VERTEX

THE SCIENCE *of* POSSIBILITY

Business Update & Full-Year and Q4'17 Financial Results

January 31, 2018

Agenda

Introduction

Michael Partridge, Vice President, Investor Relations

Key Progress and Next Steps

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

Data Highlights

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

Fourth-Quarter and Full-Year 2017 Financial Results

Ian Smith, Executive Vice President and Chief Operating Officer

Q&A

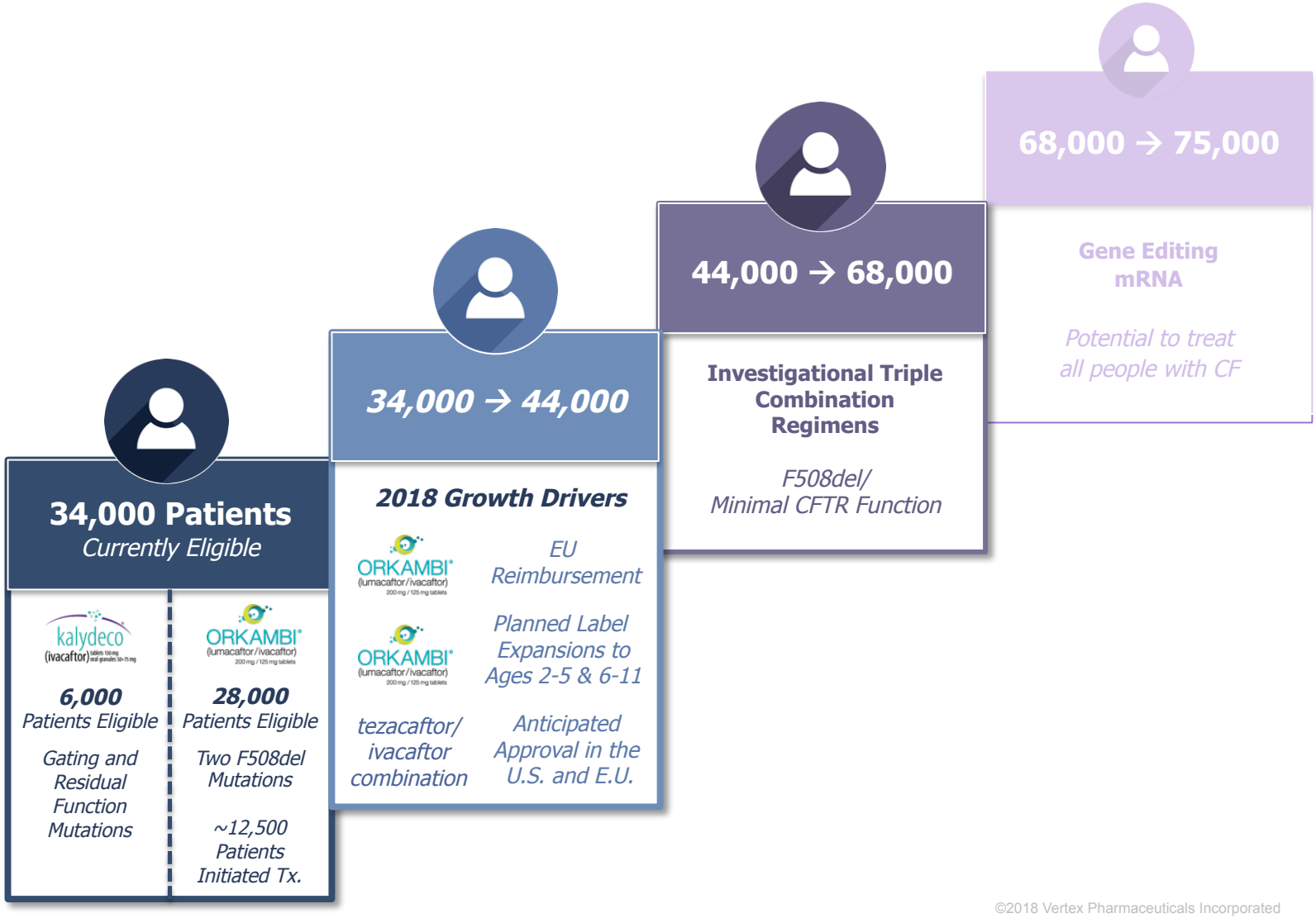
Stuart Arbuckle, Executive Vice President, Chief Commercial Officer

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, the information provided in the slide captioned "2018 Financial Guidance" and statements regarding (i) the timing and expected outcome of regulatory applications, including NDAs and MAAs and (ii) the development plan and timelines for our product development candidates, including tezacaftor in combination with ivacaftor and our next-generation triple combination regimens. 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 2018 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.

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 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 January 31, 2018 press release.

