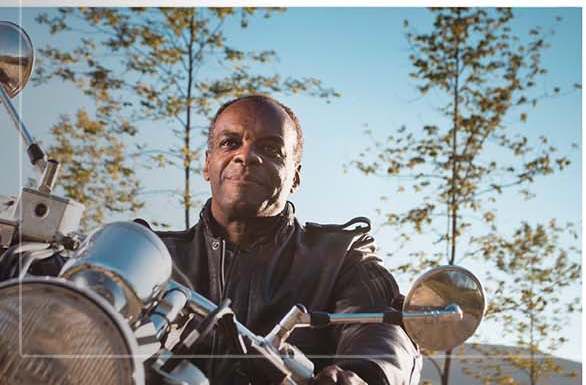







VERTEX

THE SCIENCE *of* POSSIBILITY

THIRD-QUARTER 2021 FINANCIAL RESULTS

NOVEMBER 2, 2021

AGENDA

Introduction

Michael Partridge, Senior Vice President, Investor Relations

CEO Perspective and Pipeline Update

Reshma Kewalramani, M.D., CEO and President

Commercial Update

Stuart Arbuckle, Executive Vice President and Chief Operating 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 and operations, the section captioned "Full-Year 2021 Updated Financial Guidance" and statements regarding (i) anticipated regulatory filings, data availability, approvals, and timing thereof, (ii) anticipated future label expansions, (iii) the expectations, development plans and anticipated timelines for the company's therapies and pipeline programs, including study designs, clinical site initiations, patient enrollment, data availability, and timing thereof, (iv) expectations for the CTX001 collaboration with CRISPR, including anticipated benefits of the collaboration, the potential of CTX001 to be a one-time functional cure for patients with TDT and SCD, and the expectation of regulatory filings next year, (v) expectations for uptake of and expanded access to the company's medicines, including additional reimbursement agreements and approvals, (vi) expectations for continued growth in the number of CF patients treated with our medicines, including expectations about our ability to treat up to 90% of CF patients with CFTR modulators and expansion of treatment options for the patients who do not benefit from CFTR modulators, (vii) expectations for our pain program, including our expectations for available data from bunionectomy and abdominoplasty trials in the first quarter of 2022 , (viii) our plans to advance one or more small molecules into the clinic in 2022, (ix) beliefs about commercial opportunities and operations in the disease areas in which we focus, (x) expectations for an IND submission for our T1D cells and device program in 2022, (xi) expectations for our CF pipeline program, and (xii) expectations for availability of data from VX-147 study in the fourth quarter of 2021. 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 2021 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 the company may not be able to submit the anticipated regulatory filings on the expected timeline, or at all, 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 preclinical testing or early clinical trials, especially if based on a limited number of patients, may not be indicative of final results, that the company may not realize the anticipated benefits from our collaborations with third parties, that data from the company's development programs may not be available on expected timelines, or at all, and 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 and on the SEC's website at www.sec.gov. You should not place undue reliance on these statements or the scientific data presented. 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 collaborative milestones and upfront payments, including the $900 million upfront payment to CRISPR, and certain other business development activities, (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. 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 guidance regarding its GAAP effective tax rate because it is unable to forecast with reasonable certainty the impact of excess tax benefits related to stock-based compensation and the possibility of certain discrete items, which could be material. Non-GAAP financial measures are presented compared to corresponding GAAP measures in the appendix hereto. A reconciliation of the GAAP financial results to non-GAAP financial results is included in the company's Q3 2021 press release dated November 2, 2021.

VERTEX Q3 2021:

Outstanding financial performance driven by our continued **leadership in CF; pipeline expanding and accelerating** in multiple diseases

Leadership in CF

- TRIKAFTA/KAFTRIO positioned to address 90% of CF patients
- Phase 3 clinical trials underway with next-in-class triple combination regimen VX-121/tezacaftor/VX-561
- CFTR mRNA therapy now in IND-enabling studies, with IND filing and start of clinical development planned in 2022

