Second-Quarter 2019 Financial Results

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THE SCIENCE *of* POSSIBILITY

July 31, 2019

Agenda

Introduction

Michael Partridge, Senior Vice President, Investor Relations

Business Highlights

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

Clinical Update

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

Financial Results

Charlie Wagner, Executive Vice President and Chief Financial Officer

Q&A

Stuart Arbuckle, Executive Vice President and Chief Commercial 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, (i) information pertaining to our medicines and the ongoing discovery, development and commercialization of Vertex's product candidates, (ii) 2019 financial guidance and (iii) Vertex's 2019 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'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 from Vertex's pre-tax income (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) gains or losses related to the fair value of the company's strategic investments and (iv) other adjustments. The company's non-GAAP financial results also exclude from its provision for or benefit from income taxes the estimated tax impact related to its non-GAAP adjustments to pre-tax income described above. 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 non-GAAP basis. The company also provides guidance regarding its anticipated income taxes as a percentage of pre-tax income on a non-GAAP basis. The guidance regarding GAAP research and development expenses and sales, general and administrative expenses does not include estimates associated with any potential future business development activities. A reconciliation of the GAAP financial results to non-GAAP financial results is included in the appendix of this presentation.

2019 Key Goals and Milestones

	2018	2019
ACHIEVE OUR VISION IN CYSTIC FIBROSIS	☑ 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	☑ **Phase 3 data for VX-445 in patients ages 12+** ☑ **Submit NDA for a triple combination regimen no later than mid-2019** ☑ **U.S. approval for SYMDEKO for children ages 6 through 11** ☑ **Initiate POC study of additional next-generation corrector** ☑ **Phase 2 dose-ranging study of potential once-daily regimen VX-561**
EXPAND PIPELINE BEYOND CF	☑ Advance one or more compounds from research into clinical development ☑ Initiate clinical development of CRISPR-Cas9 treatment in Beta Thalassemia & Sickle Cell Disease	☐ **Complete Phase 1 studies in at least two new diseases** ☑ **Bolster pipeline with internal and external assets** ☑ **Advance one or more compounds from research into clinical development**
BUILD FINANCIAL STRENGTH	☑ 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	☑ **Continued CF product revenue growth** ☐ **Continued uptake and reimbursement for ORKAMBI and SYMDEKO in additional countries outside the U.S.** ☐ **Continued management of non-GAAP combined R&D and SG&A expenses** ☐ **Continued expansion of non-GAAP operating margins and cash flow**

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Developing Medicines for All People with CF

