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Q1'18 Financial Results & Business Update

April 26, 2018

Agenda

Introduction

Michael Partridge, Senior Vice President, Investor Relations

Business Highlights

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

Data Highlights

Reshma Kewalramani, M.D., Executive Vice President and Chief Medical Officer

First-Quarter 2018 Financial Results

Ian Smith, Executive Vice President and Chief Operating Officer

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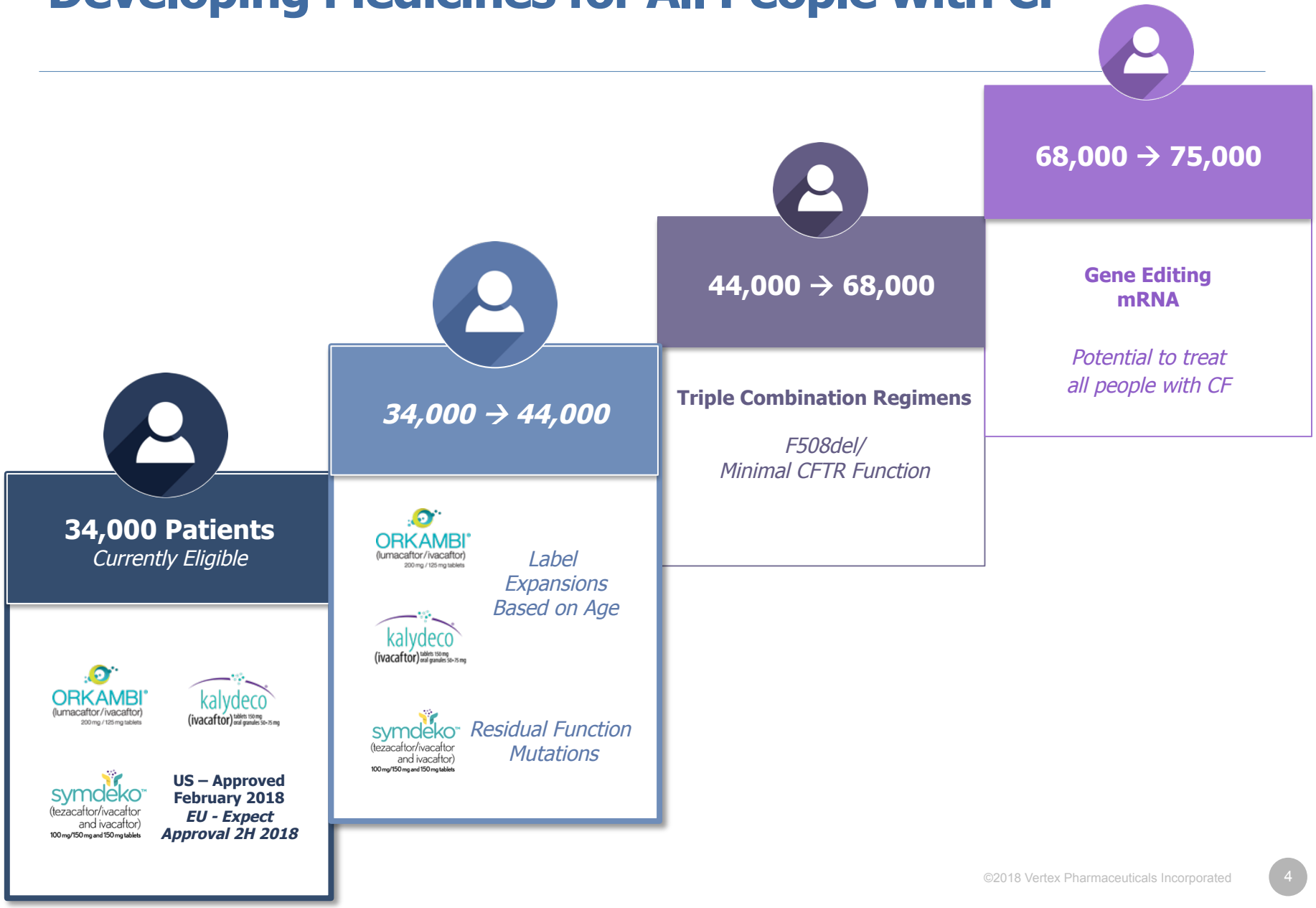
Safe Harbor Statement & Non-GAAP Financial Measures

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, including, without limitation, 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 CF net product 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.

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, asset acquisitions and consolidated variable interest entities, (iii) non-operating tax adjustments and (iv) other adjustments, including gains or losses related to the fair value of the company's strategic investments in CRISPR and Moderna Therapeutics, Inc. 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 future business development activities. A reconciliation of the GAAP financial results to non-GAAP financial results is included in the Company’s April 26, 2018 press release.