Developing Medicines for All People with CF



Key Progress and Next Steps

We have selected VX-659 and VX-445 to advance into Phase 3 development as part of two separate triple combination regimens, one of which may be a once-daily regimen

- In Phase 2, both VX-659 and VX-445 triple combination regimens were well-tolerated and have a favorable safety profile

We are finalizing designs of Phase 3 studies now and remain on track to begin the first Phase 3 program in the first half of 2018

We remain focused on bringing forward the best triple combination regimen to patients as quickly as possible

VERTEX

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 anticipated in 2H 2018) ☐ Advance additional next-generation correctors into development
EXPAND PIPELINE BEYOND CF	☑ Initiated additional Phase 2 studies of VX-150 in acute and neuropathic pain ☑ Bolstered 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	☑ Achieved total 2017 CF product revenues of $2.17B; 29% 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 2018 total CF product 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

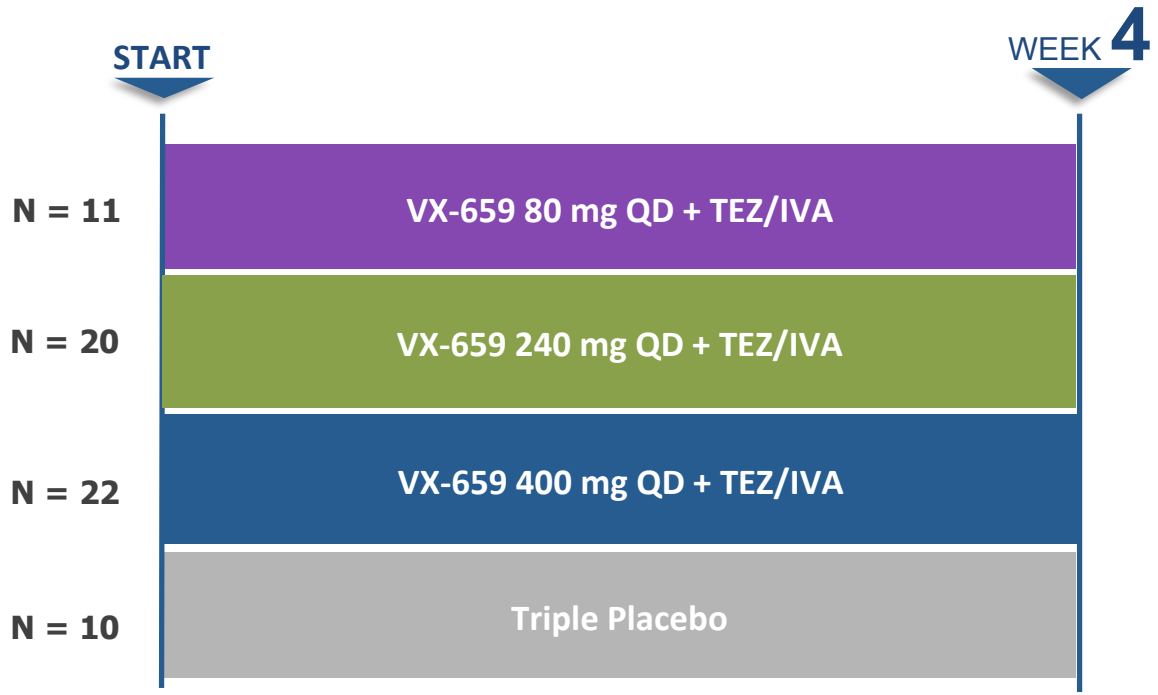
VERTEX

VX-659 & VX-445

Phase 2 Evaluations in Cystic Fibrosis Patients

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

VX-659
Dosing in CF Patients with F508del/Minimal Function Mutations



- Primary Objectives: Safety, tolerability and efficacy as assessed by mean absolute change in $ppFEV_1$ from baseline
- Secondary Endpoints: Sweat chloride and respiratory domain of CFQ-R
- Key eligibility criteria for these cohorts:
  - F508del/minimal function mutations
  - ≥18 years old
  - $ppFEV_1$, 40-90% inclusive

