VERTEX

THE SCIENCE *of* POSSIBILITY

THIRD-QUARTER 2020 FINANCIAL RESULTS

OCTOBER 29, 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

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) anticipated regulatory filings and data submissions, (ii) anticipated regulatory approvals, including the anticipated TRIKAFTA and SYMKEVI approvals, and future label expansions, (iii) the expectations, development plan and timelines, including expectations for available data, for the company's medicines, drug candidates and pipeline programs, including clinical trials, (iv) the company's expectations regarding the effects COVID-19 will have on its business and operations, (v) expectations for the continued launch of and access to KAFTRIO, (vi) expectations for expanded access to the company's medicines, including anticipated reimbursement agreements, and (vii) anticipated internal and external development. 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 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 the continued KAFTRIO launch may not be as successful as anticipated, that data from the company's development programs may not be available on expected timelines, or at all, 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 generally accepted accounting principles 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) increases or decreases in the fair value of contingent consideration, (v) acquisition-related costs and (vi) 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 should not be viewed as a substitute for the company's GAAP results and are provided as a complement to results provided in accordance with GAAP. 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 that the company believes is helpful to an understanding of its ongoing business. Management also uses these non-GAAP financial measures to establish budgets and operational goals that are communicated internally and externally, 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's calculation of non-GAAP financial measures likely differs from the calculations used by other companies. A reconciliation of the GAAP financial results to non-GAAP financial results is included in the attached financial information. The company provides guidance regarding combined R&D and SG&A expenses and effective tax rate on a non-GAAP basis. The guidance regarding combined GAAP R&D and SG&A expenses does not include estimates associated with any potential future business development activities. The company does not provide forward-looking reconciliations of these measures to the most directly comparable GAAP financial measures because it is unable, without unreasonable efforts, to calculate these GAAP measures with reasonable certainty. A reconciliation of the GAAP financial results to non-GAAP financial results is included in the attached financial information and in the company's Q3 2020 press release dated October 29, 2020.

SIGNIFICANT ACCOMPLISHMENTS ACHIEVED IN 2020

	2020 YTD Key Accomplishments
ACHIEVE OUR VISION IN CYSTIC FIBROSIS	✓ Strong launch of TRIKAFTA (U.S. ages 12+) ✓ Early approval of KAFTRIO (EU ages 12+) ✓ New and expanded reimbursement agreements across the CF portfolio ✓ Expansion of eligibility to younger patients across the CF portfolio
DEVELOP NEW TRANSFORMATIVE MEDICINES FOR ADDITIONAL SERIOUS DISEASES	✓ Achieved proof-of-concept for CTX001 in beta thalassemia patients ✓ Initiation of a Ph2 proof-of-concept study for VX-864 in AATD ✓ Initiation of a Ph2 proof-of-concept study for VX-147 in APOL1-mediated FSGS
DELIVER FINANCIAL PERFORMANCE	✓ Projected FY CF revenue growth of 52% versus 2019* ✓ Disciplined management of operating expenses, focused on R&D ✓ Operating margins >55%, among the best in peer group

*Note: 52% reflects the midpoint of the total CF product revenue guidance range provided on October 29, 2020

UPCOMING MILESTONES TO DRIVE GROWTH IN CF AND BEYOND

	Key Milestones Anticipated
ACHIEVE OUR VISION IN CYSTIC FIBROSIS	❑ Continued progress in the launch of KAFTRIO (EU ages 12+) ❑ Approval of TRIKAFTA (U.S. ages 6-11) in 2021 ❑ Approval of SYMKEVI (EU ages 6-11) in 4Q20 ❑ Advancement of the Ph3 clinical study for TRIKAFTA in children ages 2-5
DEVELOP NEW TRANSFORMATIVE MEDICINES FOR ADDITIONAL SERIOUS DISEASES	❑ New clinical data for CTX001 in SCD & beta-thalassemia patients in 4Q20 - More patients + longer follow-up; potential for SCD proof-of-concept ❑ Submission of IND in type 1 diabetes in 4Q20 ❑ Ph2 proof-of-concept clinical data for VX-864 in AATD in 1H21 ❑ Ph2 proof-of-concept clinical data for VX-147 in APOL1-mediated FSGS in 2021
DELIVER FINANCIAL PERFORMANCE	❑ Continued CF product revenue growth – expanding labels and extending access across age groups, geographies ❑ Sustained investment and high profitability; cash flow supports continued internal and external investment for future growth