Developing Medicines for All People with CF



Early 2018 Accomplishments

- **Revenue and earnings growth** driven by the increased number of patients eligible for and being treated with our CF medicines
- Received **FDA approval for SYMDEKO** for people with CF ages 12 and older who have two copies of the *F508del* mutation or who have at least one mutation that is responsive to tezacaftor/ivacaftor
- Initiated two **Phase 3 programs for VX-659 and VX-445** to be evaluated as part of two separate triple combination regimens for people with CF ages 12 and older who have two copies of *F508del* mutation or who have one *F508del* mutation and one minimal function mutation
- First clinical trial authorization (CTA) granted for **Phase 1/2 study evaluating CTX001** in B-thalassemia with partner CRISPR Therapeutics in Europe
- Announced positive data from a **Phase 2 study evaluating VX-150** for the treatment of acute pain

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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

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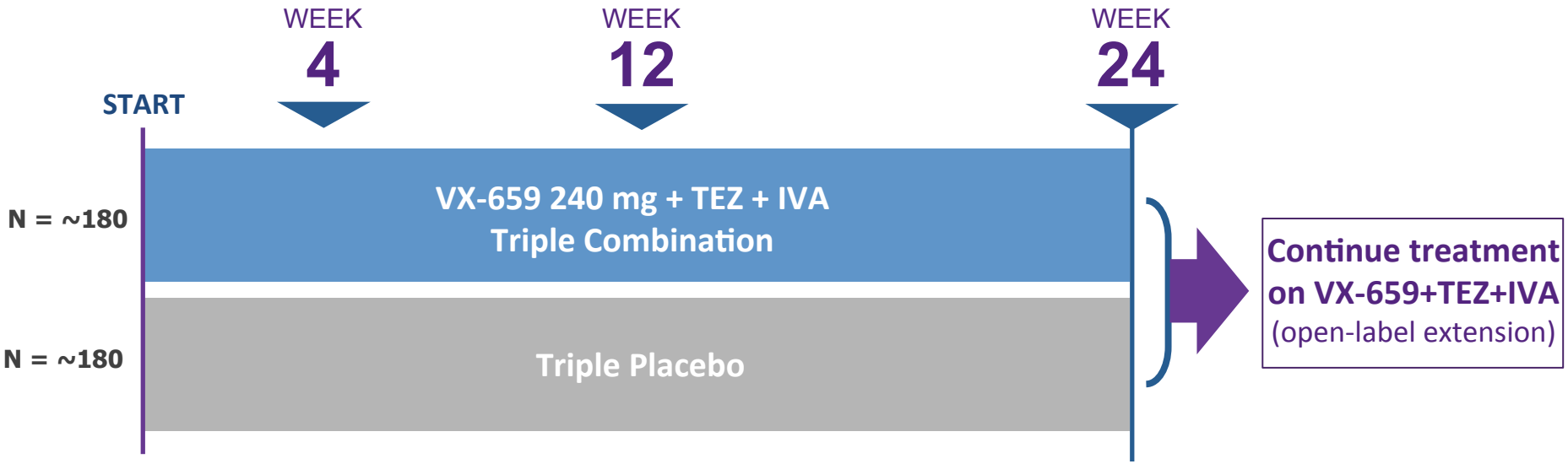
VX-659: F508del/Minimal Function Patients

Phase 3 Trial Design



- Global Phase 3 randomized, double-blind, placebo-controlled study
- Plan to enroll ~360 patients ages 12+ who have one *F508del* mutation and one minimal function mutation
- Primary endpoint is mean absolute change in lung function from baseline at week 4 of triple combination treatment compared to placebo
- Potential NDA submission based on data from 4-week primary efficacy analysis and safety data through 12 weeks
- Triple combination dose includes VX-659 240 mg + TEZ 100 mg + IVA 150 mg in AM and IVA 150 mg only in PM

