VERTEX

THE SCIENCE *of* POSSIBILITY

FIRST-QUARTER 2020 FINANCIAL RESULTS

APRIL 29, 2020

AGENDA

Introduction

Michael Partridge, Senior Vice President, Investor Relations

CEO Perspective

Reshma Kewalramani, M.D., CEO and President

Commercial Update & TRIKAFTA Launch

Stuart Arbuckle, Executive Vice President and Chief Commercial Officer

Financial Results

Charlie Wagner, Executive Vice President and Chief Financial 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 section captioned "2020 Updated Financial Guidance" and statements regarding (i) regulatory filings, (ii) the development plan and timelines for the company's drug candidates and (iii) its expectations regarding the affects COVID-19 will have on our business and operations. 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 risks and uncertainties that could cause actual events or results to differ materially from those expressed or implied by such forward-looking statements. Those risks and uncertainties include, among other things, that the company's expectations regarding its 2020 CF net product revenues, expenses and effective tax rates may be incorrect (including because one or more of the company's assumptions underlying its expectations may not be realized), that COVID-19 may have different or more significant impacts on the company's business or operations that the company currently expects, that data from the company's development programs may not support registration or further development of its potential medicines due to safety, efficacy or other reasons, and other risks listed under Risk Factors in Vertex's annual report and subsequent 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 from Vertex's pre-tax income (i) stock-based compensation expense, (ii) revenues and expenses related to collaboration agreements, (iii) gains or losses related to the fair value of the company's strategic investments, (iv) acquisition-related costs and (v) other adjustments. The company's non-GAAP financial results also exclude from its provision for income taxes the estimated tax impact related to its non-GAAP adjustments to pre-tax income described above and certain discrete items. 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 attached financial information and in the company's Q1 2020 press release dated April 29, 2020.

VERTEX STRATEGY AND BUSINESS MODEL
A BLUEPRINT FOR SERIAL INNOVATION

CORPORATE STRATEGY

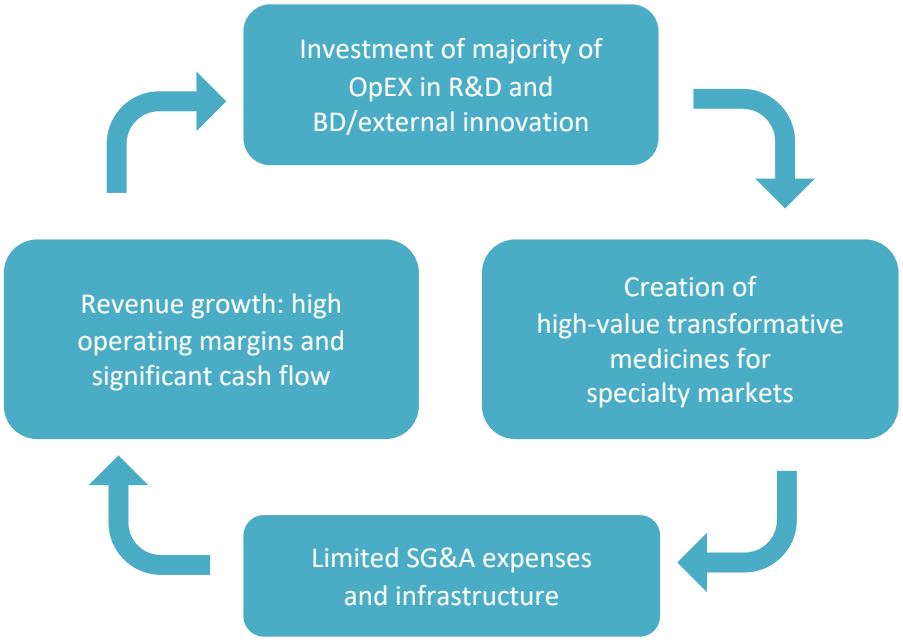
Vertex invests in **scientific innovation** to create **transformative medicines** for people with **serious diseases** with a focus on **specialty markets**

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



DEVELOPING MEDICINES FOR ALL PEOPLE WITH CF

First CFTR Modulators

~39,000 patients eligible

KALYDECO
ORKAMBI
SYMDEKO/SYMKEVI

~68,000 patients

trikafta™
(elexacaftor/tezacaftor/ivacaftor and ivacaftor)
100 mg/50 mg/75 mg and 150 mg tablets