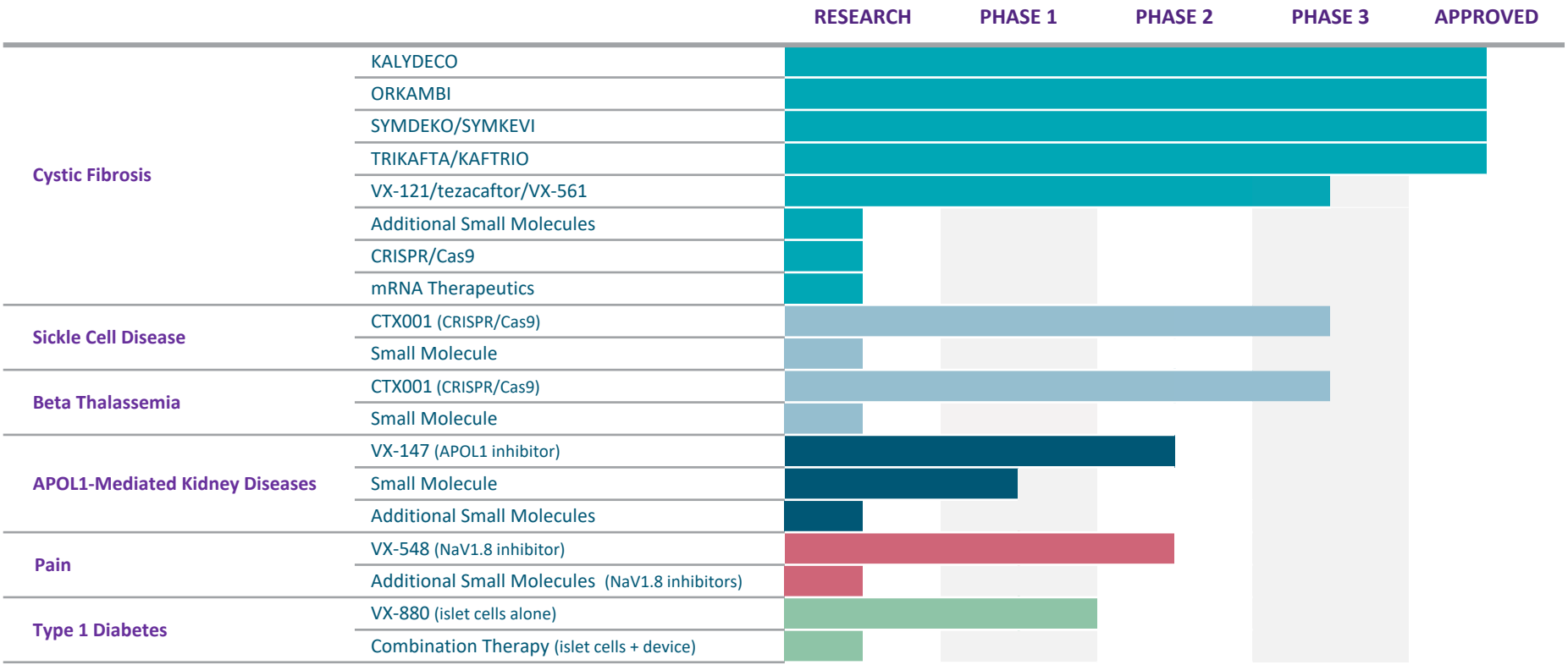
Pipeline Programs Expanding & Accelerating

- Diversified clinical pipeline spans 5 diseases outside CF and 3 therapeutic modalities, each representing multi-billion dollar opportunities
- Pipeline programs delivering; unprecedented clinical data with VX-880 announced in October
- Potential for multiple additional clinical data readouts in the next 3-6 months

Revenue Growth

- $1.98B in Q3 ’21 product revenues, a 29% increase compared to prior year
- 2021 product revenue guidance raised to a range of $7.4-$7.5B, representing 20% growth YoY at the midpoint
- CF business expected to continue to grow, based on ~30,000 CF patients still left to treat with our CFTR modulators

VERTEX PIPELINE: POTENTIALLY TRANSFORMATIVE MEDICINES IN CLINICAL DEVELOPMENT ACROSS MULTIPLE SERIOUS DISEASES



MULTIPLE PROGRAMS OUTSIDE OF CF WITH POTENTIAL FOR DATA READOUTS IN THE NEAR TERM

SMALL MOLECULES

APOL1-Mediated Kidney Diseases
VX-147 in Phase 2

Data from POC study in APOL1-mediated FSGS will be reported in Q4 '21

NaV1.8 inhibitor for Pain
VX-548 in Phase 2

Two studies in acute pain (bunionectomy and abdominoplasty) each with opioid reference arm; data anticipated in Q1 '22