VERTEX

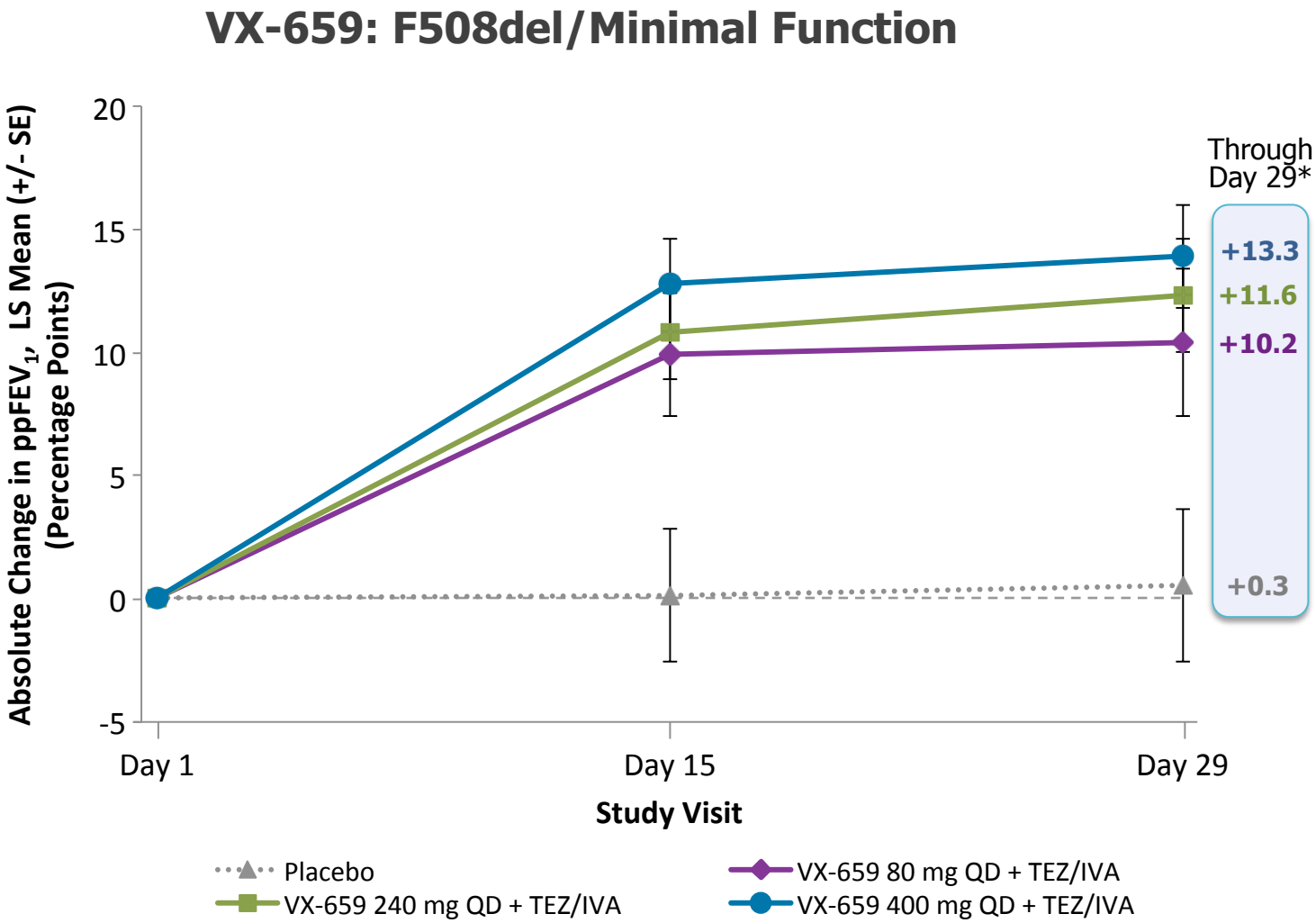
VX-659
Safety Summary

VX-659: F508del/Minimal Function

- VX-659 in combination with tezacaftor and ivacaftor was generally well tolerated and the overall safety profile was favorable
- Majority of adverse events were mild or moderate
- No discontinuations due to adverse events
  - One interruption in triple combination dosing due to rash, which resolved following interruption of treatment; Patient restarted and completed triple combination dosing without any further rash