DEVELOPING MEDICINES FOR ALL PEOPLE WITH CF

Genetic Therapies

Remaining ~10% of patients untreatable with a CFTR modulator

OF PATIENTS

First CFTR Modulators

KALYDECO
ORKAMBI
SYMDEKO/SYMKEVI

Triple combination

trikafta® (elexacaftor/tezacaftor/ivacaftor and ivacaftor)

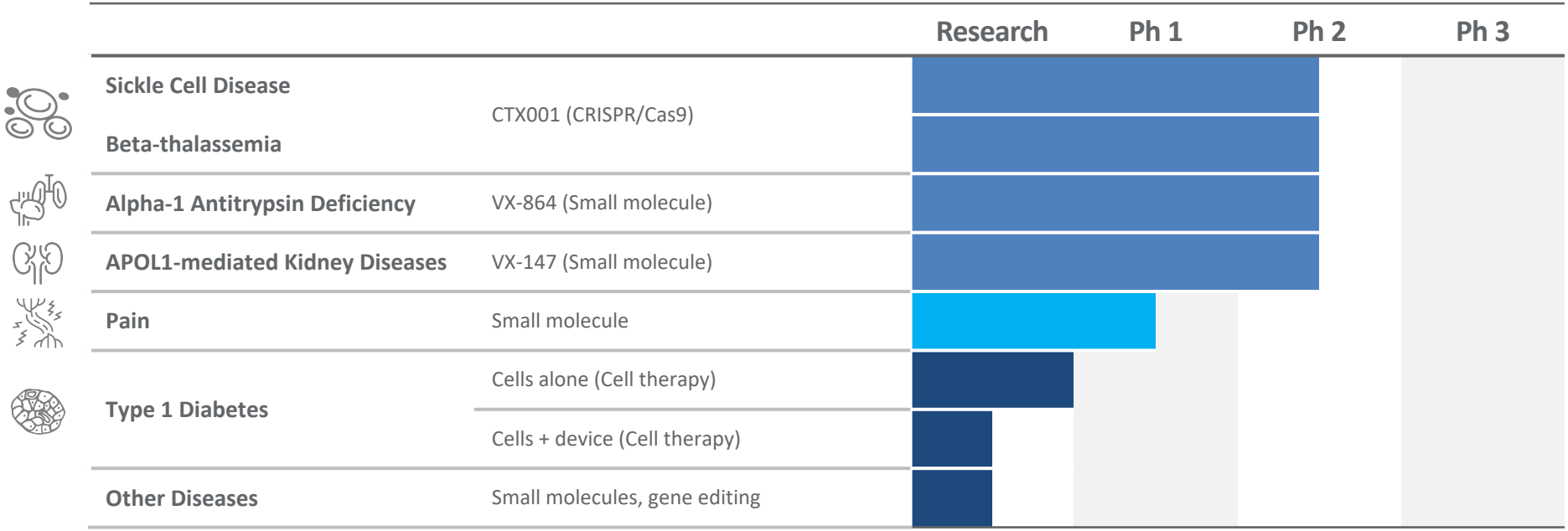
kaftrio® (ivacaftor/tezacaftor/elexacaftor) + kalydeco® (ivacaftor)

Up to 90% of CF patients eligible; Increased efficacy

Beyond 2021	WW ages <6
	EU ages 6-11
2021	U.S. ages 6-11
	WW ages 12+
TODAY	Approved in the U.S. and EU for ages 12+

TIME

BEYOND CF, ROBUST PIPELINE INCLUDES 5 FIRST-IN-CLASS PROGRAMS IN THE CLINIC

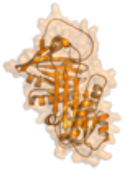


Multiple molecules are in the research/early clinical development stage in each program, reflecting our portfolio approach to drug discovery and development.

