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VERTEX

Third Quarter 2016 Financial Results

October 25, 2016

Agenda

Introduction
Michael Partridge, VP Investor Relations

CF Strategy Update
Jeff Leiden, M.D., Ph.D., Chairman and CEO

Commercial Update
Stuart Arbuckle, Chief Commercial Officer

Next-Generation Corrector Progress
Jeff Chodakewitz, M.D., Chief Medical Officer

Third Quarter 2016 Financial Results
Ian Smith, Chief Financial Officer

Q&A

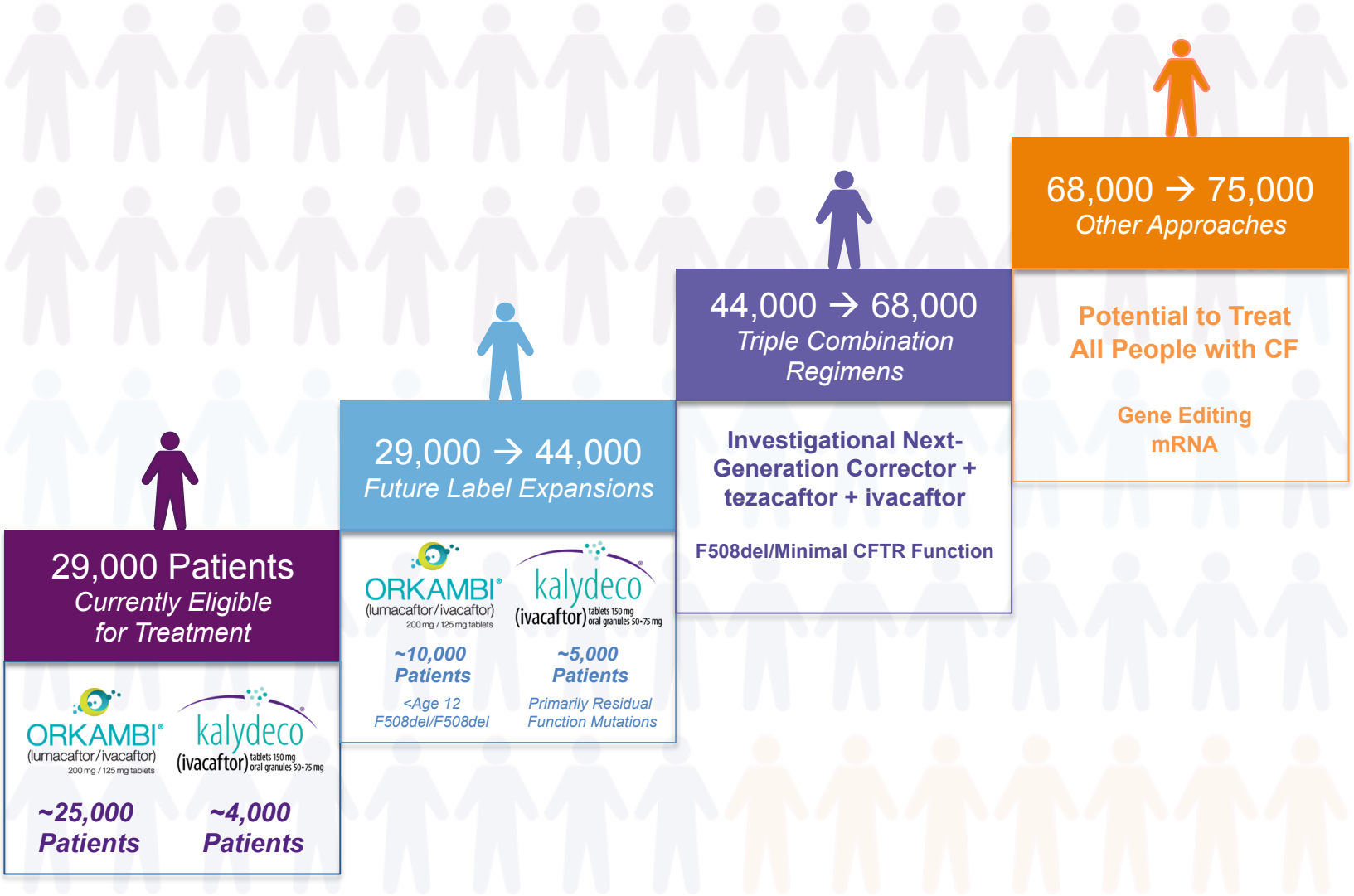
Safe Harbor Statement

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, including, without limitation, statements regarding (i) the expected timing and clinical trial designs for ongoing and planned clinical studies of ORKAMBI, tezacaftor (VX-661), and the company's next-generation correctors, including VX-659, (ii) the timing of regulatory applications, including NDA and MAAs, and (iii) 2016 financial guidance. 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 2016 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.