VERTEX

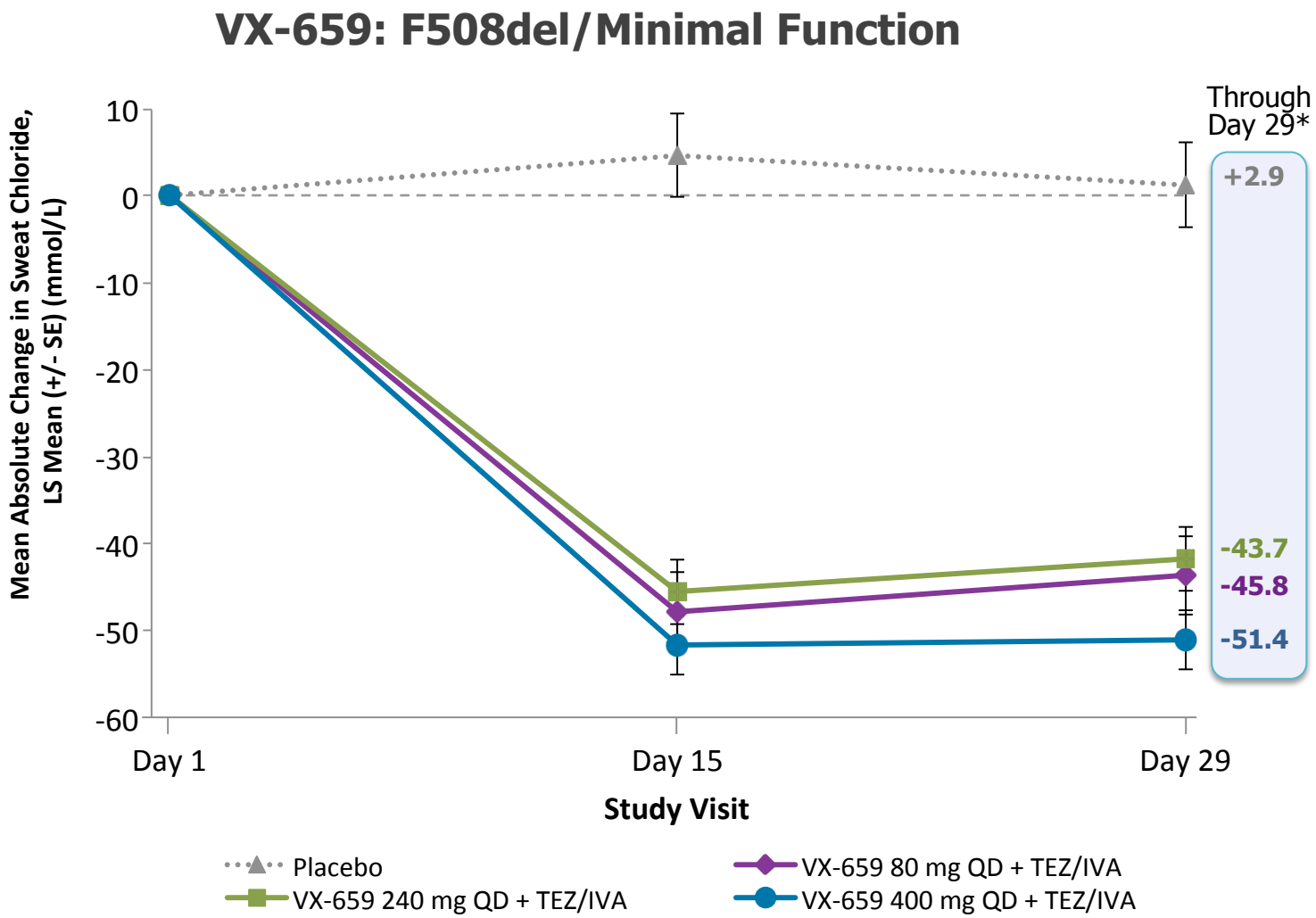
VX-659
Absolute Change in Lung Function Over Time



VERTEX

** Values expressed as "Through Day 29" are the average of Day 15 and Day 29 measures*

VX-659
Sweat Chloride Significantly Reduced



** Values expressed as "Through Day 29" are the average of Day 15 and Day 29 measures*

VX-659
Significant Improvements in Respiratory Symptoms

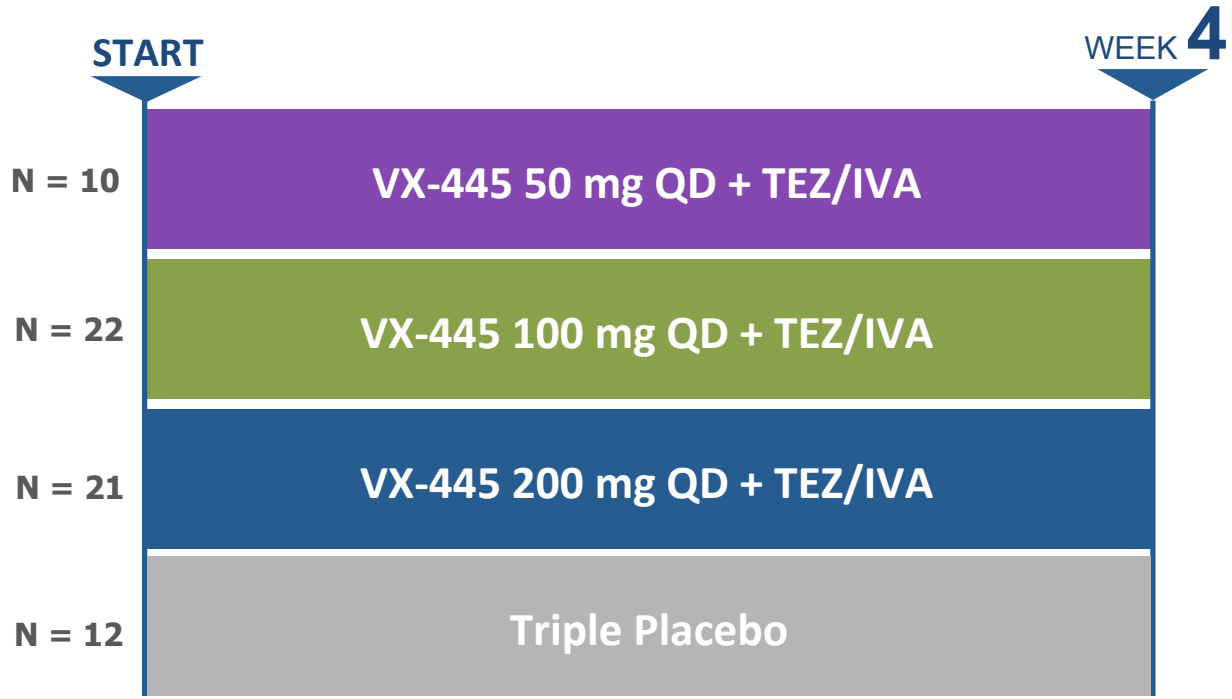
VX-659: F508del/Minimal Function

Treatment Group	Mean Absolute Change in Respiratory Domain of CFQ-R at Day 29 (mean, points)
Triple Placebo	+4.7
VX-659 80mg + TEZ/IVA	+24.6
VX-659 240mg + TEZ/IVA	+19.8
VX-659 400mg + TEZ/IVA	+21.8

