



# THIRD QUARTER 2023 FINANCIAL RESULTS

NOVEMBER 6, 2023

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# AGENDA

## Introduction

*Susie Lisa, CFA, Senior Vice President, Investor Relations*

## CEO Perspective and Pipeline Update

*Reshma Kewalramani, M.D., Chief Executive Officer 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, as amended, including, without limitation, the information provided regarding expectations for future financial and operating performance, full-year 2023 financial guidance, including expectations for raised 2023 revenue guidance, and statements regarding our (i) expectations, development plans, and timelines for the company's products, product candidates, and pipeline programs, including expectations for potential near-term launches and clinical milestones, anticipated benefits of new products, patient populations, study designs, study enrollment, data availability, anticipated regulatory filings, regulatory approvals, and timing thereof, (ii) expectations to reach all CF patients eligible for CFTRm and the last ~5,000 CF patients (ineligible for a CFTRm) with VX-522, our plans to complete a single ascending dose study and initiate multiple ascending dose study for VX-522 in 2023, and our expectations for KAFTRIO approval in the EU and UK for children 2-5 years of age by end of 2023, (iii) expectations for the benefits of vanzacaftor triple combination therapy, plans to complete Phase 3 studies in 2023, expectations for data in early 2024, and expectations for near-term launch, commercial potential and lower royalty burden, (iv) expectations for the exa-cel program, including the potential of exa-cel to be a one-time, functional cure for patients with SCD and TDT, potential of exa-cel to be the first CRISPR-based gene-editing treatment to be approved, initial patient targets, expectations regarding regulatory decisions, including timing thereof, expectations for near-term launch and commercial potential, including expected patient population, our launch readiness and expectations regarding providers and payers, expectations that 2024 will be a foundational year for exa-cel, expectations for each phase of the patient process for exa-cel, and plans for the global Phase 3 studies evaluating exa-cel in patients 5-11 years of age with SCD or TDT, (v) expectations for our pain program, including its potential to treat acute and neuropathic pain without the side effects or addictive properties of opioids, expectations to complete Phase 3 pivotal program for VX-548 in acute pain in late 2023 and have data in early 2024, expectations for data from the Phase 2 studies of VX-548 in neuropathic pain, plans to initiate a Phase 2 study evaluating VX-548 in LSR by end of 2023, commercial potential and plans for near-term commercial launch in moderate-to-severe acute pain, (vi) our expectations and beliefs regarding our pivotal program for inaxaplin, including its potential to treat the underlying cause of AMKD, plans regarding enrollment in Phase 2B portion of studies, expectations to select a dose and move to Phase 3 of the study in the first quarter of 2024, and our beliefs regarding anticipated results of the study, (vii) expectations for the development of our T1D programs, including the patient population, potential curative benefits and safety of VX-880, expectations for our VX-264 study, and expected use of CRISPR/Cas9 gene editing in our hypoimmune program, (viii) plans for continued advancement of VX-634 and VX-668, (ix) plans and expectations for our programs for muscular dystrophies, and (x) expectations regarding the company's tax rates, revenue growth, and the impact of foreign exchange rates on revenue growth. 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 future financial and operating performance may be incorrect (including because one or more of the company's assumptions underlying its expectations may not be realized), that our products may not receive regulatory approval on expected timelines, or at all, that external factors may impact the company's business or operations differently than the company currently expects, that data from preclinical testing or clinical trials, especially if based on a limited number of patients, may not be indicative of final results, that patient enrollment in our trials may be delayed, that actual patient populations able to participate in our trials or eligible for our products may be smaller than anticipated, that reimbursement for our therapies may be more difficult to obtain or maintain than expected, 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 filed with the Securities and Exchange Commission (SEC) and available through the company's website at [www.vrtx.com](http://www.vrtx.com) and on the SEC's website at [www.sec.gov](http://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) gains or losses related to the fair value of the company's strategic investments, (iii) increases or decreases in the fair value of contingent consideration, (iv) acquisition-related costs, (v) an intangible asset impairment charge, 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's calculation of non-GAAP financial measures likely differs from the calculations used by other companies. The company provides guidance regarding combined R&D, Acquired IPR&D and SG&A expenses and effective tax rate on a non-GAAP basis. Unless otherwise noted, the guidance regarding combined GAAP and non-GAAP R&D, Acquired IPR&D and SG&A expenses does not include estimates associated with any potential future business development transactions, including collaborations, asset acquisitions and/or licensing of third-party intellectual property rights. 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 2023 press release dated November 6, 2023.

