



SECOND-QUARTER 2020 FINANCIAL RESULTS

JULY 30, 2020

AGENDA

Introduction

Michael Partridge, Senior Vice President, Investor Relations

CEO Perspective and R&D Update

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 information provided regarding future financial performance, the section captioned "Full Year 2020 Updated Financial Guidance" and statements regarding (i) regulatory filings and data submissions, (ii) anticipated regulatory approvals, including the anticipated KAFTRIO and SYMKEVI approvals, and future label expansions, (iii) the development plan and timelines for the company's medicines, drug candidates and pipeline programs, (iv) the company's expectations regarding the effects COVID-19 will have on its business and operations, and (v) the anticipated commercial launch and access to KAFTRIO, if approved. 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 than 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 Q2 2020 press release dated July 30, 2020.

SIGNIFICANT RECENT ACCOMPLISHMENTS AND UPCOMING MILESTONES

2020 YTD Key Accomplishments

- ✓ Successful launch of TRIKAFTA (U.S. ages 12+)
- ✓ Positive CHMP opinion for KAFTRIO (EU ages 12+)
- ✓ KAFTRIO reimbursement agreement with NHS England

ACHIEVE OUR VISION IN CYSTIC FIBROSIS

Key Milestones Ahead

- ❑ European Commission approval of KAFTRIO (ages 12+)
- ❑ Submission of TRIKAFTA sNDA (U.S. ages 6-11)
- ❑ European Commission approval of SYMKEVI (ages 6-11)

- ✓ Proof-of-concept for CTX001 in beta thalassemia patients
- ✓ Enrollment underway in the Ph2 study for VX-147 in APOL1-mediated FSGS
- ✓ Initiated Ph2 for VX-864 in AAT deficiency

DEVELOP NEW TRANSFORMATIVE MEDICINES FOR ADDITIONAL SERIOUS DISEASES

- ❑ Potential for proof-of-concept in AAT deficiency
- ❑ Potential for proof-of-concept for CTX001 in sickle cell disease
- ❑ Submission of IND in type 1 diabetes

- ✓ Significant CF product revenue growth
- ✓ Disciplined management of operating expenses

DELIVER FINANCIAL PERFORMANCE

- ❑ Continued internal and external investment for future growth
- ❑ FY CF revenue growth of 45% versus 2019

DEVELOPING MEDICINES FOR ALL PEOPLE WITH CF

Genetic Therapies

Remaining ~10% of patients untreatable with a CFTR modulator

Triple Combination

~68,000 patients


trikafta[®]
(elexacaftor/tezacaftor/ivacaftor
and ivacaftor)


kaftrio[®]
(ivacaftor/tezacaftor/elexacaftor)


+ kalydeco[®]
(ivacaftor)

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

Approved in the U.S. for ages 12+

Positive CHMP opinion in EU for ages 12+

First CFTR Modulators

~39,000 patients eligible

KALYDECO
ORKAMBI
SYMDEKO/SYMKEVI

MULTIPLE PROGRAMS ON TRACK FOR POTENTIAL PROOF-OF-CONCEPT

SMALL MOLECULES

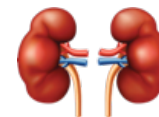
Alpha-1 Antitrypsin Deficiency



VX-814 & VX-864 in Phase 2
VX-814 data anticipated late 2020 or Q121

Small molecules to correct protein misfolding, enabling secretion of AAT from the liver and increased functional AAT in serum