KALYDECO
ORKAMBI
SYMDEKO

39,000 Patients
Currently Eligible

39,000 → 44,000

- *Treating younger patients*
- *Label expansions*

44,000 → 68,000

VX-445+ tezacaftor+ivacaftor Triple Combination Regimen

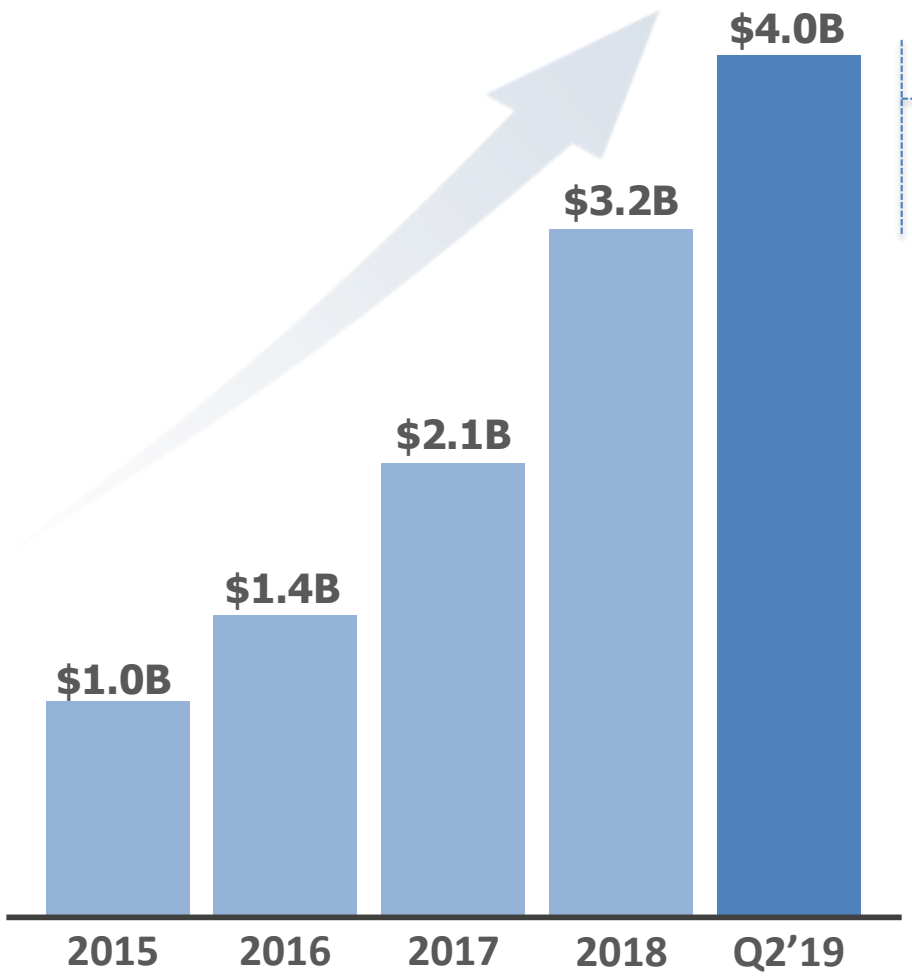
F508del/ Minimal CFTR Function

68,000 → 75,000

Gene Editing mRNA

Potential to treat all people with CF

Increasing Cash Flow Enables Investment for Future Growth



Total Cash at Period-End

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

Business Development and Capital Allocation Strategy

- Complement ongoing R&D in CF
- Access novel platform technologies and targets
- In-license or acquire pipeline assets

CRISPR THERAPEUTICS · exonics THERAPEUTICS · arbor · MERCK · X-CHEM · KYMERA · GENOMICS PLC

Note: *Period-end cash includes cash, cash equivalents and marketable securities.*

Vertex Strategy and Business Model

A Blueprint for Serial Innovation

CORPORATE STRATEGY

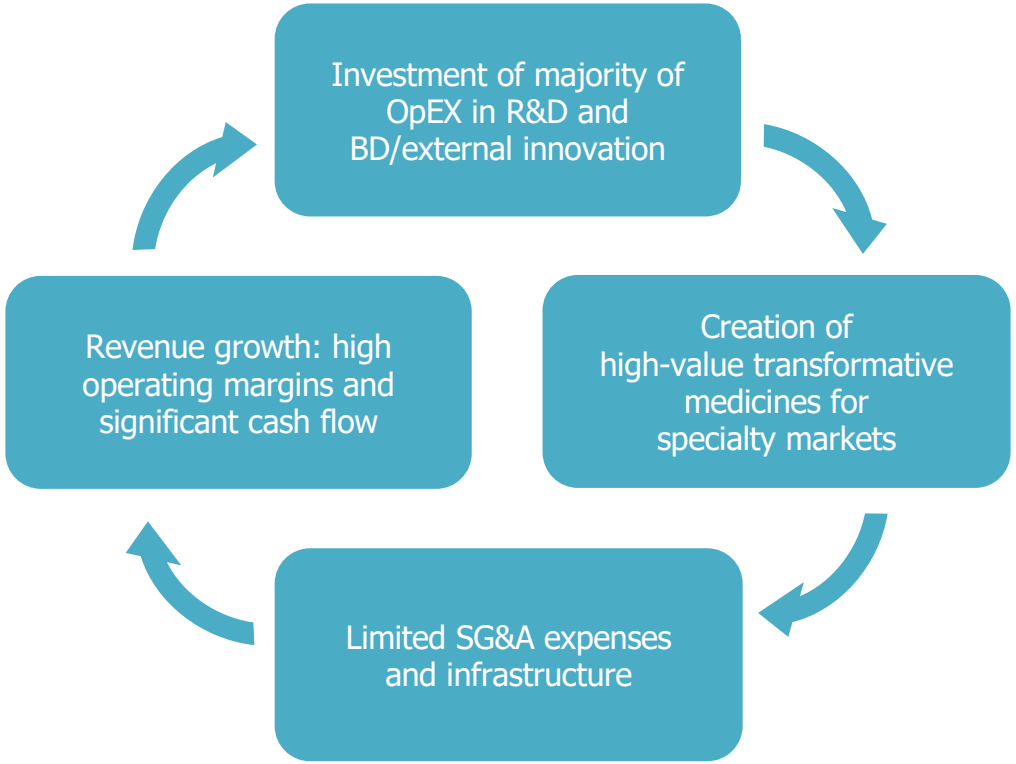
Vertex invests in **scientific innovation** to create **transformative medicines** for people with **serious diseases** with a focus on **specialty markets**