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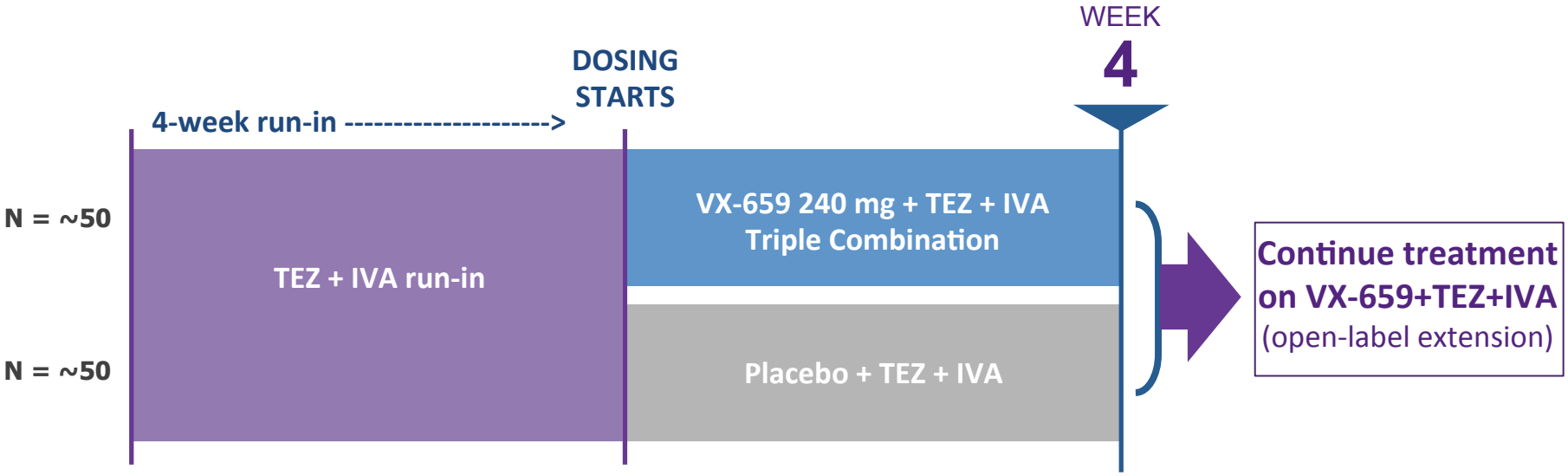
VX-659: F508del/F508del Patients

Phase 3 Trial Design

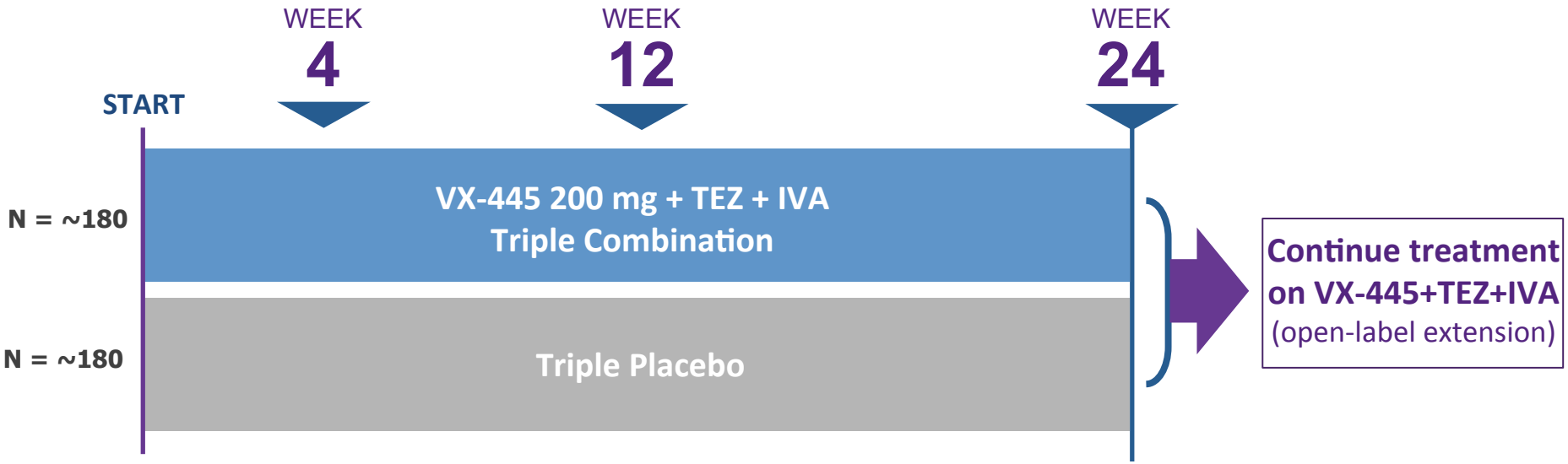


- Global Phase 3 randomized, double-blind, active-controlled study
- Plan to enroll ~100 patients ages 12+ with two copies of the *F508del* mutation
- Primary endpoint is mean absolute change in lung function from baseline (end of 4-week TEZ+IVA run-in) at week 4 of triple combination treatment compared to placebo+TEZ+IVA
- Potential regulatory submission in the U.S. based on 4-week primary efficacy analysis and secondary safety analysis and on 24-week safety data from Phase 3 F/MF study of VX-659+TEZ+IVA
- Triple combination dose includes VX-659 240 mg + TEZ 100 mg + IVA 150 mg in AM and IVA 150 mg only in PM