CFQ-R results reported are based on a mixed effect model not adjusted for baseline CFQ-R

VX-445

Dosing in CF Patients with F508del/Minimal Function Mutations



- Primary Objectives: Safety, tolerability and efficacy as assessed by mean absolute change in ppFEV$_1$ from baseline
- Secondary Endpoints: Sweat chloride and respiratory domain of CFQ-R
- Key eligibility criteria for these cohorts:
  - F508del/minimal function mutations
  - ≥18 years old
  - ppFEV$_1$, 40-90% inclusive

VERTEX

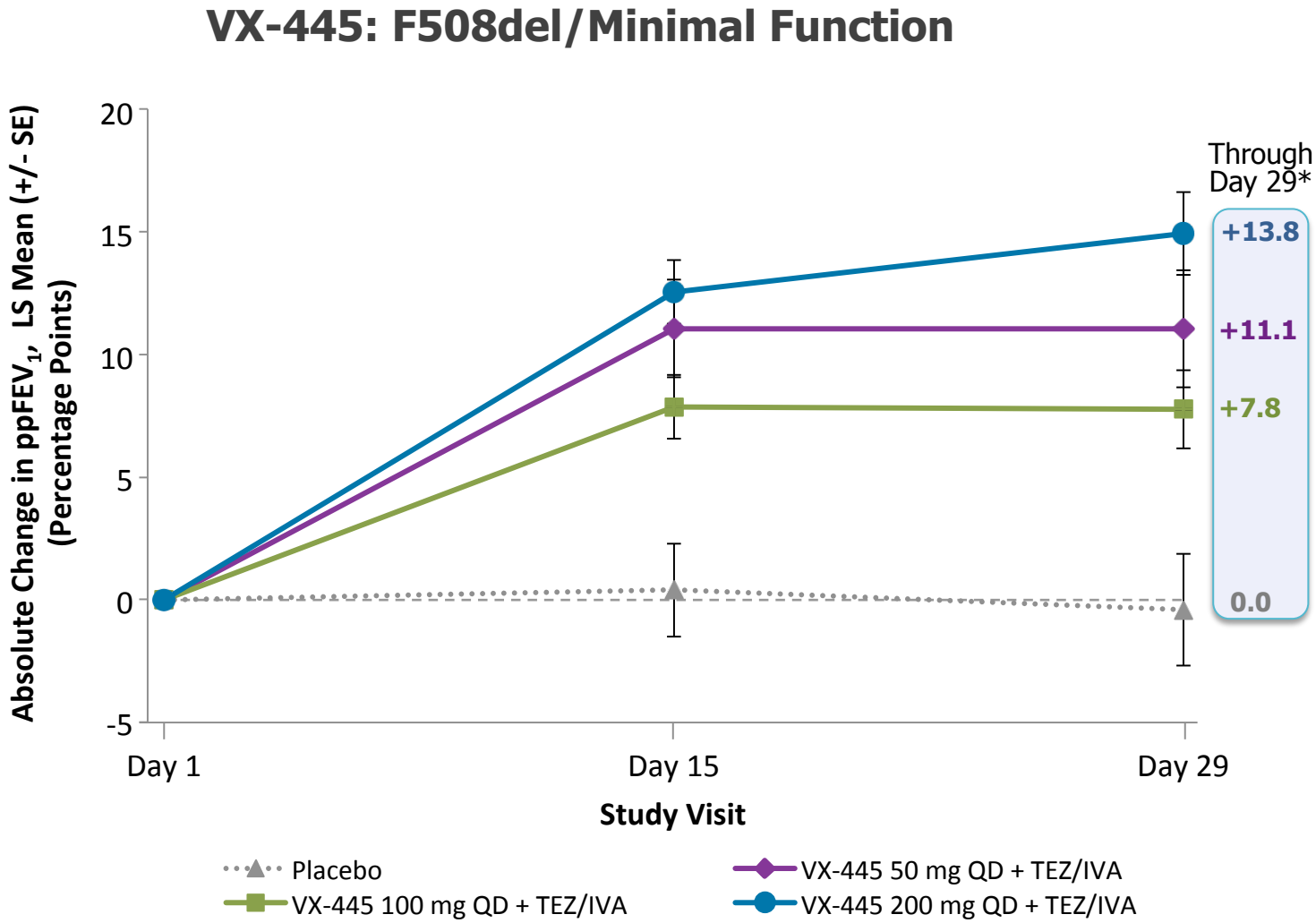
VX-445
Safety Summary

VX-445: F508del/Minimal Function

- VX-445 in combination with tezacaftor and ivacaftor was generally well tolerated and the overall safety profile was favorable
- Majority of adverse events were mild or moderate
- Two discontinuations due to adverse events in triple combination treatment groups (none in the placebo group):
  - Increased bilirubin (without concomitant transaminase elevations) - observed on final day of dosing; patient's bilirubin levels returned to baseline during safety follow-up period after discontinuation of treatment
  - Rash – resolved following discontinuation of treatment