APOL1-Mediated Kidney Diseases



VX-147 in Phase 2
Data anticipated 2021

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

CELL AND GENETIC THERAPIES

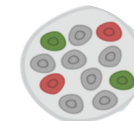
Sickle Cell Disease & Beta Thalassemia



CTX001 in Phase 1/2
Additional data anticipated 2H20

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

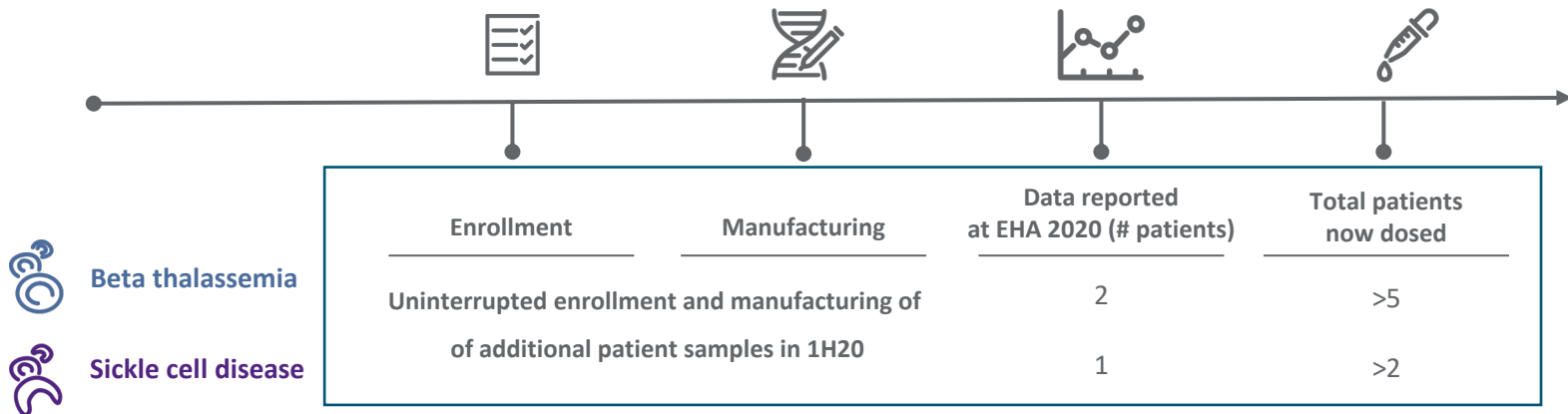
Type 1 Diabetes



Preclinical
IND on track for late 2020

Potentially curative cell-based treatment and delivery system

CTX001 PROGRAM GAINING MOMENTUM WITH ADDITIONAL DATA EXPECTED IN 2H20



Proof-of-concept achieved in beta thalassemia and expected in 2H20 for SCD

TDT patients: Transfusion-independent at 15 and 5 months post-CTX001 infusion

SCD patient: VOC-free at 9 months post-CTX001 infusion

Conditioning and dosing is ongoing in both studies, and data in additional patients expected in 2H20

U.S. TRIKAFTA LAUNCH

- Early FDA approval received on October 21, 2019 for people ages 12+ who have at least one *F508del* mutation
- Vast majority of the ~18,000 eligible patients in the U.S. initiated TRIKAFTA therapy
- Continued strong uptake from all eligible patients, including new initiations as well as patients transitioning from another VRTX CF medicine
- Achieved broad reimbursement from public and private payers
- Positive CHMP opinion for the *elexacaftor/tezacaftor/ivacaftor* triple combination



GEOGRAPHICAL AND LABEL EXPANSIONS ANTICIPATED TO CONTINUE TO DRIVE CF GROWTH BEYOND 2020



CHMP positive opinion for *elexacaftor/tezacaftor/ivacaftor* (KAFTRIO); European Commission approval anticipated



Expansion of the reimbursement agreement with NHS England to include KAFTRIO for the treatment of patients 12+ with one *F508del* mutation and one minimal function mutation or two *F508del* mutations



Submission of an sNDA with at least one *F508del* mutation to U.S. FDA in Q4 2020 for TRIKAFTA for the treatment of patients ages 6-11