VERTEX

VX-445: F508del/Minimal Function Patients

Phase 3 Trial Design



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- Triple combination dose includes VX-445 200 mg + TEZ 100 mg + IVA 150 mg in AM and IVA 150 mg only in PM

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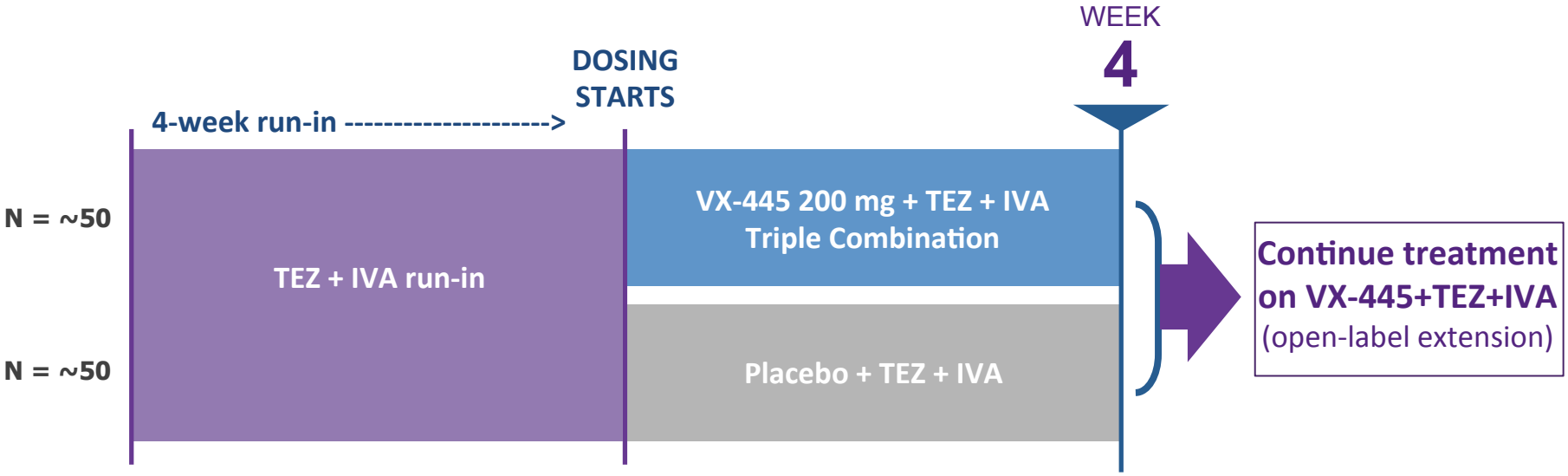
VX-445: F508del/F508del Patients

Phase 3 Trial Design



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- Primary endpoint is mean absolute change in lung function from baseline (end of 4-week TEZ+IVA run-in) at week 4 of triple combination treatment compared to placebo+TEZ+IVA
- Potential regulatory submission in the U.S. based on 4-week primary efficacy analysis and secondary safety analysis and on 24-week safety data from Phase 3 F/MF study of VX-445+TEZ+IVA
- Triple combination dose includes VX-445 200 mg + TEZ 100 mg + IVA 150 mg in AM and IVA 150 mg only in PM

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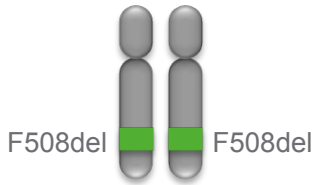
Phase 2 Studies Show Consistent Improvements Across Multiple Patient Groups

PHASE 2 RESULTS

VX-659 or VX-445 IN COMBINATION WITH TEZACAFTOR AND IVACAFTOR



Homozygous

Incremental to Tezacaftor/Ivacaftor Treatment

Heterozygous

	Absolute $ppFEV_1$ from baseline (Through Day 29)	Sweat Chloride (Through Day 29)	CFQ-R (at Day 29)	Absolute $ppFEV_1$ from baseline (Through Day 29)	Sweat Chloride (Through Day 29)	CFQ-R (at Day 29)
	VX-659 (400mg) + tezacaftor + ivacaftor			*VX-659 (240mg) + tezacaftor + ivacaftor*		
VX-659 *Active Arm n=18 F/F, n=20 F/MF*	**+9.7**	**-42.2**	**+19.5**	**+11.6**	**-43.7**	**+19.8**
	VX-445 (200mg) + tezacaftor + ivacaftor			*VX-445 (200mg) + tezacaftor + ivacaftor*		
VX-445 *Active Arm n=21 F/F, n=21 F/MF*	**+11.0**	**-39.6**	**+20.7**	**+13.8**	**-39.1**	**+25.7**