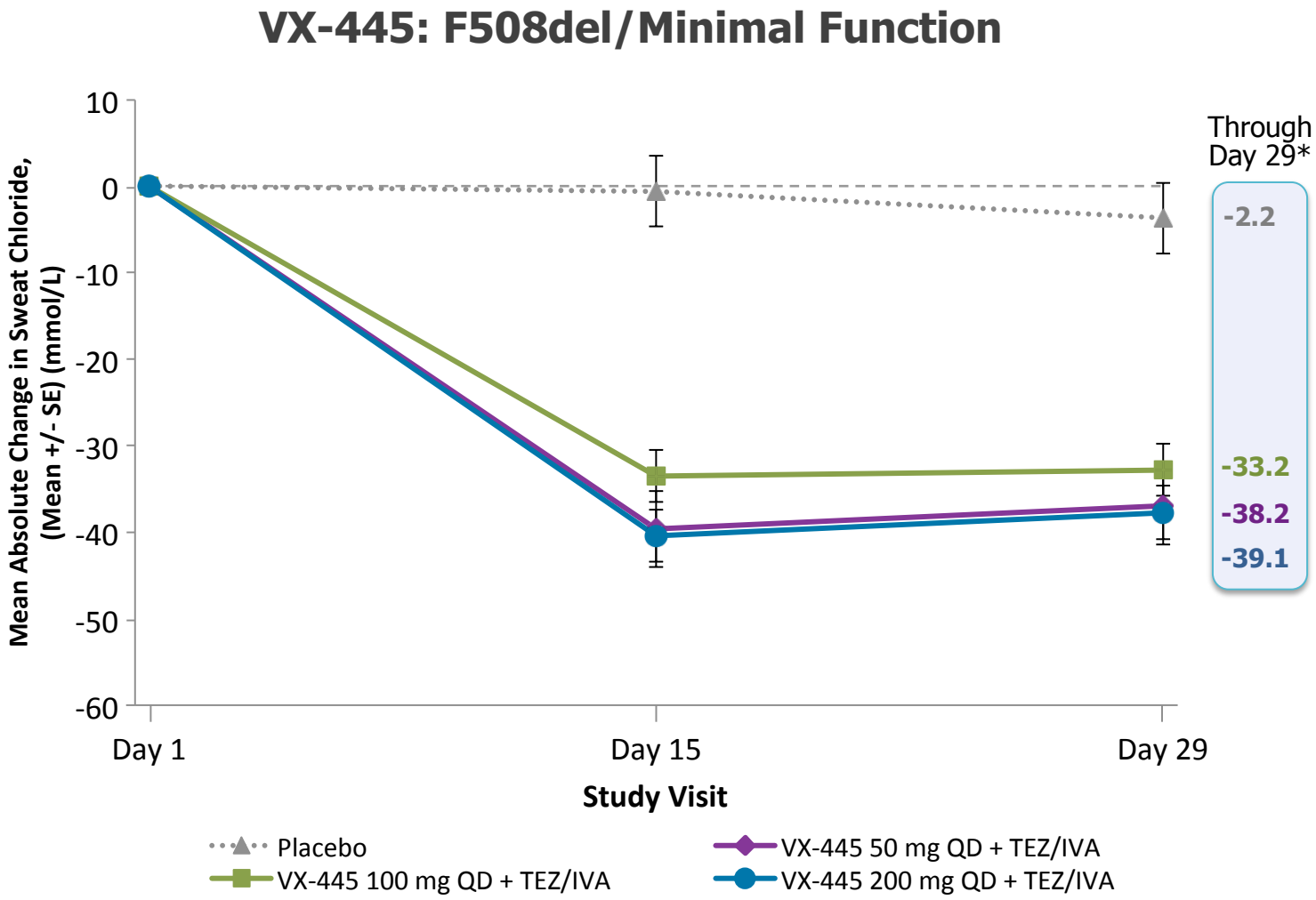
VERTEX

VX-445
Absolute Change in Lung Function Over Time



** Values expressed as "Through Day 29" are the average of Day 15 and Day 29 measures*

VX-445
Sweat Chloride Significantly Reduced



** Values expressed as "Through Day 29" are the average of Day 15 and Day 29 measures*

VX-445
Significant Improvements in Respiratory Symptoms

VX-445: F508del/Minimal Function

Treatment Group	Mean Absolute Change in Respiratory Domain of CFQ-R at Day 29 (mean, points)
Triple Placebo	+4.2
VX-445 50 mg + TEZ/IVA	+20.8
VX-445 100 mg + TEZ/IVA	+15.4
VX-445 200 mg + TEZ/IVA	+25.7