RESEARCH STRATEGY

Combine **transformative advances** in the **understanding of human disease** and in the **science of therapeutics** to dramatically advance human health

- Focus on **validated targets** that address causal human biology
- Create **predictive lab assays** and **clinical biomarkers**
- Identify **rapid path to registration** and approval
- Discover and develop medicines that offer transformative benefit, **regardless of modality**

DIFFERENTIATED BUSINESS MODEL



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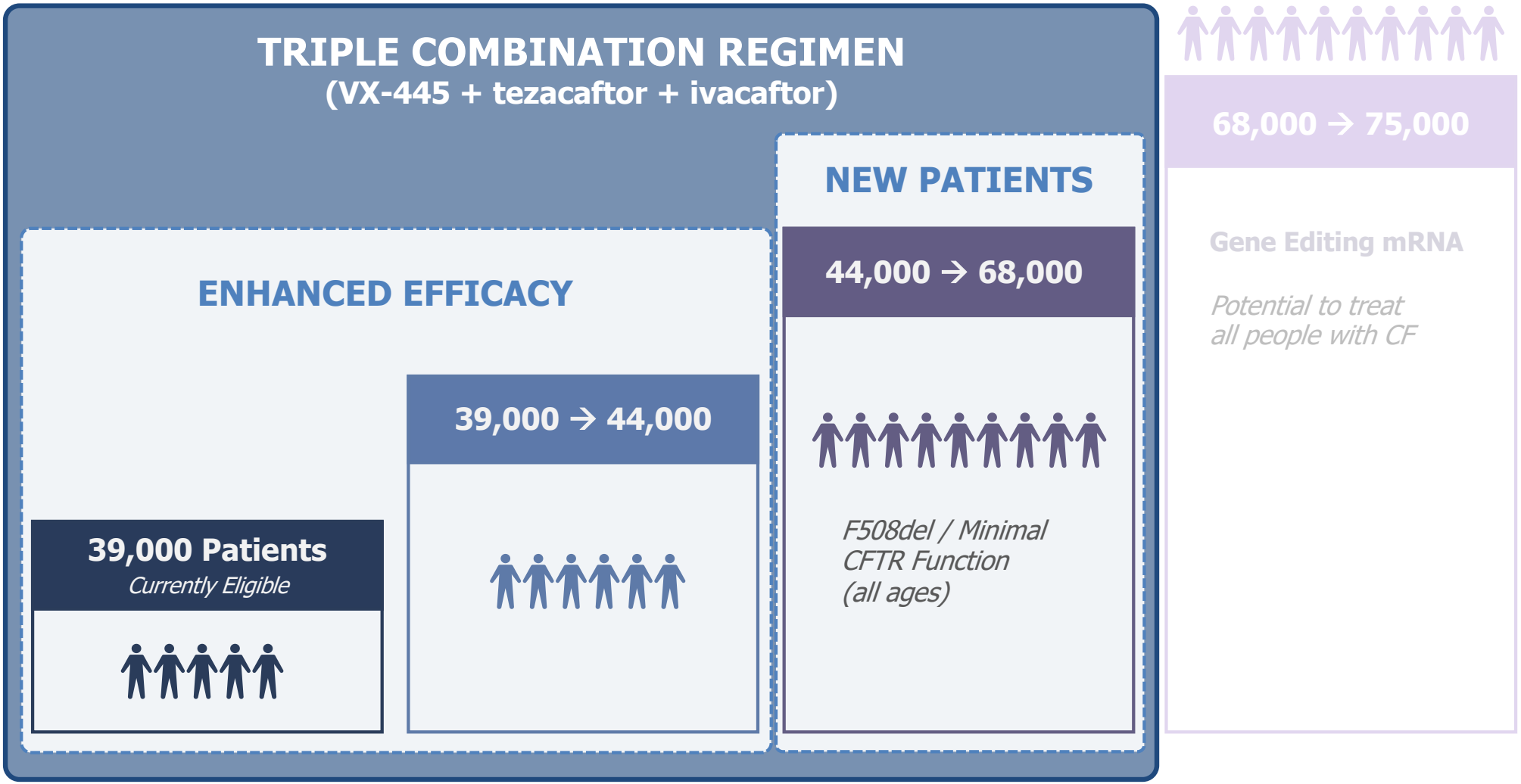
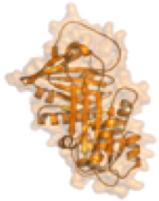
VX-445 + tezacaftor + ivacaftor Triple Combination Regimen Has Potential to Treat Up to 90% of CF Patients