- *F/F = F508del/F508del; F/MF = F508del/minimal function*
- *VX-659 F/F Ph2 trial only evaluated 400mg dose as shown above; VX-659 F/MF Ph2 dose shown as 240mg as being evaluated in Ph3*
- *VX-445 F/F Ph2 trial only evaluated 200mg dose as shown above; VX-445 F/MF Ph2 dose shown as 200mg as being evaluated in Ph3*
- *Data provided as within-group changes for doses noted; complete safety and efficacy data available in 2/1/18, 3/1/18 and 4/26/18 press releases*
- *Change in $ppFEV_1$ provided as percentage points, sweat chloride as mmol/L, CFQ-R as points*
- *CFQ-R results reported are based on a mixed effect model not adjusted for baseline CFQ-R*

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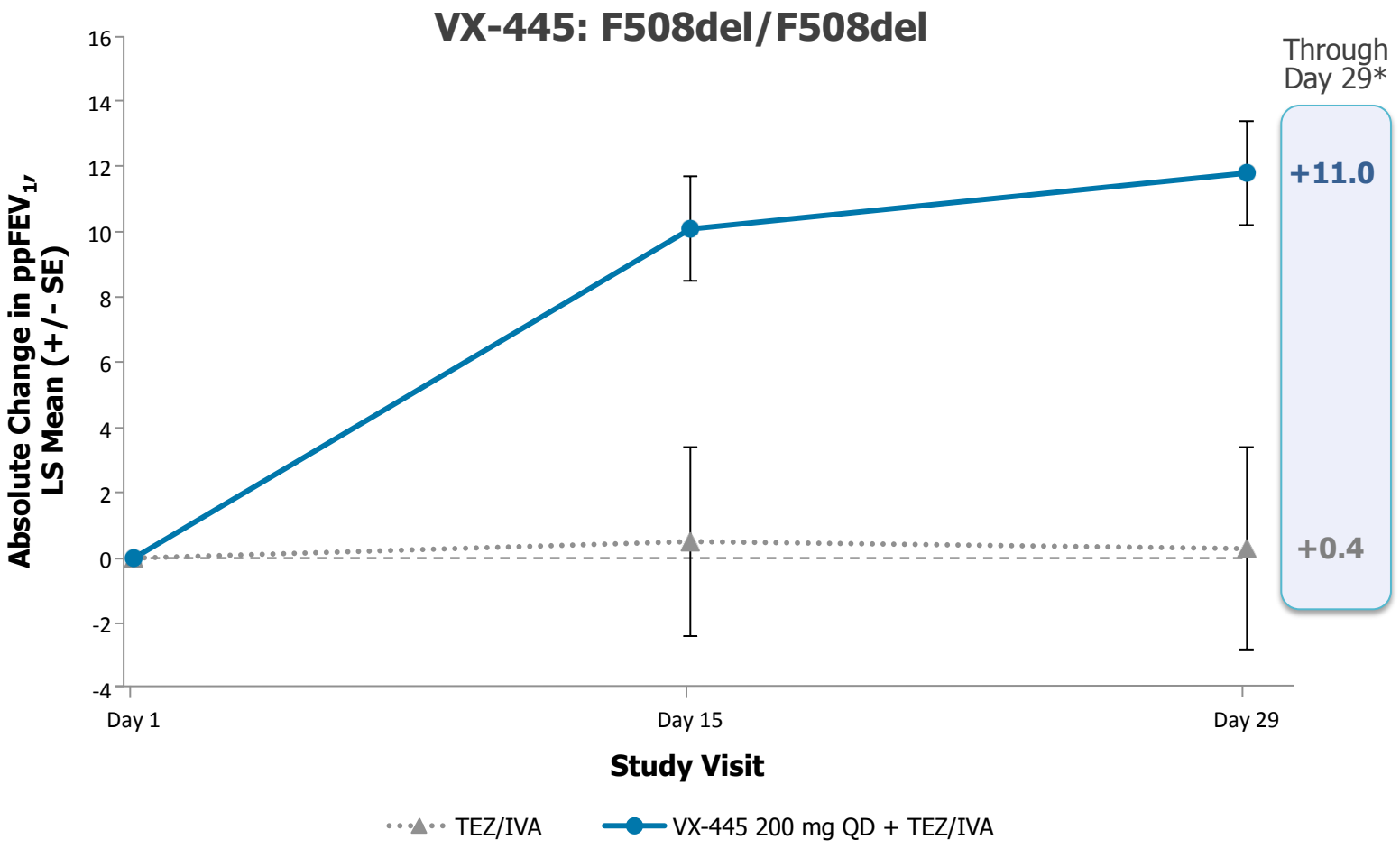
VX-445 + tezacaftor + ivacaftor