There is no guarantee that the investigational compounds listed will be approved by a Health Authority or will be marketed. Safety and effectiveness of investigational medicines have not been established.

MULTIPLE POTENTIALLY TRANSFORMATIVE PROGRAMS IN DEVELOPMENT

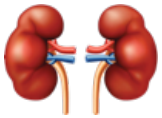
SMALL MOLECULES



Alpha-1 Antitrypsin Deficiency

VX-864 in Phase 2
Potential POC data anticipated 1H21

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
Potential POC data anticipated 2021

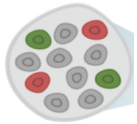
Small molecule inhibitor of APOL1 function, an underlying genetic cause of FSGS/other proteinuric kidney diseases

CELL AND GENETIC THERAPIES

Sickle Cell Disease & Beta Thalassemia

CTX001 in Phase 2
POC achieved for beta-thalassemia program
Potential POC data anticipated for sickle cell disease program
New data anticipated 4Q20: more patients + longer follow-up

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



Type 1 Diabetes

Preclinical
IND filing for islet cells alone program anticipated 4Q20

Cell therapy that uses fully differentiated islet cells derived from stem cells

ON THE PATH TO TREATING UP TO 90% OF CF PATIENTS WITH CFTR MODULATORS
TRIKAFTA & KAFTRIO LAUNCHES

- Early FDA approval in the U.S. received on October 21, 2019 for people ages 12+ who have at least one *F508del* mutation
- Achieved broad reimbursement from public and private payers
- Vast majority of the ~18,000 eligible patients in the U.S. have initiated TRIKAFTA therapy

- Early EC approval in the EU received on August 21, 2020 for people ages 12+ who have two *F508del* mutations or one *F508del* mutation and one minimal function mutation
- Reimbursement agreements secured in several countries (England, Scotland, Wales, Northern Ireland, Denmark and Ireland) and immediate access is available in Germany

KEY PROGRESS TOWARDS GEOGRAPHIC AND LABEL EXPANSIONS ANTICIPATED TO CONTINUE TO DRIVE CF GROWTH BEYOND 2020

EXPANSION TO ADDITIONAL GEOGRAPHIES

Launch of KAFTRIO in certain EU countries, with plans to seek reimbursement agreements beyond initial launch countries

EXPANSION TO YOUNGER AGE GROUPS

Submission of an sNDA to FDA anticipated in 4Q20 for the triple combination in children with CF ages 6-11

FDA approval and positive CHMP opinion for KALYDECO in infants with CF > 4 months of age

Positive CHMP opinion for SYMKEVI in children with CF ages 6-11

Planned initiation of a Phase 3 study for the triple combination in children with CF ages 2-5

EXPANSION TO ADDITIONAL PATIENT POPULATIONS

Acceptances of three sNDAs for TRIKAFTA, SYMDEKO and KALYDECO intended to expand the labels of these drugs to include additional people with CF who have rare CFTR mutations

POTENTIAL FOR LONG-TERM CF GROWTH WITH CFTR MODULATORS

FUTURE GROWTH

>20,000 Patients currently not reimbursed or not eligible

KEY DRIVERS FOR FUTURE GROWTH

- ADDITIONAL KAFTRIO EU REIMBURSEMENTS AGES 12+
- ADDITIONAL TRIKAFTA/KAFTRIO OUS APPROVALS AND REIMBURSEMENTS AGES 12+
- TRIKAFTA/KAFTRIO APPROVALS AND REIMBURSEMENTS AGES 6-11
- TRIKAFTA/KAFTRIO AGES <6 & OTHER CFTR MODULATOR APPROVALS/LABEL EXPANSIONS