Alpha-1 Antitrypsin Deficiency

One or more small molecules expected to enter the clinic in '22

CELL AND GENETIC THERAPIES

Sickle Cell Disease & Beta Thalassemia
CTX001 in Phase 3

- Have now achieved target enrollment in both studies
- Plan to submit regulatory filings for approval by year-end '22

Type 1 Diabetes
Phase 1/2 ongoing with VX-880

- Clinical data from the first patient dosed with single infusion of a half dose of VX-880 showed rapid and robust improvements through day 90 across multiple measures of islet cell function
- IND submission for the cells + device program expected in '22

RAPID UPTAKE OF OUR CFTR MODULATORS AROUND THE WORLD

NORTH AMERICA

- Nearly all patients eligible for TRIKAFTA ages 12+ with at least one *F508del* mutation in the U.S. have initiated therapy
- Strong uptake across all patient subgroups in the U.S., including children ages 6-11
- Multiple provincial reimbursement agreements reached in Canada, providing ~90% of patients 12 and older covered by government insurance with reimbursed access to TRIKAFTA

EUROPE and OTHER MARKETS

- Strong continued launch of KAFTRIO to people ages 12+ with at least one *F508del* mutation across multiple key countries where patients have access, including the major new markets of France and Italy
- Achieved reimbursement agreements for KAFTRIO/TRIKAFTA in more than 20 countries in the one year since ex-US approval
- Regulatory submission filed in Europe for children ages 6-11

CTX001: LAUNCH PREPARATION ACTIVITIES WELL UNDERWAY

People

Hired many of the key people who will support the launch of CTX001

Manufacturing

Processes designed to ensure that we can supply a consistent and high-quality product to the large number of patients we believe could benefit from the medicine on day one of the launch

Patients

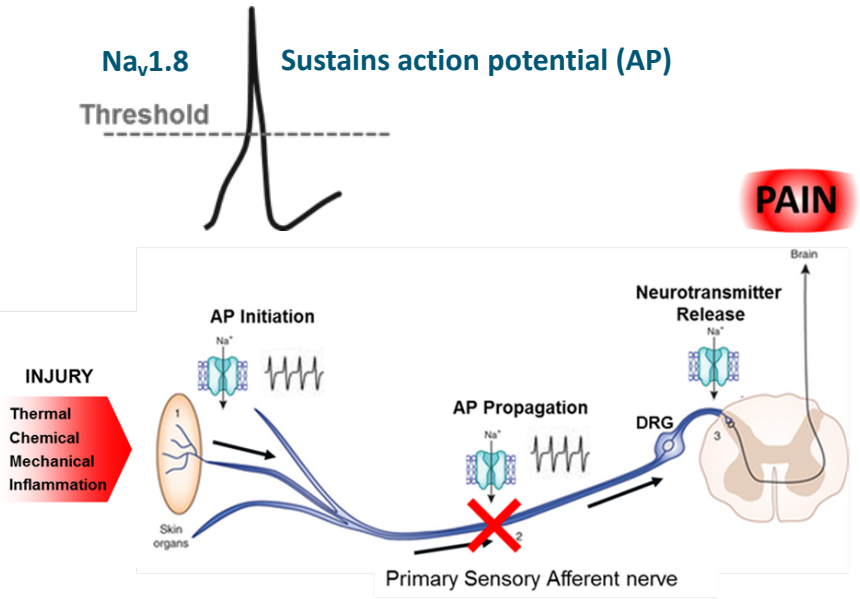
Understand the patients and their experience so we can provide them at launch with the information, resources and support they need as they consider treatment with CTX001

ACUTE PAIN IS A SIGNIFICANT MARKET OPPORTUNITY THAT CAN BE SERVED WITH A SMALL COMMERCIAL FOOTPRINT

There is a **need for new pain medicines** without the limitations of opioids, particularly their addictive potential

Acute pain is estimated to be a **$4B market** despite 90% of prescriptions being generic

Treatment is **highly concentrated** where 25% of hospitals account for 80% of the opioid prescriptions in the U.S.