Absolute Change in ppFEV$_1$



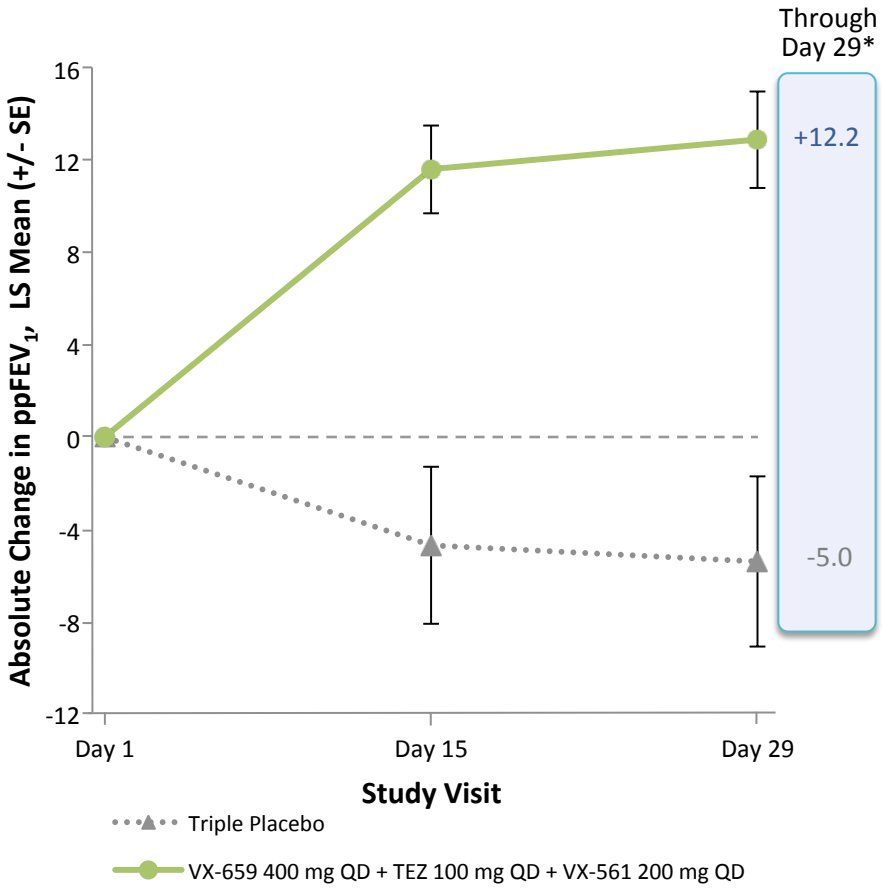
**Values expressed as "Through Day 29" are the average of Day 15 and Day 29 measures; baseline reflects the end of the 4-week tezacaftor/ivacaftor run-in period*

TEZ/IVA= tezacaftor (100 mg qd) + ivacaftor (150 mg q12h)

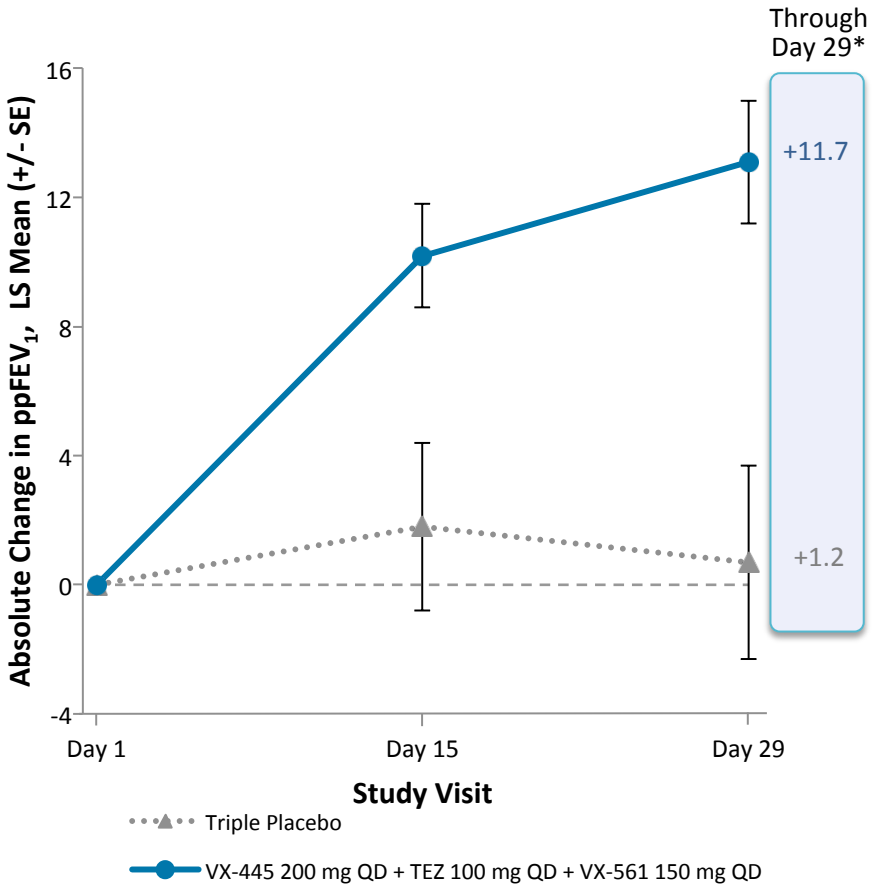
Phase 2 Studies of VX-561 as Part of Potential Once-Daily Triple Combination Regimen