Beyond CF

Multiple Opportunities for Transformative Medicines

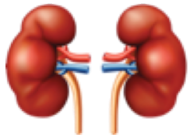


Alpha-1 Antitrypsin Deficiency

Phase 1 evaluation of single and multiple ascending doses of VX-814 complete; VX-814 to advance into Phase 2 development; Clinical data in people with two Z mutations anticipated in 2020; Second molecule (VX-864) advanced into Phase 1 development

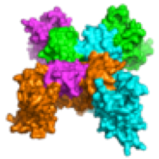
Sickle Cell Disease / Beta Thalassemia

First patients dosed in Phase 1/2 study of CTX001 for severe sickle cell disease and beta-thalassemia



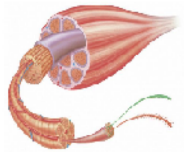
APOL1-Mediated Kidney Diseases

First molecule (VX-147) advanced into Phase 1 development; Potential to advance to Phase 2 POC study in 2020; Multiple other APOL1 inhibitors advancing through preclinical development



Pain

Proof-of-concept for NaV1.8 inhibition in acute, musculoskeletal and neuropathic pain; Ongoing research to discover/develop additional NaV1.8 inhibitors and will choose best molecule(s) to advance into late-stage development; Initiating Phase 1 study of VX-961



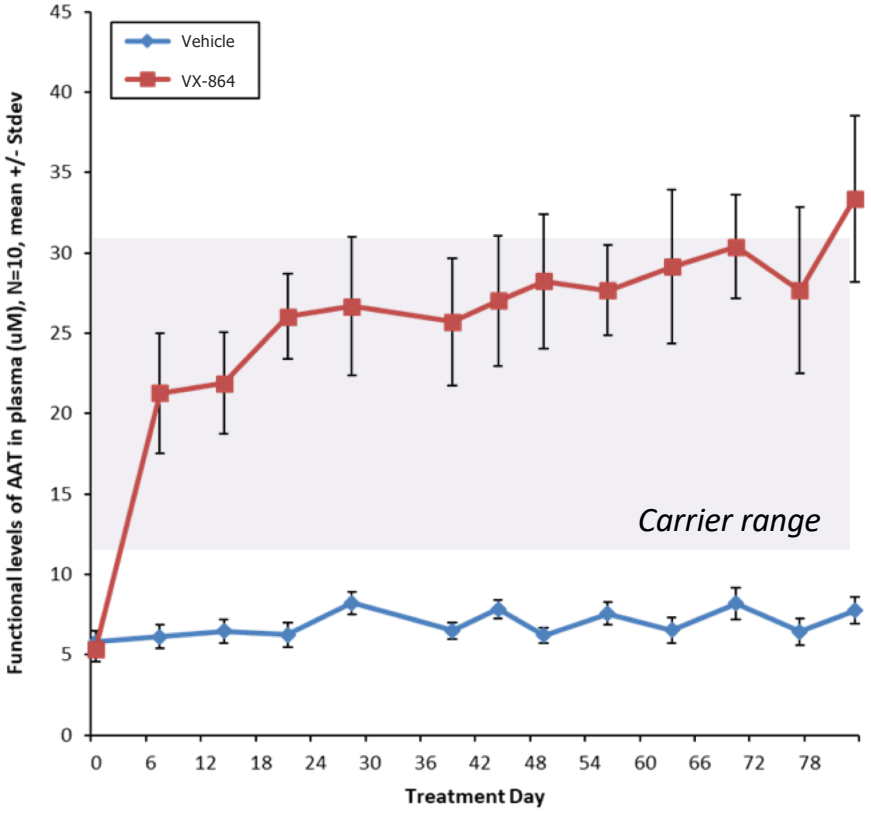
Duchenne Muscular Dystrophy / Myotonic Dystrophy Type 1

