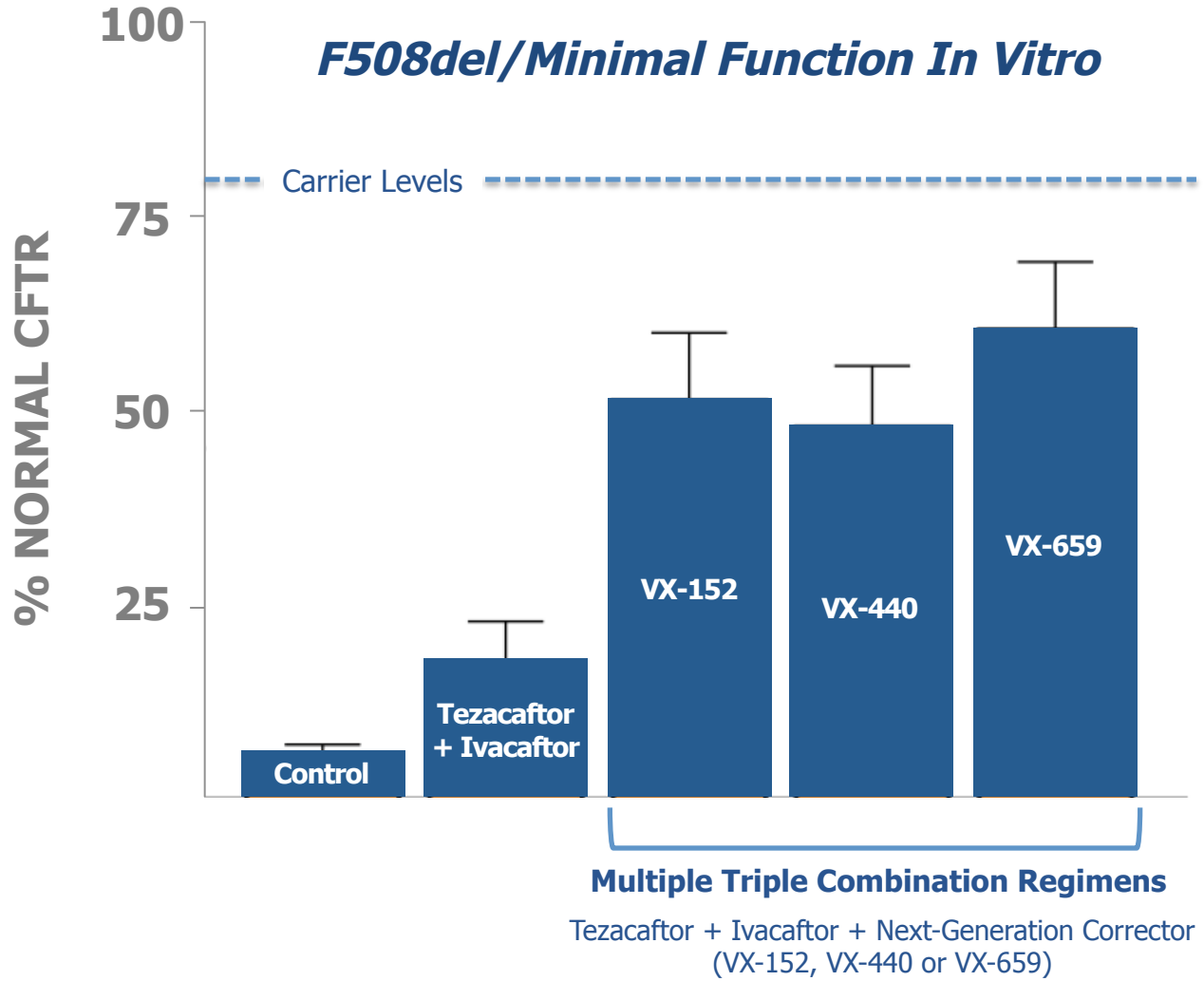
Untreated F508del Cell



Treated F508del Cell



Multiple Next-Generation Correctors Highly Active in Triple Combination in HBE Cells



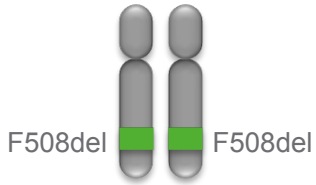
N = 4 donors (2 G542X; 1 3905InsT; 1 E585X); 96-well Ussing + 20% serum; Top of bar charts represent EC 90 concentrations

Van Goor F, et al. Presented at the 30th North American Cystic Fibrosis Conference, Orlando, Florida, October 27-29, 2016. Symposium S14.4.