# **STRONG THIRD QUARTER: CONTINUE TO DRIVE EXECUTION ACROSS THE COMPANY**

## **Continue the journey in cystic fibrosis (CF)**

- Serially innovate to bring highly efficacious therapies to all CF patients

## **Prepare for potential near-term commercialization opportunities**

- Exa-cel: SCD PDUFA: December 8, 2023; TDT PDUFA: March 30, 2024; regulatory decisions in the EU and U.K. expected in the coming months
- Vanzacaftor triple in CF: all Phase 3 studies expected to complete by end of 2023; data in early 2024
- VX-548 in moderate to severe acute pain: all Phase 3 studies expected to complete by end of 2023; data in early 2024

## **Accelerate diversified R&D pipeline**

- VX-548 in peripheral neuropathic pain:
  - Phase 2 DPN trial has completed; data by end of 2023
  - Phase 2 LSR trial to initiate by end of 2023
- Inaxaplin in AMKD: completion of enrollment in Phase 2B portion of Phase 2/3 trial this year
- VX-880 in T1D: completed enrollment in Part C of Phase 1/2 study
- VX-522 in CF: expect to complete the single ascending dose (SAD) portion in CF patients and initiate the multiple ascending dose (MAD) portion of the study by the end of 2023

## **Deliver financial performance**

- Raising full year 2023 CF product revenue guidance to ~\$9.85B; specialty model sustains strong operating margins while allowing for significant investments in pipeline and commercial capabilities

# CONTINUING OUR SERIAL INNOVATION IN CYSTIC FIBROSIS

ON TRACK TO COMPLETE VANZACAF TOR TRIPLE STUDIES BY THE END OF 2023 WITH DATA IN EARLY 2024



## Vanzacaftor Triple

- Next-in-class CFTR modulator triple therapy
- On track to complete all three Phase 3 studies by the end of 2023: SKYLINE 102 and SKYLINE 103 in patients ages 12+, RIDGELINE in patients ages 6-11 years
- Expect to share results from all three pivotal studies in early 2024
- Convenient, once-daily dosing
- Meaningfully lower royalty burden



## VX-522

- CFTR mRNA therapy in development for ~5,000 CF patients who cannot benefit from CFTR modulators
- On track to complete single ascending dose (SAD) portion in CF patients in 2023 and initiate multiple ascending dose (MAD) portion of the study by the end of 2023
- Program developed in partnership with Moderna



# NEAR-TERM LAUNCH POTENTIAL: EXA-CEL

FDA ADVISORY COMMITTEE COMPLETED FOR SCD, NOW APPROACHING REGULATORY DECISIONS FROM U.S., U.K., AND EU IN THE NEAR TERM

## Exa-cel holds potential for one-time, functional cure



The first CRISPR-based gene-editing treatment potentially to be approved

Plans to initially target the most severe patients (~32,000) across the U.S. and Europe



SCD PDUFA: December 8, 2023  
TDT PDUFA: March 30, 2024

Expect regulatory decisions from the U.K. and the EU in the coming months

Submitted MAA to the Kingdom of Saudi Arabia; exa-cel is first ever to receive Breakthrough Medicines designation in KSA



Updated clinical data in TDT and SCD accepted for oral presentation at ASH

Continue to enroll and dose two global Phase 3 studies in patients 5-11 years of age with SCD or TDT