From Waxman and Zamponi, Nature Neuroscience, 2014

VX-880 ADDRESSES A VERY LARGE MARKET OPPORTUNITY IN TYPE 1 DIABETES

Patients potentially eligible for VX-880

(stem cell-derived, allogeneic, fully differentiated, insulin secreting islet cells with standard immunosuppression)

~45K
Severe T1D

People with T1D who have a severe and difficult-to-control form of T1D characterized by impaired awareness of hypoglycemia and severe hypoglycemic events

+

~15K
Previously transplanted

People with T1D who have previously received a kidney transplant and are already immunosuppressed

Device-encapsulated and gene-edited hypoimmune stem cell-derived islet cells
hold the potential to address a much larger opportunity – the **2.6M people** with type 1 diabetes in U.S. and Europe

Q3 2021 FINANCIAL HIGHLIGHTS

($ in millions except as noted, per share data and percentages)	Q3 20	FY 20	Q3 21
Total CF product revenues	$1.54B	$6.20B	**$1.98B**
TRIKAFTA/KAFTRIO	960	3.86B	**1.56B**
SYMDEKO/SYMKEVI	156	629	**81**
ORKAMBI	226	908	**185**
KALYDECO	194	803	**162**
Combined non-GAAP R&D and SG&A expenses	497	1.98B	**561**
Non-GAAP operating income	854	3.49B	**1.19B**
Non-GAAP operating margin	56%	56%	**60%**
Non-GAAP net income	697	2.72B	**926**
Non-GAAP net income per share - diluted	$2.64	$10.32	**$3.56**
Cash, cash equivalents & marketable securities (period-end)	$6.2B	$6.7B	**$7.0B**

Notes: An explanation of non-GAAP financial measures and reconciliation of combined non-GAAP R&D and SG&A expenses, non-GAAP operating income and non-GAAP net income to corresponding GAAP measures are included in the company's Q3 2021 press release dated November 2, 2021. Non-GAAP financial measures are presented compared to corresponding GAAP measures in the appendix of this presentation. Totals above may not add due to rounding.

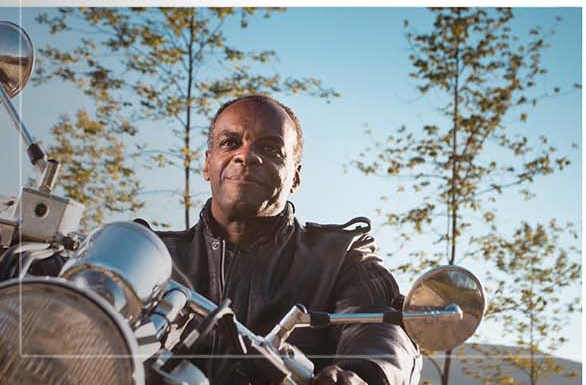
FULL-YEAR 2021 UPDATED FINANCIAL GUIDANCE

	Current FY 2021 Guidance	Previous FY 2021 Guidance	FY 2021 Commentary
Total CF Product Revenues	**$7.4 - $7.5B**	$7.2 - $7.4B	Increased guidance reflects strong year-to-date performance in the U.S. and internationally
Combined GAAP R&D and SG&A Expenses	**Unchanged**	$3.8 -$3.95B	
Combined Non-GAAP R&D and SG&A Expenses	**Unchanged**	$2.25 -$2.3B	
Non-GAAP Effective Tax Rate	**Unchanged**	21-22%	

Note: An explanation of non-GAAP financial measures and a reconciliation between the company's full-year 2021 combined GAAP R&D and SG&A expenses and combined non-GAAP R&D and SG&A expenses guidance is included in the company's Q3 2021 press release dated November 2, 2021





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APPENDIX

GAAP TO NON-GAAP FINANCIAL INFORMATION

($ in millions except as noted, per share data and percentages)	Q3 20	FY 20	Q3 21
Combined R&D and SG&A expenses			
GAAP	678	**2.60B**	692
Non-GAAP	497	**1.98B**	561
Operating income			
GAAP	672	**2.86B**	1.05B
Non-GAAP	854	**3.49B**	1.19B
Operating Margin %:			
GAAP	44%	**46%**	53%
Non-GAAP	56%	**56%**	60%
Net income			
GAAP	667	**2.71B**	852
Non-GAAP	697	**2.72B**	926
Net income per share - diluted			
GAAP	$2.53	**$10.29**	$3.28
Non-GAAP	$2.64	**$10.32**	$3.56

Note: An explanation of non-GAAP financial measures and reconciliation of combined non-GAAP R&D and SG&A expenses, non-GAAP operating income and non-GAAP net income to corresponding GAAP measures are included in the company's Q3 2021 press release dated November 2, 2021.