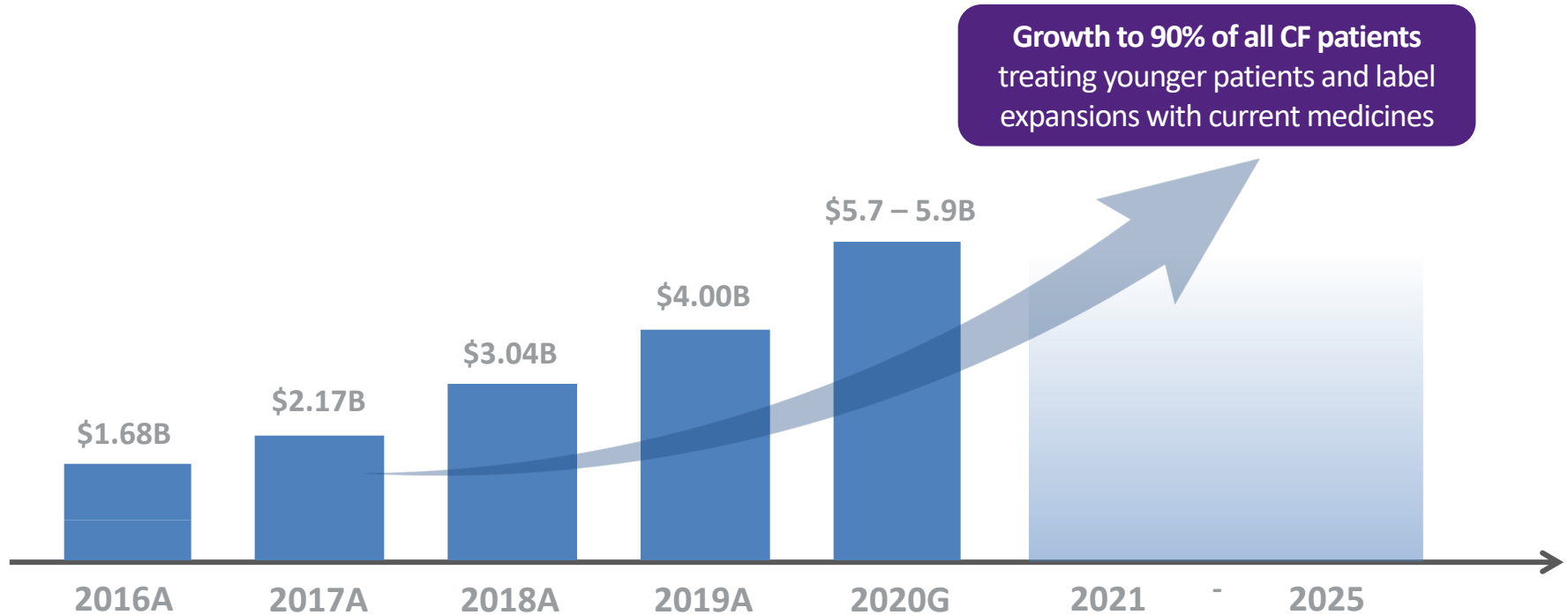
Q2 2020 FINANCIAL HIGHLIGHTS

<i>(\$ in millions except where noted or per share data and percentages)</i>	Q2 19	FY 19	Q2 20
Total non-GAAP CF product revenues	<u>\$940</u>	<u>\$4.00B</u>	<u>\$1.52B</u>
TRIKAFTA	-	420	918
SYMDEKO/SYMKEVI	362	1.42B	172
ORKAMBI	316	1.18B	232
KALYDECO	262	991	203
Combined non-GAAP R&D and SG&A	<u>394</u>	<u>1.69B</u>	<u>467</u>
Non-GAAP operating income	413	1.79B	874
Non-GAAP operating margin	44%	45%	57%
Non-GAAP net income	327	1.39B	687
Non-GAAP net income per share - diluted	\$1.26	\$5.33	\$2.61
Cash, cash equivalents & marketable securities (period-end)	\$4.0B	\$3.8B	\$5.5B

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 2020 press release dated July 30, 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

ANTICIPATED CF REVENUE GROWTH IN 2020 AND BEYOND



Notes:

- 2020 reflects the midpoint of the total CF product revenue guidance range provided on July 30, 2020
- 2021 - 2025 potential growth in CF revenues is provided as a graphical representation
- All figures are non-GAAP

GLOBAL CF PRODUCT REVENUES

FULL YEAR 2020 UPDATED FINANCIAL GUIDANCE

	Prior	Current	Commentary
Total CF Product Revenues	\$5.3-\$5.6B	\$5.7 - \$5.9B	Updated guidance reflects strong year-to-date performance driven by the TRIKAFTA launch in the U.S.
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 and credits 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 2020 press release dated July 30, 2020



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APPENDIX

RECONCILIATION OF GAAP TO NON-GAAP FINANCIAL INFORMATION

	Q2 2019	FY 2019	Q2 2020
GAAP total revenues	\$941	\$4.16B	\$1.52B
Non-GAAP total revenues	\$941	\$4.01B	\$1.52B
GAAP operating income	270	1.20B	718
Stock compensation expense	90	360	117
Other adjustments	53	228	39
Non-GAAP operating income	413	1.79B	874
Operating Margin %:			
GAAP	29%	29%	47%
Non-GAAP	44%	45%	57%
Net income			
GAAP	267	1.18B	837
Non-GAAP	327	1.39B	687
Net income per share - diluted			
GAAP	\$1.03	\$4.51	\$3.18
Non-GAAP	\$1.26	\$5.33	\$2.61

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