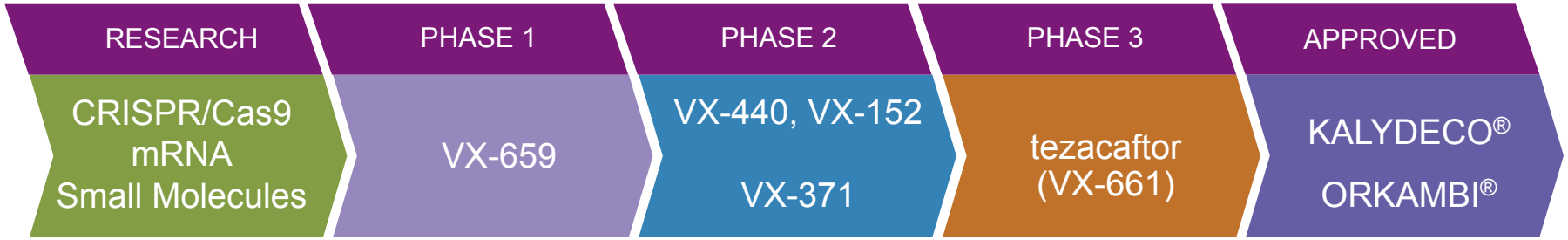
Non-GAAP Financial Measures

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 non-GAAP research and development and sales, general, and administrative expenses. The company does not provide guidance regarding GAAP research and development and sales, general, and administrative expenses because of the difficulty of estimating stock-based compensation expenses, and predicting whether or not there will be additional expense items for which adjustments are appropriate.

Path to Treating All CF Patients



Vertex CF Pipeline



RESEARCH

CRISPR/Cas9

- Gene editing research collaboration with initial focus in CF and Sickle Cell Disease/ Hemoglobinopathy

mRNA

- Research collaboration and licensing agreement to develop mRNA Therapeutics™ for the treatment of CF

Small Molecules

- Additional next-gen correctors potentially increasing benefit

PHASE 1

- Phase 1 study of VX-659 planned to begin in 2016; Phase 2 planned for 2H17, pending data
- Additional next-generation corrector expected to enter clinical development in 2017

PHASE 2

Next-Generation Correctors:

- Planned initiation of Phase 2 studies for VX-440 and VX-152 in 2016

ENaC:

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

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 29,000 patients eligible for treatment with ORKAMBI or KALYDECO in U.S., E.U., Canada and Australia

~29,000 People Currently Eligible for ORKAMBI or KALYDECO

ORKAMBI®
(lumacaftor/ivacaftor)
200 mg / 125 mg tablets

- Q3'16 revenues of $234M, including:
  - $211M in U.S.
  - $23M ex-U.S.
- ~6,400 patients have started treatment in U.S. as of September 30, 2016
- Approved in September 2016 for people ages 6-11 who have two copies of F508del mutation in the U.S.

kalydeco®
(ivacaftor) tablets 150 mg oral granules 50•75 mg

- Q3'16 revenues of $176M, including:
  - $101M in U.S.
  - $75M ex-U.S.
- Most eligible patients on therapy