POTENTIAL TO TREAT 90% OF CF POPULATION WITH CFTR MODULATORS

Q3 2020 FINANCIAL HIGHLIGHTS

($ in millions except where noted or per share data and percentages)	Q3 19	FY 19	Q3 20
Total non-GAAP CF product revenues	$950	$4.00B	**$1.54B**
TRIKAFTA/KAFTRIO	-	420	**960**
SYMDEKO/SYMKEVI	404	1.42B	**156**
ORKAMBI	297	1.18B	**226**
KALYDECO	249	991	**194**
Combined non-GAAP R&D and SG&A	416	1.69B	**497**
Non-GAAP operating income	403	1.79B	**854**
Non-GAAP operating margin	42%	45%	**56%**
Non-GAAP net income	322	1.39B	**697**
Non-GAAP net income per share - diluted	$1.23	$5.33	**$2.64**
Cash, cash equivalents & marketable securities (period-end)	$4.0B	$3.8B	**$6.2B**

Notes

- An explanation of non-GAAP financial measures and reconciliation of non-GAAP CF product revenues, combined non-GAAP R&D and SG&A expense, non-GAAP net income and non-GAAP net income per share-diluted to corresponding GAAP measures are included in the company's Q3 2020 press release dated October 29, 2020.
- Reconciliation of non-GAAP operating income and non-GAAP operating margin to corresponding GAAP measures are included in the appendix of this presentation; totals may not add due to rounding.

FULL YEAR 2020 UPDATED FINANCIAL GUIDANCE

	Prior	Current	Commentary
Total CF Product Revenues	$5.7-$5.9B	**$6.0 - $6.2B**	Updated guidance reflects strong year-to-date performance driven by the TRIKAFTA launch in the U.S.
Combined GAAP R&D and SG&A	$2.4 -$2.55B	**$2.5 -$2.6B**	GAAP guidance reflects the effect of a new collaboration agreement in 3Q20
Combined Non-GAAP R&D and SG&A	$1.95 -$2.0B	**Unchanged**	Non-GAAP guidance unchanged
Non-GAAP Effective Tax Rate	21% - 22%	**20-21%**	Adjusted non-GAAP effective tax rate guidance includes a change in the utilization of certain tax assets

Note: An explanation of non-GAAP financial measures and reconciliation of combined non-GAAP R&D and SG&A expense and non-GAAP effective tax rate to corresponding GAAP measures are included in the company's Q3 2020 press release dated October 29, 2020.

VERTEX POSITIONED FOR LONG-TERM GROWTH

- Successful execution has enabled creation of our leading CF franchise, and positions Vertex to drive future growth, including via geographic and label expansions

- Beyond CF, we have a pipeline of potentially transformative therapies in development across multiple diseases, with multiple important clinical readouts in the next 12 months

- R&D and corporate strategy drives continued investment in internal R&D and external innovation, with clear priorities and diseases of interest

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APPENDIX
RECONCILIATION OF GAAP TO NON-GAAP FINANCIAL INFORMATION

	Q3 19	FY 19	Q3 20
GAAP total revenues	$950	$4.16B	**$1.54B**
Non-GAAP total revenues	950	4.01B	**1.54B**
GAAP operating income	99	1.20B	**672**
Stock compensation expense	85	360	**100**
Other adjustments	218	228	**82**
Non-GAAP operating income	403	1.79B	**854**
Operating Margin %:			
GAAP	10%	29%	**44%**
Non-GAAP	42%	45%	**56%**
Net income			
GAAP	58	1.18B	**667**
Non-GAAP	322	1.39B	**697**
Net income per share - diluted			
GAAP	$0.22	$4.51	**$2.53**
Non-GAAP	$1.23	$5.33	**$2.64**

Notes: All numbers in the above reconciliation table are in the millions except where noted, per share data and percentages. Reconciliations of non-GAAP total revenue and non-GAAP Net income to corresponding GAAP measures are included in the company's Q3 2020 press release dated October 29, 2020; totals may not add due to rounding.