Up to 90% of CF patients eligible; Increased efficacy

Beyond 2021
- WW ages <6
- OUS ages 6-11

2020/2021
- U.S. ages 6-11
- OUS ages 12+

TODAY
18,000 patients eligible
Approved in the U.S. for ages 12+

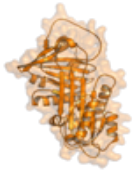
Genetic Therapies

Remaining ~10% of patients untreatable with a CFTR modulator

BEYOND CF
MULTIPLE OPPORTUNITIES FOR TRANSFORMATIVE MEDICINES

SMALL MOLECULES

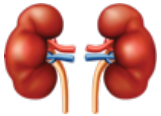
Alpha-1 Antitrypsin Deficiency



VX-814 in Phase 2

Small molecule that corrects protein misfolding, enables secretion of AAT from the liver, and increases functional serum AAT levels

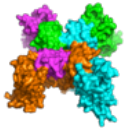
APOL1-Mediated Kidney Diseases



VX-147 in Phase 2

Small molecule inhibitor of APOL1 function, a causal genetic factor in FSGS/other proteinuric kidney diseases

Pain



Phase 1

Small molecule inhibitors of NaV1.8 as a novel treatment for pain

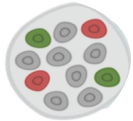
CELL AND GENETIC THERAPIES

Sickle Cell Disease & Beta Thalassemia

CTX001 in Phase1/2

Ex vivo gene editing with goal of providing one-time curative therapy

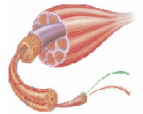
Type 1 Diabetes



Preclinical

Potentially curative cell-based treatment and delivery system

DMD and DM1



Preclinical

Novel gene editing platform to potentially restore dystrophin production in DMD

U.S. TRIKAFTA LAUNCH

- Early FDA approval received on October 21, 2019 for people ages 12+ who have at least one *F508del* mutation
- Majority of the ~18,000 eligible patients in the U.S. already initiated TRIKFATA therapy
- Strong uptake from all eligible patients, including new initiations as well as patients transitioning from another VRTX CF medicine
- Broad coverage and reimbursement from both commercial and government payers in the U.S.
- MAA review underway for EU approval

KEY GROWTH DRIVERS FOR CF PORTFOLIO

EXPANDING INTO NEW COUNTRIES

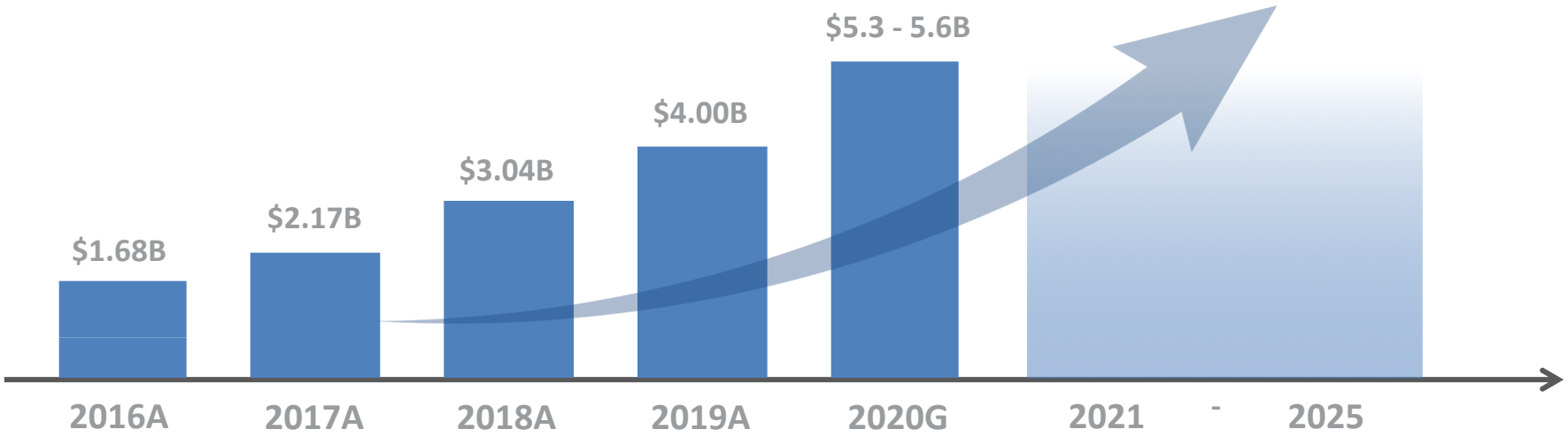
- MAA for *elexacaftor/tezacaftor/ivacaftor* in patients with at least one F508del mutation aged 12+ has been filed and is under review with the EMA
- Applications have also been submitted for *elexacaftor/tezacaftor/ivacaftor* in patients with at least one *F508del* mutation aged 12+ in Australia and Switzerland
- Patients in Switzerland can now access ORKAMBI and SYMDEKO through a new portfolio reimbursement agreement that will also encompass *elexacaftor/tezacaftor/ivacaftor* upon that regimen's approval