Phase 1 and 2 Studies Show Consistent Clinical Benefit Across Multiple Patient Groups

INITIAL PHASE 1 & 2 RESULTS

VX-440, VX-152 and VX-659 IN COMBINATION WITH TEZACAFTOR AND IVACAFTOR



Homozygous

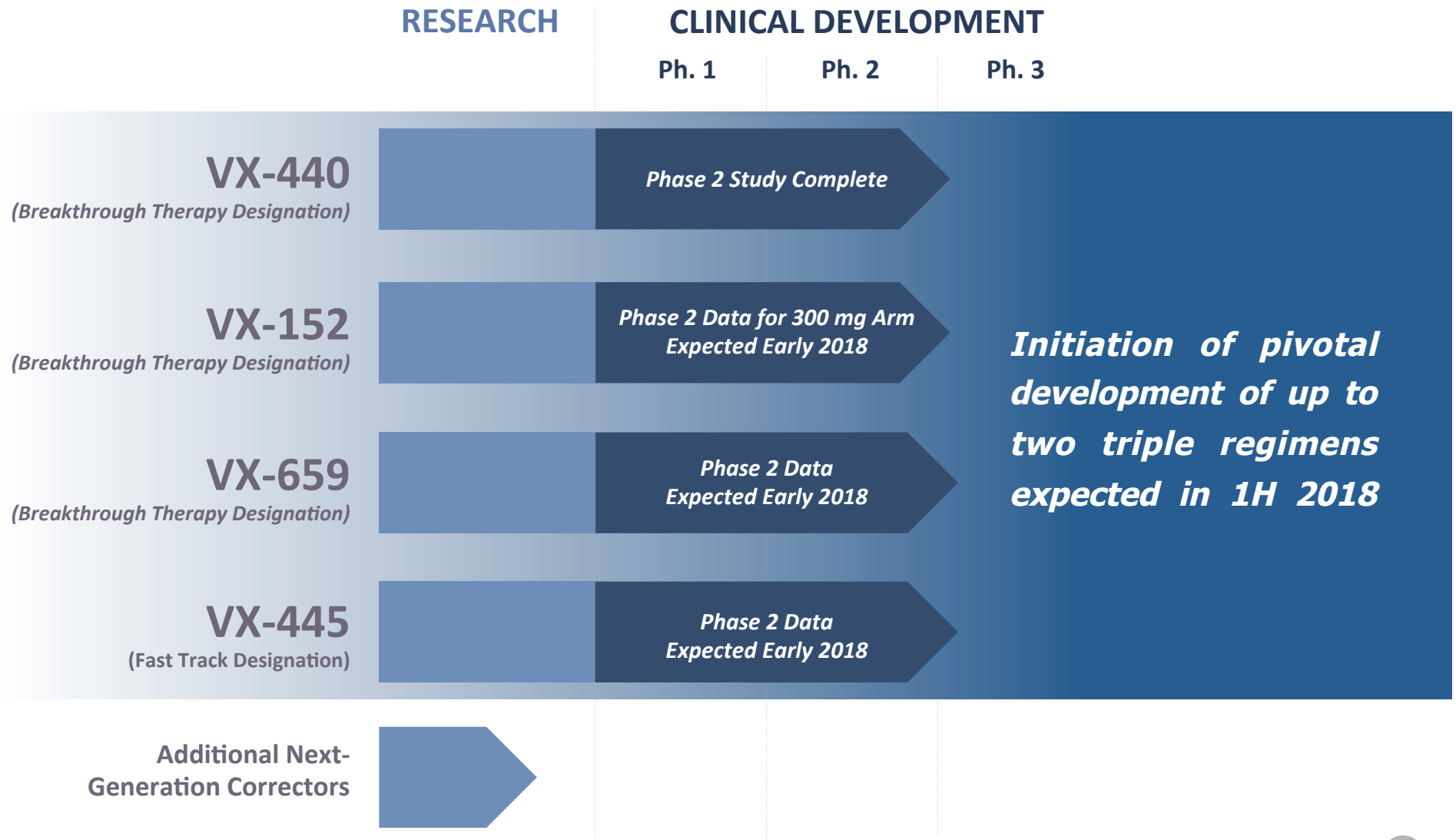
Incremental to Tezacaftor/Ivacaftor Treatment