In July 2019, VRTX completed its acquisition of Exonics Therapeutics and expanded its collaboration with CRISPR Therapeutics with a goal of developing novel gene editing therapies for DMD and DM1

Small Molecule Corrector for Alpha-1 Antitrypsin Deficiency

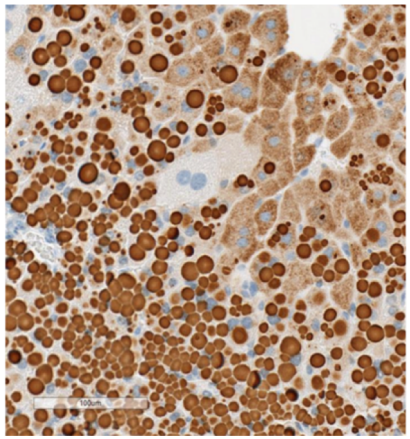
Proof of Mechanism in Preclinical Studies over 12 Weeks

RAISING CIRCULATING LEVELS OF AAT IN PIZ TRANSGENIC MOUSE

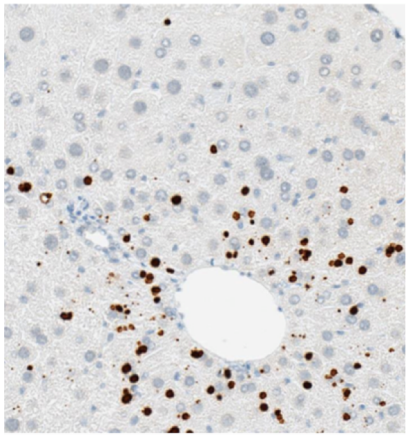


REDUCING TOXIC POLYMER IN THE LIVER OF PIZ TRANSGENIC MICE

Vehicle 12 weeks



VX-864 12 weeks



75% reduction in polymer (p<0.001)

Potential to prevent disease progression in the lung

Potential to address pathology in the liver

Notes:

- *Animal studies using PiZ transgenic mouse model that carries human Z-AAT gene*
- *Mouse baseline in this experiment corresponds well with approximate average human ZZ baseline (~5uM)*
- *"Carrier range" corresponds to values above the "protective threshold" (11 uM)*

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Focal Segmental Glomerulosclerosis

Proof of Mechanism in Animal Model of APOL1-Mediated Kidney Disease

Severity of Disease

FSGS is a severe kidney disease characterized by proteinuria and progressive loss of kidney function. ~10,000 people in the U.S. have FSGS and are homozygous for APOL1 mutations

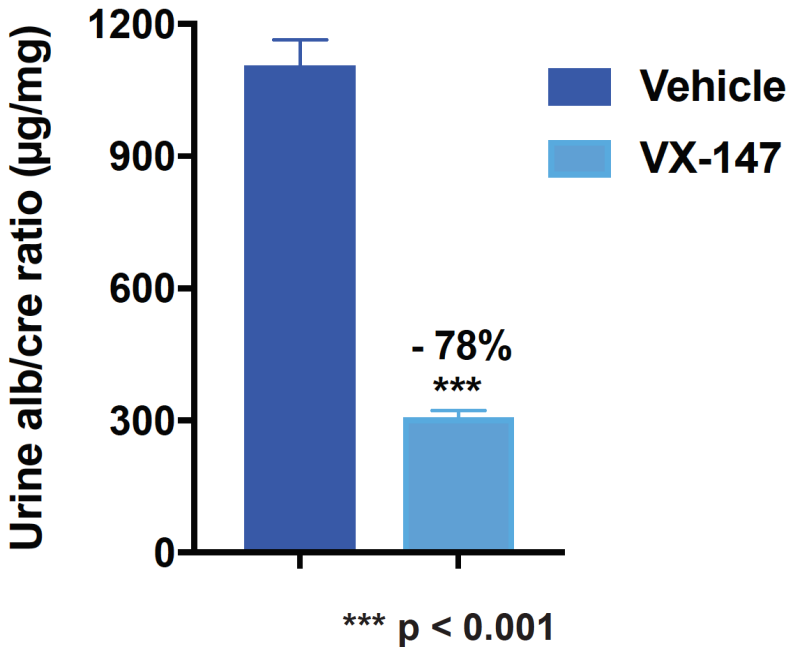
Human Biology

Precision medicine approach targeting APOL1 protein function in people with two APOL1 mutations – a causal genetic factor in FSGS and other proteinuric kidney diseases