Absolute Change in ppFEV$_1$

VX-659 + tezacaftor + VX-561: F508del/Minimal Function



VX-445 + tezacaftor + VX-561: F508del/Minimal Function



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

Q1 2018 Financial Highlights

($ in millions except per share data and percentages)	Q1 17	FY 2017	Q1 18
Total CF product revenues	$481	$2.17B	**$638**
Combined non-GAAP R&D and SG&A	313	$1.33B	**360**
Non-GAAP operating income	122	564	**208**
Non-GAAP operating margin	25%	26%	**33%**
Non-GAAP net income	101	495	**196**
Non-GAAP net income per share - diluted	$0.41	$1.95	**$0.76**
Cash, cash equivalents & marketable securities (quarter-end)		$2.09B	**$2.48B**

- *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 Q1 2018 press release dated April 26, 2018*
- *Reconciliation of non-GAAP operating income and non-GAAP operating margin to corresponding GAAP measures is included in the Appendix of this presentation*

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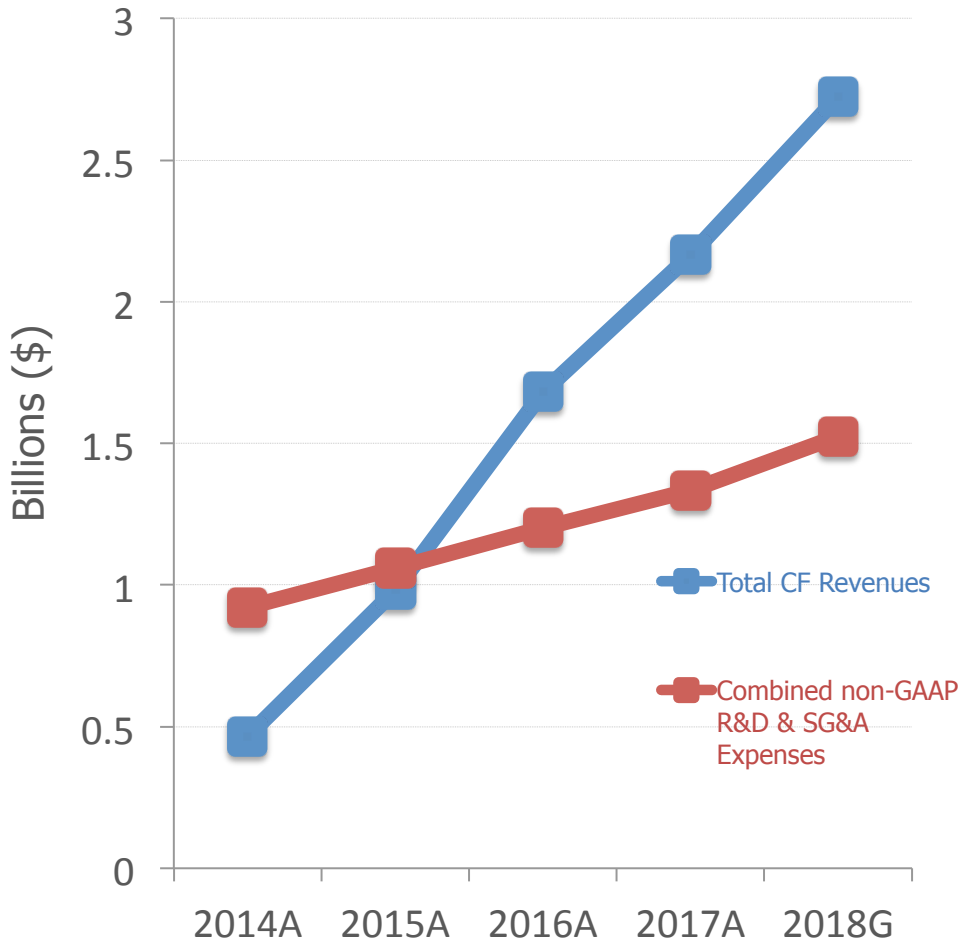
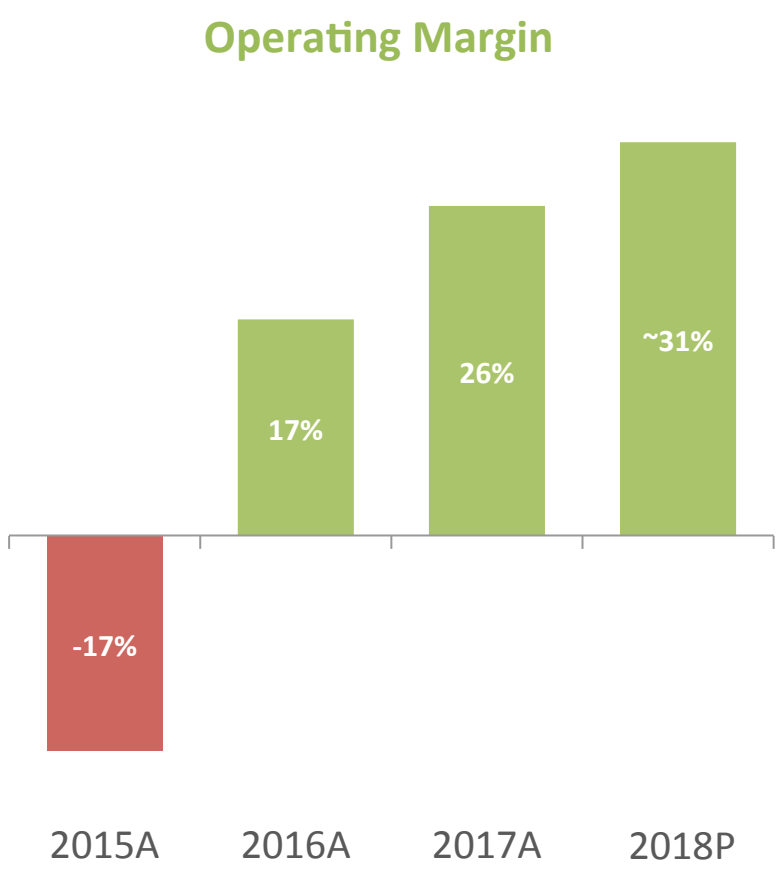
2018 Financial Guidance