Heterozygous

	Absolute ppFEV$_1$ from baseline	Sweat Chloride	CFQ-R	Absolute ppFEV$_1$ from baseline	Sweat Chloride	CFQ-R
VX-440 (600 mg) *Through Day 29; n=20/18*	+9.5	-31.3	---	+12.0	-33.1	+20.7
VX-152 (200 mg) *At Day 15; n=10/10*	+7.3	-20.9	---	+9.7	-14.1	---
VX-659 (120 mg) *At Day 15; n=9*	---	---	---	+9.6	-41.6	---

Data provided as within-group changes for highest dose reported to date; complete safety and efficacy data available in 7/18/17 press release; ppFEV1 provided as percentage points, sweat chloride as mmol/L, CFQ-R as points

Planned Initiation of Pivotal Development



2018 and Beyond

Achieving our Vision in Cystic Fibrosis

Expanding Pipeline Beyond CF

Increasing Financial Strength

Learnings in CF Have Transformed Our Investments in Research

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

- **Sickle Cell Disease & Beta Thalassemia**
- **Adrenoleukodystrophy**
- **Alpha-1 Antitrypsin Deficiency**
- **Polycystic Kidney Disease**

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Gene Editing Approach to Sickle Cell Disease

A Transformative Opportunity

- ✓ **Validated Target**
  Naturally occurring variants in BCL11A increase fetal hemoglobin and ameliorate symptoms of sickle cell disease
- ✓ **Biomarkers Predict Outcomes**
  Level of HbF correlates with disease outcomes and is measurable in vitro and in humans (>30% HbF expected to prevent disease symptoms)
- ✓ **Transformative Potential**
  One-time treatment using CRISPR/Cas9 gene editing aimed at functional cure
- ✓ **Rapid Development Path**
  Short-term biological POC based on HbF levels