CFQ-R results reported are based on a mixed effect model not adjusted for baseline CFQ-R

Phase 3 Program Next Steps

Focused on finalizing design of Phase 3 programs and remain on track to initiate first Phase 3 program for VX-659 in 1H 2018 upon completion of discussions with FDA

Expect to conduct two separate studies for each VX-659 and VX-445 triple combination regimen - F508del/minimal function and F508del/F508del

Plan to initiate Phase 3 studies for VX-445 triple regimen in mid-2018 and evaluate VX-445 in combination with tezacaftor and VX-561 as potential once-daily triple combination regimen, pending Phase 2 data and completion of long-term nonclinical toxicology studies for VX-445

VERTEX

Full-Year and Fourth-Quarter 2017 Financial Results

Ian Smith, Executive Vice President and Chief Operating Officer

Full-Year and Q4 2017 Financial Highlights

($ in millions except per share data and percentages)	FY 2016	Q1 17	Q2 17	Q3 17	Q4 17	FY 2017
ORKAMBI	980	295	324	336	365	**1.32B**
KALYDECO	703	186	190	213	256	**845**
Total CF product revenues	$1.68B	481	514	550	621	**$2.17B**
Combined non-GAAP R&D and SG&A	$1.20B	313	333	334	355	**$1.33B**
Non-GAAP operating income	288	122	112	145	184	**564**
Non-GAAP operating margin	17%	25%	22%	26%	30%	**26%**
Non-GAAP net income	211	101	99	136	158	**495**
Non-GAAP net income per share - diluted	$0.85	$0.41	$0.39	$0.53	$0.61	**$1.95**
Cash, cash equivalents & marketable securities (quarter-end)	$1.43B					**$2.09B**

(1) An explanation of non-GAAP financial measures and reconciliation of non-GAAP combined R&D and SG&A expense, non-GAAP net income and non-GAAP net income per share is included in the company's January 31, 2018 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