EXPANDING TO YOUNGER PATIENTS

- Enrollment is completed for a Ph3 study for TRIKAFTA in children ages 6-11. An sNDA planned for 2H 2020 in people with at least one *F508del* mutation
- Recently completed submission of an sNDA to the FDA and Type 2 variation to the EMA for the use of KALYDECO in infants ages 4 - <6 months

CONTINUED CF REVENUE GROWTH IN 2020 AND BEYOND

Growth to 90% of all CF patients
treating younger patients and label expansions with current medicines



GLOBAL CF PRODUCT REVENUES

Notes:
- 2020 reflects the midpoint of the total CF product revenue guidance range provided on April 29, 2020
- 2021 - 2025 potential growth in CF revenues is provided as a graphical representation

Q1 2020 FINANCIAL HIGHLIGHTS

($ in millions except where noted or per share data and percentages)	Q1 19	FY 19	Q1 20
Total non-GAAP CF product revenues	$857	$4.00B	**$1.52B**
TRIKAFTA	-	420	**895**
SYMDEKO/SYMKEVI	320	1.42B	**173**
ORKAMBI	293	1.18B	**234**
KALYDECO	244	991	**213**
Combined non-GAAP R&D and SG&A	388	1.69B	**477**
Non-GAAP operating income	377	1.79B	**877**
Non-GAAP operating margin	44%	45%	**58%**
Non-GAAP net income	296	1.39B	**674**
Non-GAAP net income per share - diluted	$1.14	$5.33	**$2.56**
Cash, cash equivalents & marketable securities (period-end)	$3.5B	$3.8B	**$4.2B**

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 Q1 2020 press release dated April 29, 2020
- 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

FY 2020 UPDATED FINANCIAL GUIDANCE

	Prior	Current	Commentary
Total CF Product Revenues	$5.1-$5.3B	**$5.3 - $5.6B**	At the midpoint of the new guidance, this represents 36% growth over 2019
Combined Non-GAAP R&D and SG&A	$1.95 -$2.0B	**Unchanged**	Non-GAAP guidance unchanged
Combined GAAP R&D and SG&A	$2.4 -$2.55B	**Unchanged**	GAAP guidance unchanged
Non-GAAP Effective Tax Rate	21% - 22%	**Unchanged**	A portion 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 Q1 2020 press release dated April 29, 2020

VERTEX

THE SCIENCE *of* POSSIBILITY

FIRST-QUARTER 2020 FINANCIAL RESULTS

APRIL 29, 2019

APPENDIX
RECONCILIATION OF GAAP TO NON-GAAP FINANCIAL INFORMATION

	Q1 2019	FY 2019	Q1 2020
GAAP total revenues	$858	$4.16B	**$1.52B**
Non-GAAP total revenues	$858	$4.01B	**$1.52B**
GAAP operating income	277	1.20B	**720**
Stock compensation expense	94	360	**116**
Other adjustments	6	228	**41**
Non-GAAP operating income	377	1.79B	**877**
Operating Margin %:			
GAAP	32%	29%	**48%**
Non-GAAP	44%	45%	**58%**
Net income			
GAAP	269	1.18B	**603**
Non-GAAP	296	1.39B	**674**
Net income per share - diluted			
GAAP	$1.03	$4.51	**$2.29**
Non-GAAP	$1.14	$5.33	**$2.56**

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