***GOAL:** Develop one-time BCL11A gene-editing approach to increase HbF levels and functionally cure the disease*

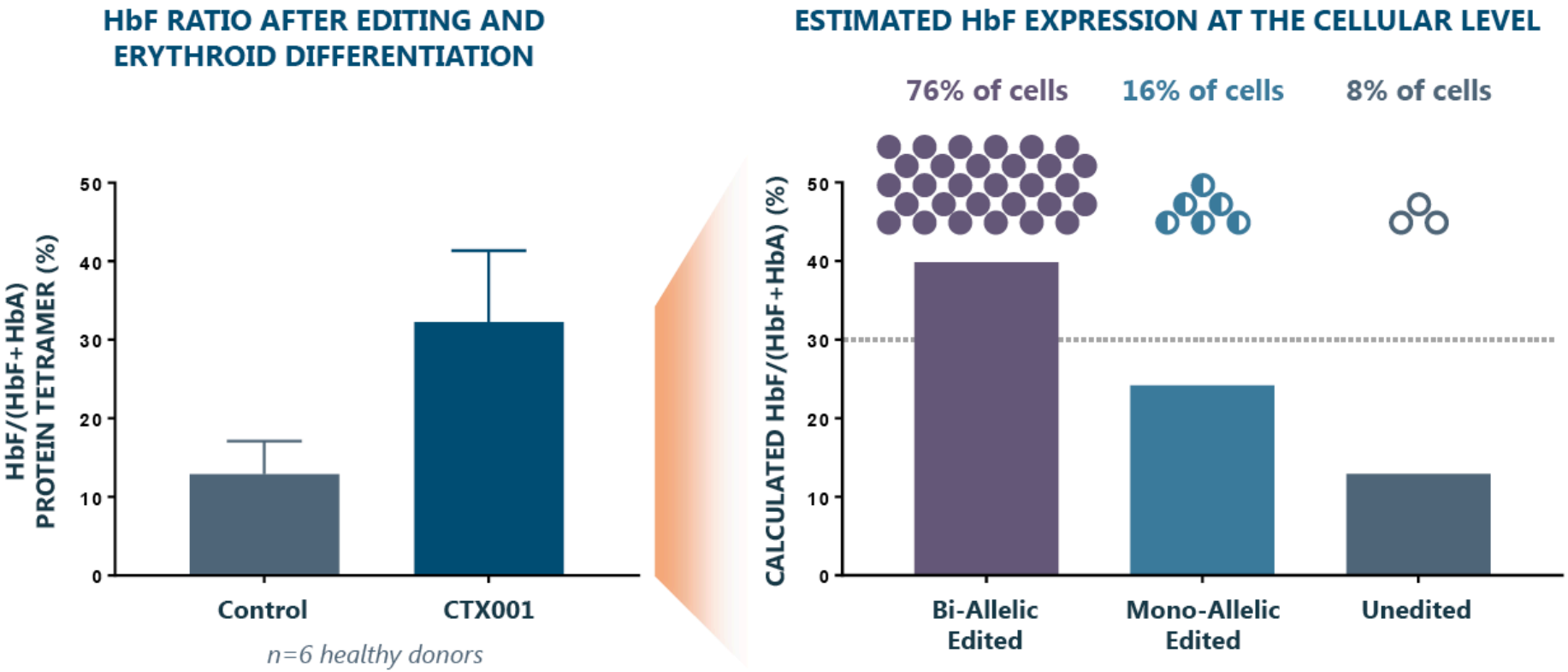
KEY FACTS

~100,000 People
in the U.S.

Current Treatment
Only Helps Certain Patients

Life-Threatening
Complications and
Frequent Hospitalizations

CTX001 Gene Editing Therapy Increases Fetal Hemoglobin In Vitro



Planned initiation of Phase 1/2 clinical studies of CTX001 in β Thalassemia and Sickle Cell Disease in 2018