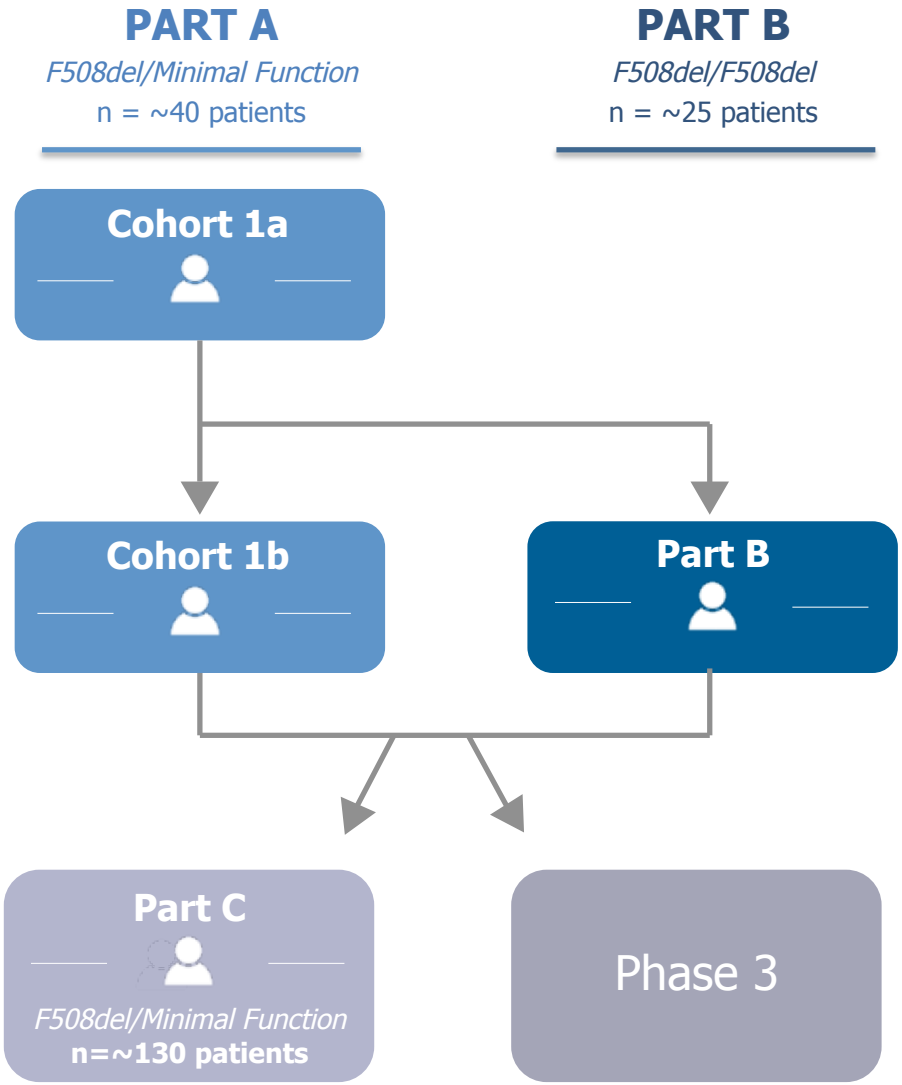
VX-440 Phase 2 Study Design

Regimen
4 Weeks of Triple Combination or Placebo (Parts A & B):
- ***VX-440/tezacaftor/ivacaftor***
- ***Part B includes 4-week lead-in and washout periods of only tezacaftor/ivacaftor***

Patient Genotypes:
F508del/Minimal Function (Part A)
F508del/F508del (Part B)

Endpoints:
- **Primary: Safety, Tolerability and Abs. Change in $ppFEV_1$**
- **Secondary: Rel. Change in $ppFEV_1$, Sweat Cl-, CFQ-R Resp. Score, others.**

Data Expectation:
2H 2017 (Parts A & B)



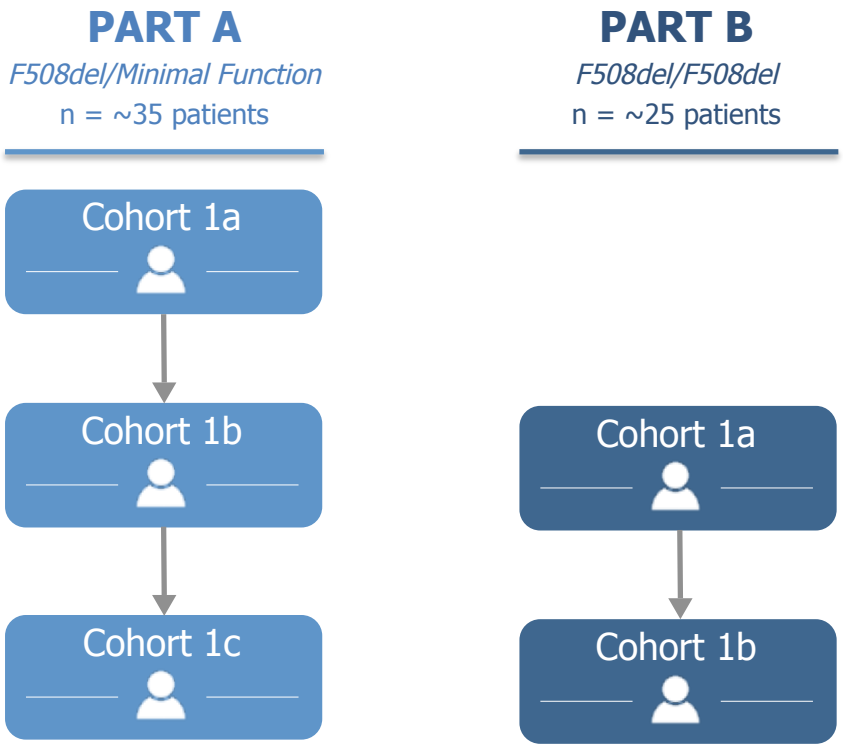
VX-152 Phase 2 Study Design

Regimen
2 Weeks of Triple Combination or Placebo:
- ***VX-152/tezacaftor/ivacaftor***
- ***Part B includes a 4-week lead-in and 2-week washout period of only tezacaftor/ivacaftor***