# VX-548 FOR ACUTE AND NEUROPATHIC PAIN HOLDS THE PROMISE OF EFFECTIVE PAIN RELIEF WITHOUT THE SIDE EFFECTS OR ADDICTIVE PROPERTIES OF OPIOIDS



ACUTE PAIN: PIVOTAL PROGRAM TO COMPLETE BY END OF 2023 WITH DATA IN EARLY 2024

PNP: PHASE 2 DPN TRIAL COMPLETE, PHASE 2 LSR TRIAL TO INITIATE BY END OF 2023

## Significant Unmet Need

- Millions in the U.S. each year suffer from acute and peripheral neuropathic pain
- Existing therapies have challenging side effects and/or abuse potential

## Validated Target

- Na<sub>v</sub>1.8 is genetically and pharmacologically validated
- 5 successful proof-of-concept studies across both VX-150 and VX-548 in major pain types

## Acute pain

### Near-term launch potential:

- On track to complete pivotal program by end of 2023
  - ✓ Completed Ph 3 trial in abdominoplasty
  - ✓ On track to complete Ph3 bunionectomy and single arm safety and effectiveness trial by end of 2023
- Results from all three Phase 3 studies expected in early 2024
- Granted Fast Track and Breakthrough Therapy designations

## Peripheral neuropathic pain

### Diabetic peripheral neuropathy (DPN):

- Completed the Phase 2, 12-week, dose-ranging, proof-of-concept study
- Expect to share results by the end of 2023

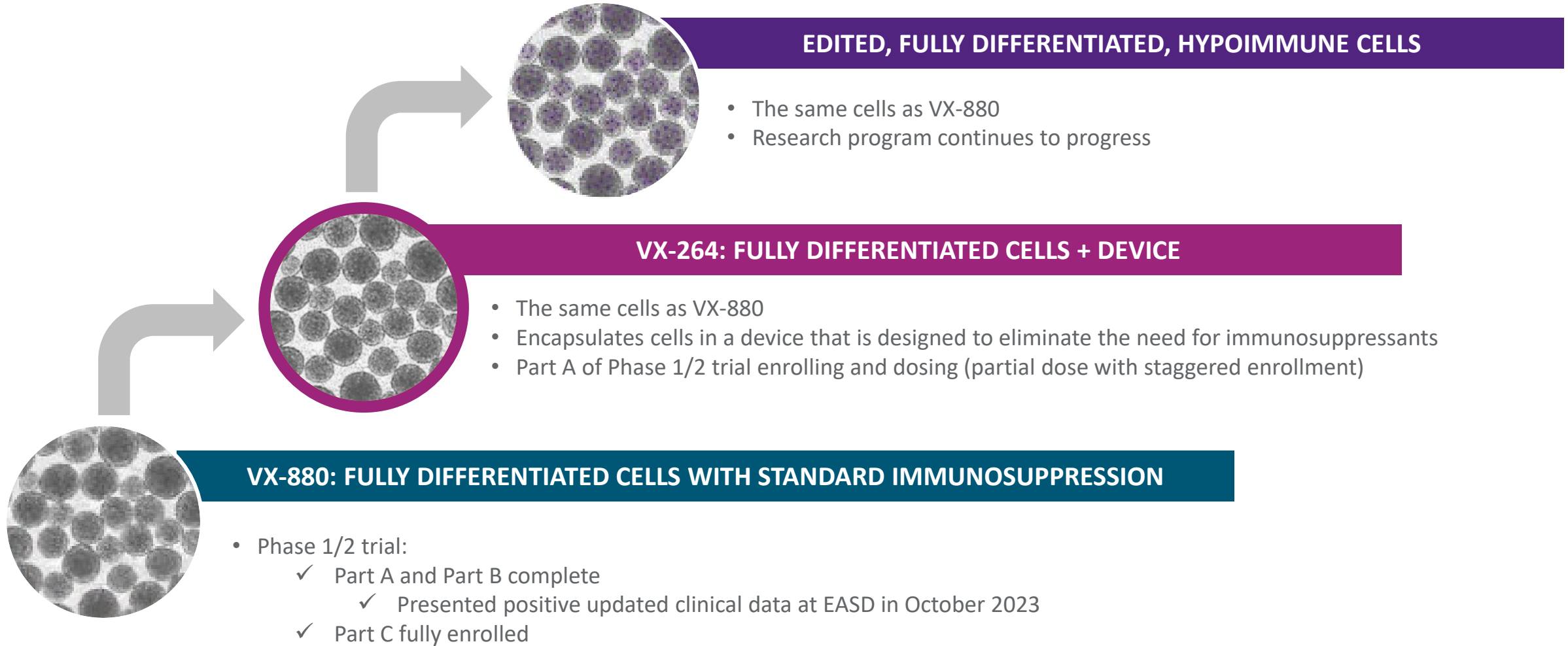
### Lumbosacral radiculopathy (LSR):