CTA Submitted in Europe in December 2017 for Phase 1/2 trial in β Thalassemia

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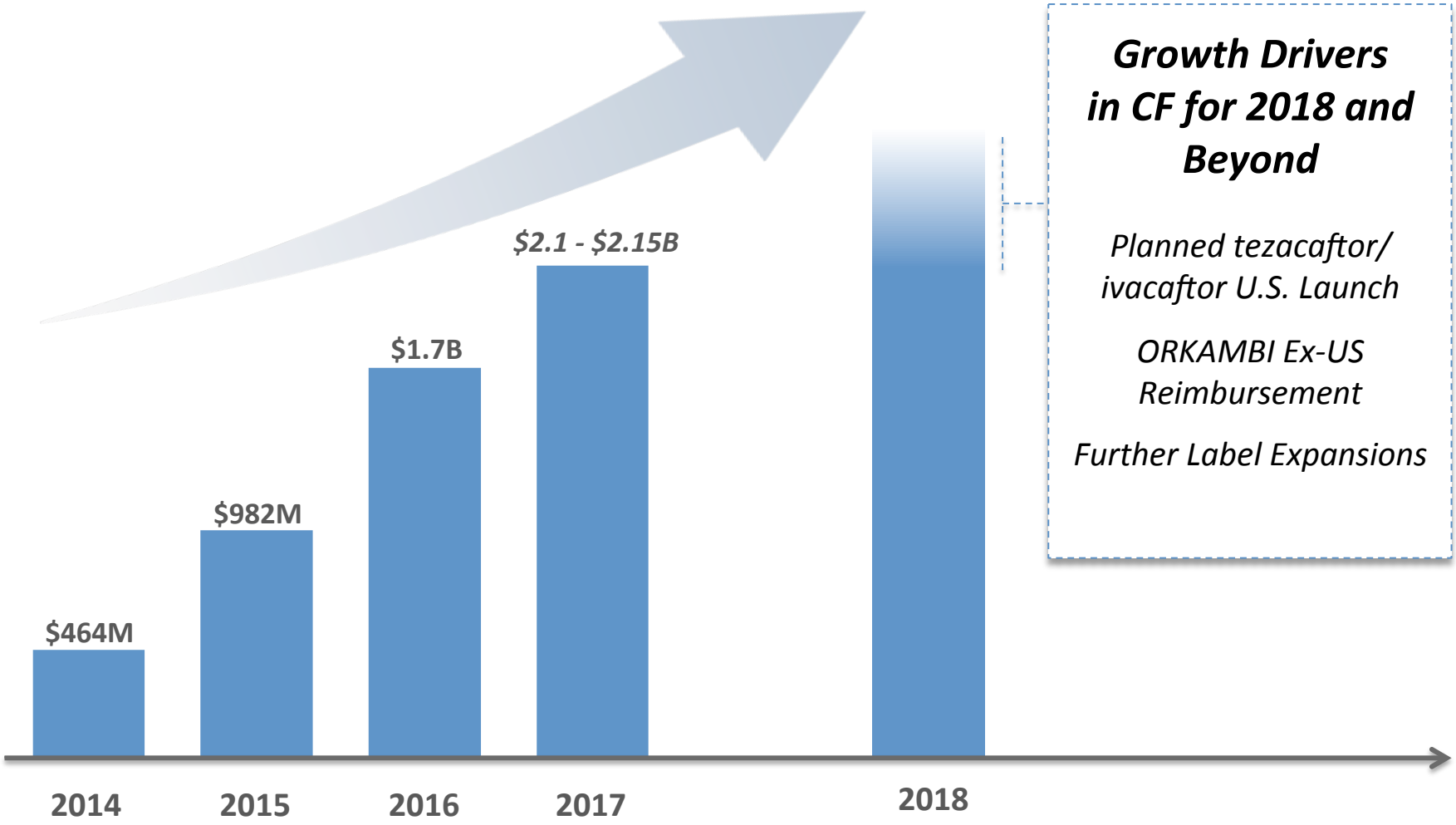
CF Revenues Are Expected to Continue to Grow