	FY 2017 Actuals	2018 Guidance	2018 Guidance Commentary
Total CF Product Revenues	$2.17B	**$2.65 - $2.80B**	Expected revenue growth primarily from: • 12+ launch of SYMDEKO in U.S. • Increased number of patients treated with ORKAMBI outside the U.S.
Combined non-GAAP R&D and SG&A	$1.33B	**$1.50 - $1.55B**	Year-over-year increase based on: • Execution of Phase 3 studies for two separate triple combination regimens • Supply chain investment for triple combination regimens • Incremental investment to support SYMDEKO launch
Combined GAAP R&D and SG&A	$1.82B	**$1.80 - $1.95B**	

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 Q1 2018 press release dated April 26, 2018

Significant Growth in Revenue Driving Operating Margin Expansion





- *2018 Total CF Revenues (guidance: $2.65 – $2.80B) and Non-GAAP R&D and SG&A expenses (guidance: $1.50 - $1.55B) reflect the midpoint of guidance ranges.*
- *Operating margins reflect total CF revenues, combined non-GAAP R&D and SG&A expenses and cost of sales.*
- *2018 projected operating margin based on the midpoint of guidance ranges and assumes a ~13.5% cost of sales; not intended as financial guidance.*

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Appendix

Reconciliation of GAAP to non-GAAP Financial Information

($ in millions except per share data and percentages)	Q1 2017	Q4 2017	FY 2017	Q1 2018
GAAP total revenues	$715	$652	$2,489	$641
Non-GAAP total revenues	$482	$623	$2,174	$639
GAAP income from operations	$271	$126	$123	$129
Stock compensation expense	69	75	291	78
Collaborative and transaction revenues and expenses	(228)	(18)	(133)	1
Other adjustments	11	1	17	0
Non-GAAP income from operations	$122	$184	$564	$208
Operating Margin %:				
GAAP	38%	19%	5%	20%
Non-GAAP	25%	30%	26%	33%
Net income				
GAAP	248	101	263	210
Non-GAAP	101	158	495	196
Net income per share - diluted				
GAAP	$0.99	$0.39	$1.04	$0.81
Non-GAAP	$0.41	$0.61	$1.95	$0.76

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

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