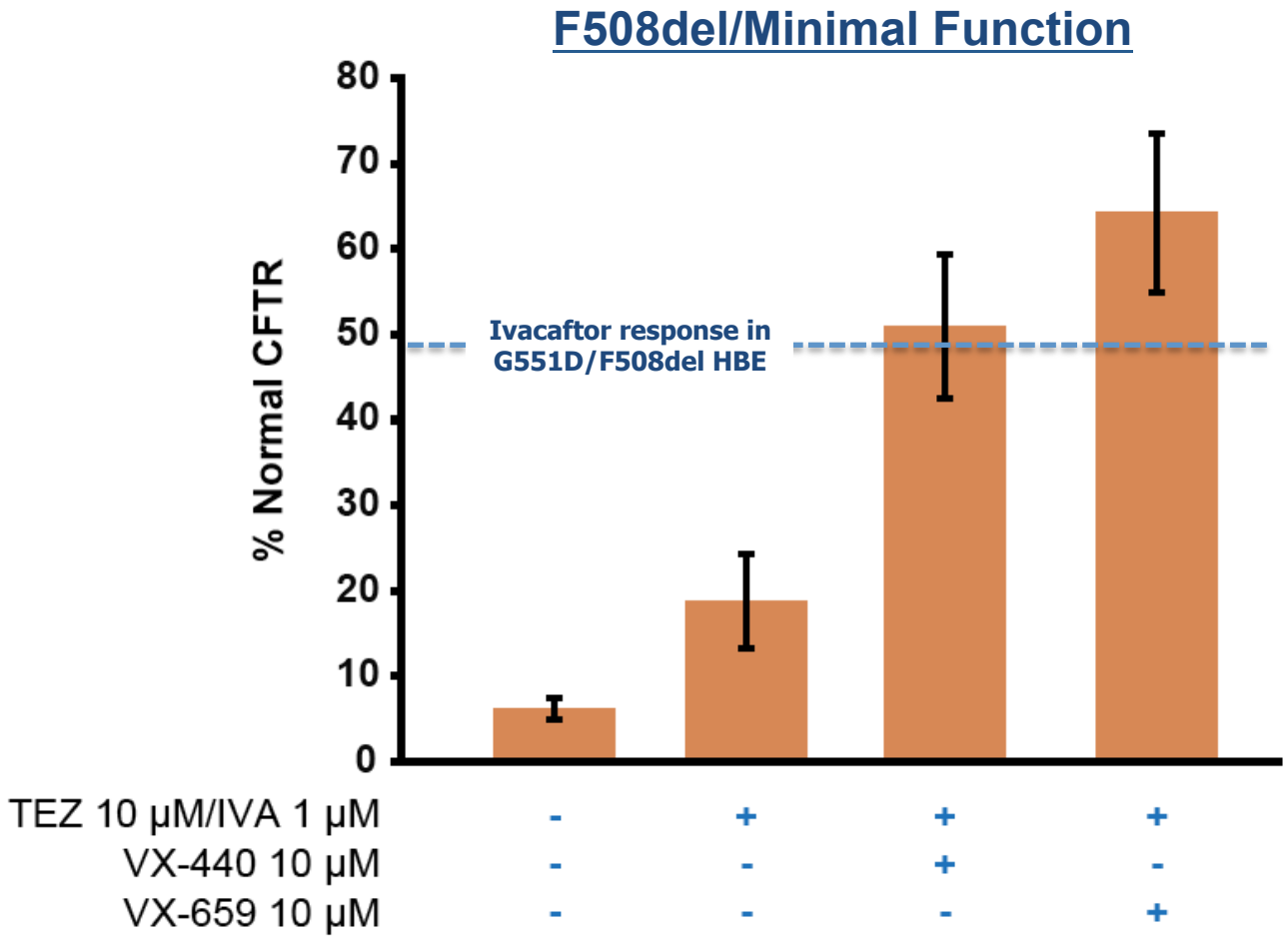
Patient Genotypes:
F508del/Minimal Function (Part A)
F508del/F508del (Part B)

Endpoints:
1 & 2
- **Primary: Safety and Tolerability**
- **Secondary: Abs. & Rel. Change in $ppFEV_1$, Sweat Cl-, CFQ-R Resp. Score, others.**

Data Expectation:
2H 2017 (Parts A & B)



VX-659 Preclinical Profile



Preclinical Profile

- Higher maximal efficacy vs. VX-440 & VX-152 triple combinations
- Greater potency

Development Path

- Phase 1 start by end of 2016
- Phase 2 in second half of 2017, pending data

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.