Growth Drivers in CF for 2018 and Beyond

Planned tezacaftor/ivacaftor U.S. Launch

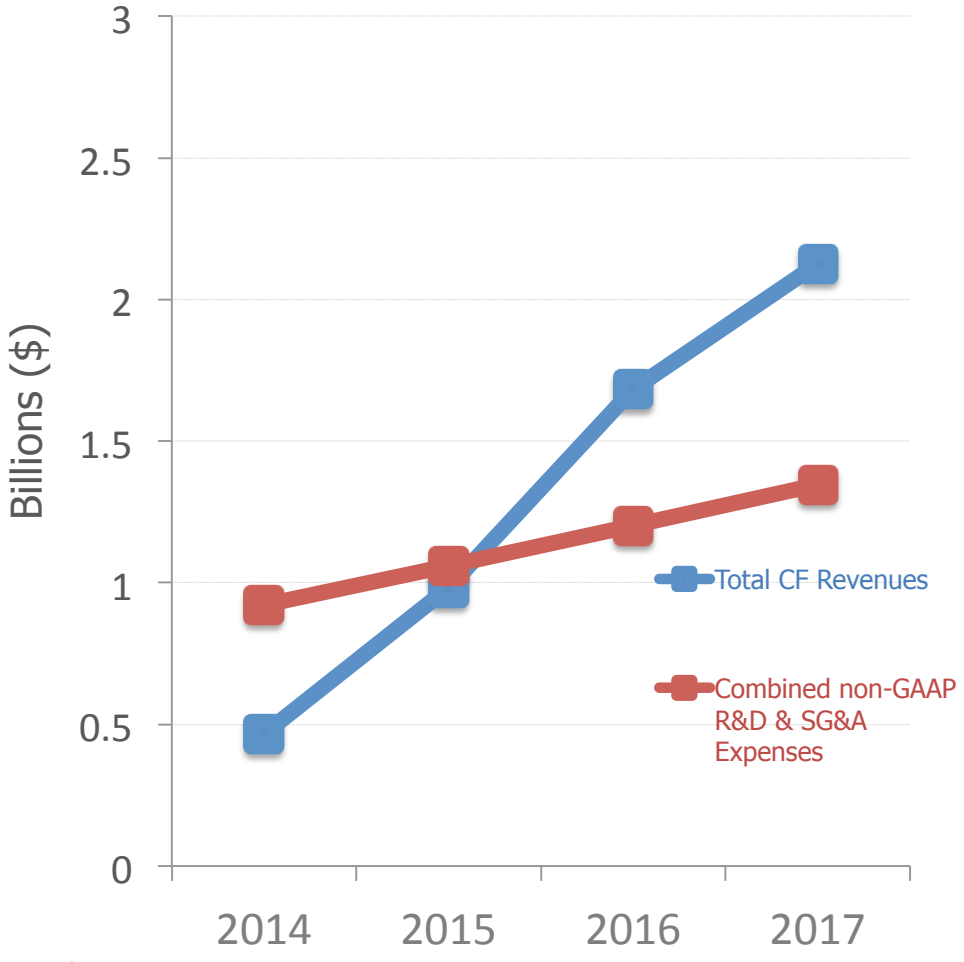
ORKAMBI Ex-US Reimbursement

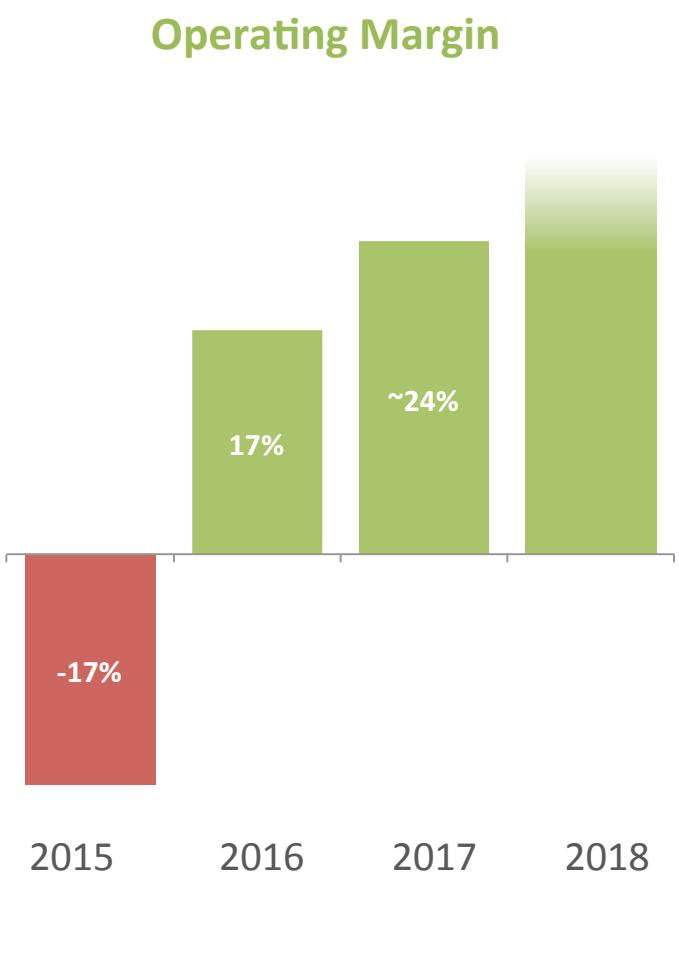
Further Label Expansions

GLOBAL CF PRODUCT REVENUES

Notes: 2017 reflects the midpoint of the total CF revenue guidance provided on 10/25/17; not meant as a reiteration of guidance; 2018 potential growth in CF revenues provided as a graphical representation and not intended as financial guidance.