Therapeutic Approach & Biomarkers

VX-147 is an inhibitor of APOL1 function and demonstrates dose-dependent therapeutic efficacy in cell and in animal models of APOL1-mediated kidney disease, where it reduces protein levels in urine

REDUCED PROTEINURIA AFTER 4 DAYS OF TREATMENT WITH VX-147



Notes:

- *Animal studies using transgenic mouse model that carries mutant human APOL1 gene*
- *Treatment with VX-147 was initiated after establishment of proteinuria*

Q2 2019 Financial Highlights

($ in millions except per share data and percentages)	Q2 18	FY 2018	Q1 19	Q2 19	1H 2019
Total CF product revenues	$750	$3.04B	$857	**$940**	$1.80B
KALYDECO	253	1.01B	244	**262**	506
ORKAMBI	311	1.26B	293	**316**	609
SYMDEKO/SYMKEVI	186	769	320	**362**	682
Combined non-GAAP R&D and SG&A	388	1.53B	388	**394**	782
Non-GAAP operating income	260	1.11B	377	**413**	790
Non-GAAP operating margin	35%	37%	44%	**44%**	44%
Non-GAAP net income	244	1.06B	296	**327**	623
Non-GAAP net income per share - diluted	$0.94	$4.08	$1.14	**$1.26**	2.40
Cash, cash equivalents & marketable securities (period-end)		$3.2B		**$4.0B**	

Notes

- *An explanation of non-GAAP financial measures and reconciliation of combined non-GAAP R&D and SG&A expense, non-GAAP net income and non-GAAP net income per share is included in the company's Q2 2019 press release dated July 31, 2019*
- *Reconciliation of non-GAAP operating income and non-GAAP operating margin to corresponding GAAP measures is included in the appendix of this presentation; totals may not add due to rounding*

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2019 Financial Guidance Update

	FY 2018 Actuals	FY 2019 Guidance	FY 2019 Guidance Commentary
Total CF Product Revenues	$3.04B	**$3.60 - $3.70B**	Increased guidance from $3.45 - $3.55B reflects strong commercial performance in 1H 2019
Combined Non-GAAP R&D and SG&A	$1.53B	**$1.65 - $1.70B**	Non-GAAP guidance unchanged
Combined GAAP R&D and SG&A	$1.97B	**$2.25 - $2.40B**	
Non-GAAP Effective Tax Rate		**21% - 22%**	The vast majority of the company's tax provision will be a non-cash expense until NOLs are fully utilized

Note: *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 Q2 2019 press release dated July 31, 2019*

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Appendix

Reconciliation of GAAP to non-GAAP Financial Information

	Q2 2018	FY 2018	Q1 2019	Q2 2019	1H 2019
GAAP total revenues	$752	$3,048	$858	**$941**	$1,800
Non-GAAP total revenues	$751	$3,043	$858	**$941**	$1,800
GAAP operating income	173	635	277	**270**	547
Stock compensation expense	82	325	94	**90**	183
Other adjustments	5	152	6	**53**	60
Non-GAAP operating income	260	1.11B	377	**413**	790
Operating Margin %:					
GAAP	23%	21%	32%	**29%**	30%
Non-GAAP	35%	37%	44%	**44%**	44%
Net income					
GAAP	207	2.10B	269	**267**	536
Non-GAAP	244	1.06B	296	**327**	623
Net income per share - diluted					
GAAP	$0.80	$8.09	$1.03	**$1.03**	$2.06
Non-GAAP	$0.94	$4.08	$1.14	**$1.26**	$2.40

Note: *All numbers in the above reconciliation table are in millions except per share data and percentages; totals may not add due to rounding*