Third Quarter 2016 Financial Highlights

(in $M except per share data)	3Q'16	3Q'15
Total CF Revenues	410	297
ORKAMBI Revenues	234	131
KALYDECO Revenues	176	166
Non-GAAP Operating Expense*	298	278
Non-GAAP R&D Expense*	214	202
Non-GAAP SG&A Expense*	84	76
Non-GAAP Net Income (Loss)*	40	(32)
Non-GAAP Net Income (Loss) Per Share*	0.16	(0.13)
*Cash Balance at September 30, 2016**	*1.13B*	

**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 October 25, 2016.*

**The company's GAAP net loss was $42M and $95M, respectively, GAAP R&D expense was $275M and $246M, respectively, and GAAP SG&A expense was $106M and $100M, respectively, in Q3'16 and Q3'15.*

** Cash includes cash, cash equivalents and marketable securities. As of September 30, 2016 the company had $300M of term debt.*

2016 Financial Guidance

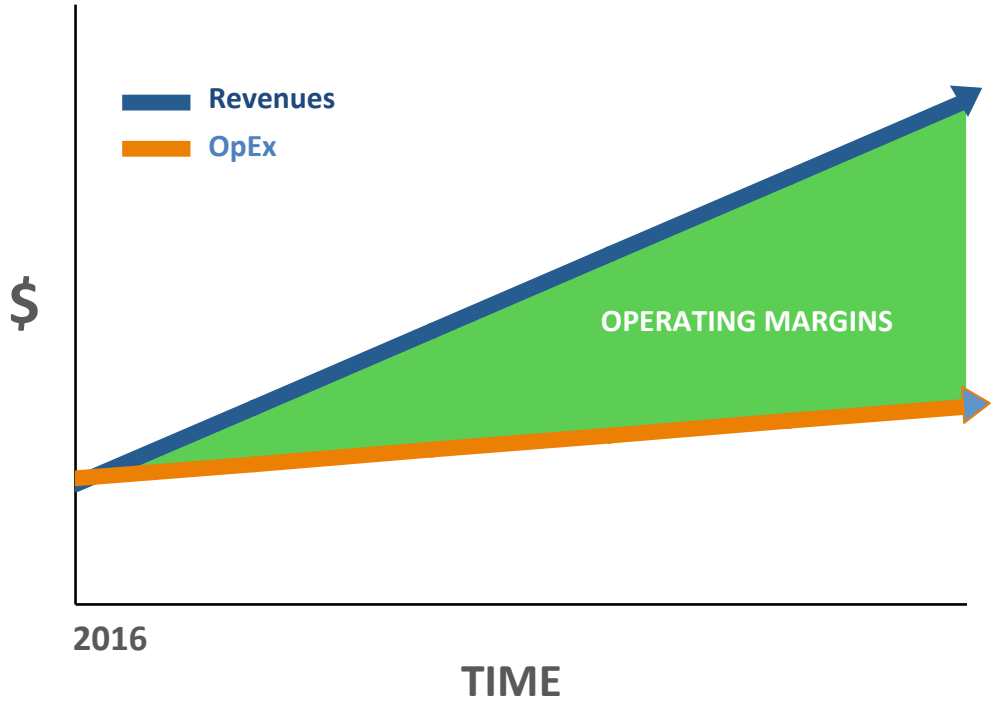
	FY 2016 Guidance
ORKAMBI Revenues	$950 - 990M
KALYDECO Revenues	$685 - 705M
Non-GAAP Operating Expenses	$1.18 - 1.23B
Non-GAAP R&D Expense	$850 - 880M
Non-GAAP SG&A Expense	$330 - 350M

Notes

- *2016 KALYDECO net revenue guidance excludes any potential revenues from approval for residual function.*
- *Combined non-GAAP operating expenses exclude stock-based compensation expense and certain other expenses.*

CF Expansion Drives Sustainable Revenue and Earnings Growth & Enables Investment in Pipeline Assets

CF Execution & Value Creation Beyond CF



Anticipated Profile Moving Forward

- Significant revenues from multiple high-value medicines
- Modest growth in operating expenses, enabling operating margin expansion
- Broadening CF portfolio
  - tezacaftor combination
  - Next-gen corrector portfolio
  - Other modalities and complementary approaches
- Diversify and expand pipeline through internal research productivity and external collaborations / in-licensing
- Strengthening balance sheet through significant cash generation

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