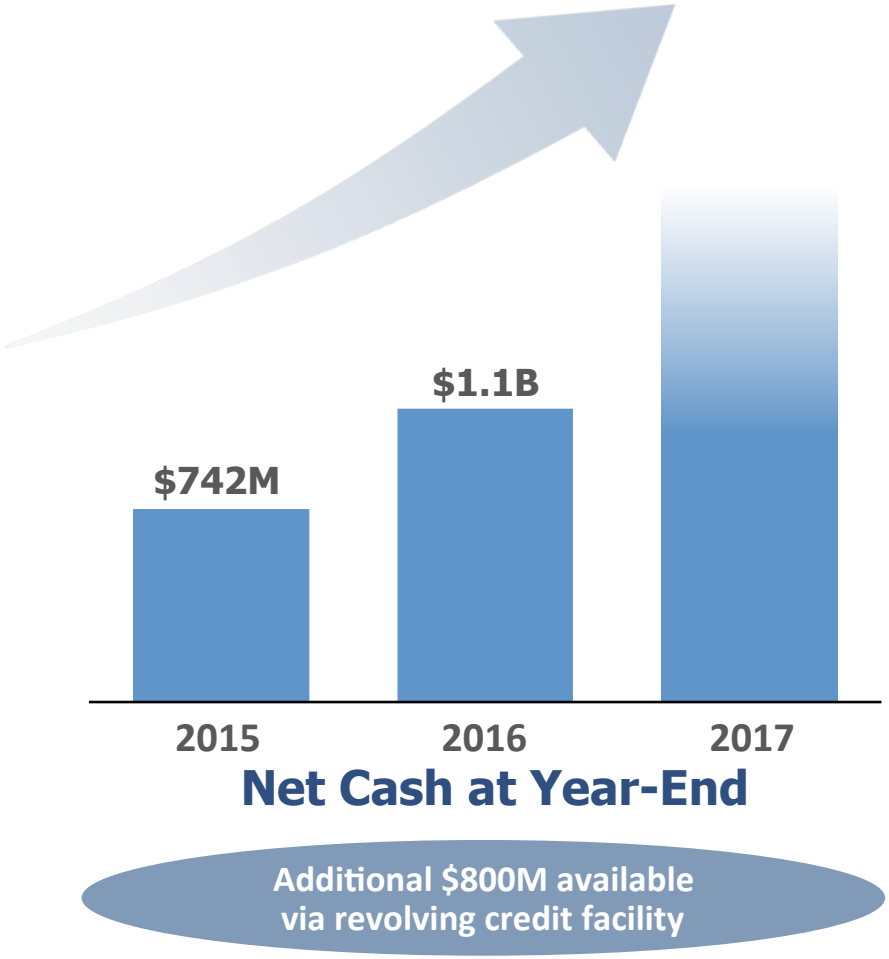
Significant Growth in Revenue Driving Operating Margin Expansion





Notes: Operating margins reflect total non-GAAP revenues, combined non-GAAP R&D & SG&A expenses & cost of revenues; 2017 values reflect the midpoint of the total CF revenue guidance & non-GAAP combined R&D & SG&A expenses guidance provided on 10/25/17; not meant as a reiteration of guidance; 2018 operating margin provided as graphical representations and not intended as financial guidance; Operating margins reflect an estimate of approximately 13% for COR in 2017.

Increasing Cash Flow Drives Return for Shareholders and Enables Investment for Future Growth



Growing Cash Position Enables Continued Investment in Internal R&D and Execution of Business Development Strategy

Business Development Strategy

Complement Ongoing R&D in CF

Access Promising Platform Technologies

Bolster Pipeline with Internal and External Assets

CRISPR THERAPEUTICS

CoNCERT Pharmaceuticals Inc.®

moderna® messenger therapeutics

Notes: Cash noted in 2015 and 2016 as net of $300M outstanding debt related to revolving credit facility, which was repaid in full in Q1 2017; 2017 potential growth in year-end cash provided as a graphical representation and not intended as financial guidance

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Our Mission

Vertex invests in scientific innovation to create transformative medicines for serious diseases

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