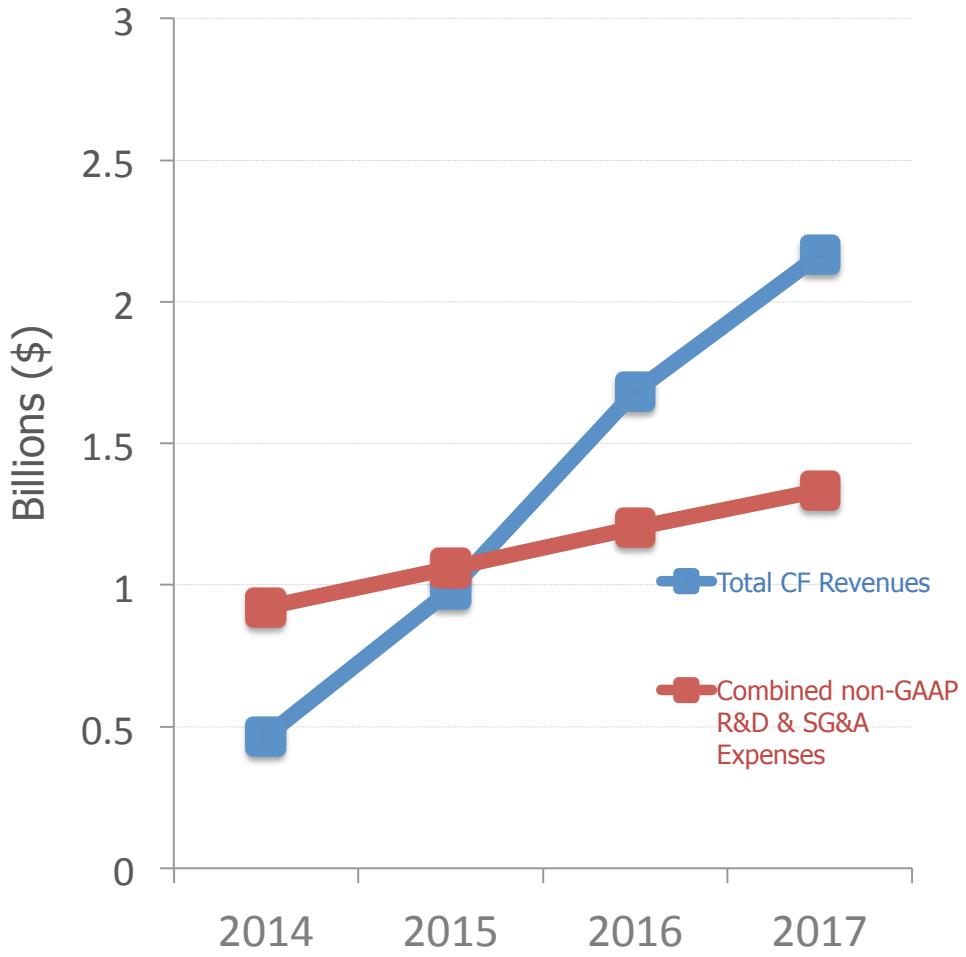
2018 Financial Guidance

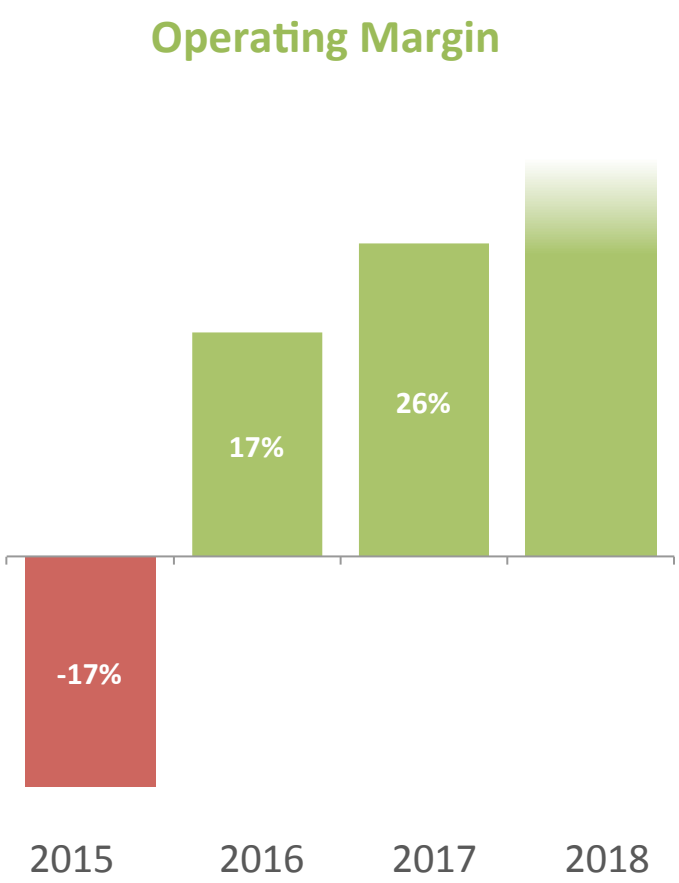
	FY 2017 Actuals	2018 Guidance	2018 Guidance Commentary
Combined non-GAAP R&D and SG&A	$1.33B	**$1.50 - $1.55B**	Year-over-year increase from: • Execution of Phase 3 studies for two separate triple combination regimens • Supply chain investment for triple combination regimens • Incremental investment for tezacaftor/ivacaftor planned launch
Combined GAAP R&D and SG&A	$1.82B	**$1.80 - $1.95B**	

The company expects to provide 2018 total CF product revenue guidance upon the anticipated U.S. approval of the tezacaftor/ivacaftor combination

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 January 31, 2018 press release

Significant Growth in Revenue Driving Operating Margin Expansion





Operating margins reflect total CF revenues, combined non-GAAP R&D and SG&A expenses and cost of revenues

Thank You

…to the hundreds of patients who took part in our clinical trials, and the physicians, nurses, families and others who care for them.

…to our employees for their dedication to helping advance the treatment of CF.

…and to the CF community for their support and commitment to changing the course of CF.

Appendix A

Reconciliation of GAAP to non-GAAP Financial Information

($ in millions except per share data and percentages)	FY 2016	Q1 2017	Q2 2017	Q3 2017	Q4 2017	FY 2017
GAAP total revenues	$1,702	$715	$544	$578	$652	$2,489
Non-GAAP total revenues	$1,701	$482	$517	$552	$623	$2,174
GAAP income (loss) from operations	$10	$271	$53	$(326)	$126	$123
Stock compensation expense	238	69	73	74	75	291
Concert upfront and transaction expenses	-	-	4	161	-	165
Revenues and expenses related to VIEs	10	2	(18)	(16)	1	(32)
Other collaborative and transaction revenue and expenses	33	(230)	(3)	252	(19)	0
Other adjustments	(2)	11	4	1	1	17
Non-GAAP income from operations	$288	$122	$112	$145	$184	$564
Operating Margin %:						
GAAP	1%	38%	10%	-56%	19%	5%
Non-GAAP	17%	25%	22%	26%	30%	26%
Net income (loss)						
GAAP	(112)	248	18	(103)	101	263
Non-GAAP	211	101	99	136	158	495
Net income (loss) per share - diluted						
GAAP	$(0.46)	$0.99	$0.07	$(0.41)	$0.39	$1.04
Non-GAAP	$0.85	$0.41	$0.39	$0.53	$0.61	$1.95

All numbers in the above reconciliation table are in millions except per share data, totals may not add due to rounding