- Expect to initiate a Phase 2 study in LSR, pain caused by impairment of nerve roots in the area of the lumbar spine, by the end of 2023



# TYPE 1 DIABETES: ADVANCING POTENTIALLY CURATIVE TREATMENTS FOR ~2.5M PATIENTS IN NORTH AMERICA & EUROPE

PART C FULLY ENROLLED IN VX-880 TRIAL





# INAXAPLIN: FIRST POTENTIAL MEDICINE TO TARGET THE UNDERLYING CAUSE OF AMKD



100,000  
patients in the  
U.S. and Europe

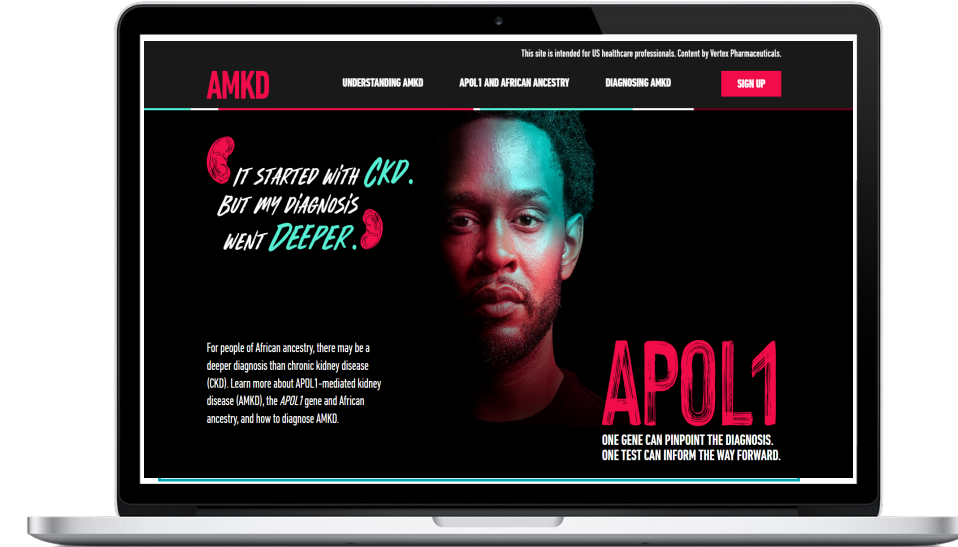
## APOL1-MEDIATED KIDNEY DISEASE

- Two APOL1 variants
- Proteinuric kidney disease
- Rapid progression to ESKD



## PIVOTAL TRIAL UNDERWAY

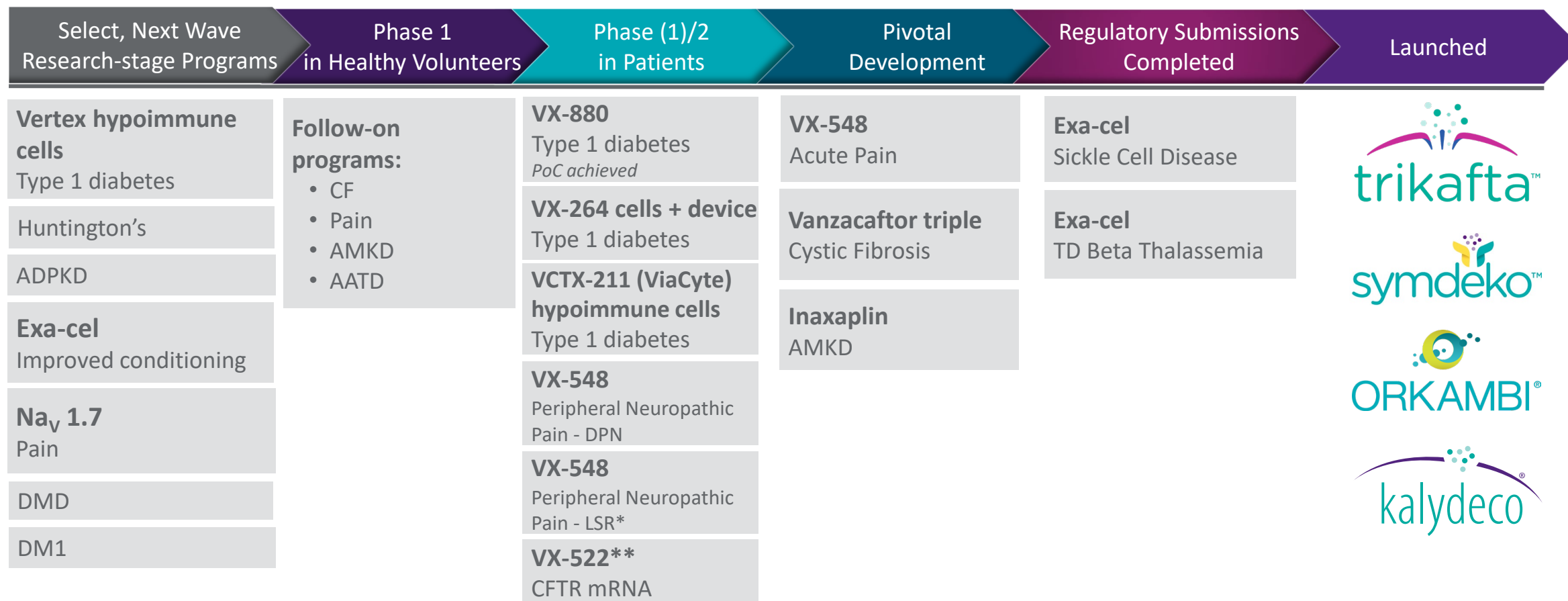
- Phase 2B dose-ranging portion of the study continues to enroll and dose patients
- Expect to select a dose and move to Phase 3 of the study in the first quarter of 2024
- Path to accelerated approval with interim analysis at 48 weeks of treatment
- Final analysis at ~2 years of treatment



## RAISING DISEASE AWARENESS AND ONGOING GENETIC TESTING EFFORTS

- Education outreach with physicians and patients
- Building trust with historically underserved communities
- Multiple ongoing initiatives to increase awareness of the importance of genetic testing for AMKD

# CLINICAL PORTFOLIO IS BROAD, DIVERSE AND RAPIDLY ADVANCING



# SUSTAINING AND EXPANDING LEADERSHIP IN CF WITH SERIAL INNOVATION

RECEIVED TRIKAFTA APPROVAL IN CANADA FOR AGES 2-5

EXPECT KAFTRIO APPROVALS IN EU AND U.K. FOR AGES 2-5 BY END OF 2023



**88,000 PATIENTS WITH CF**

vs. 83,000 estimated in 2021

*U.S., Europe, Australia and Canada*



**TREATED TODAY WITH CFTRm**

**>20,000 REMAINING  
ADDRESSABLE WITH CFTRm**

**~5,000 ADDRESSABLE  
WITH VX-522**

## DRIVERS OF GROWTH

- 1. Treating younger patients and securing additional reimbursements**
  - Strong U.S. launch of TRIKAFTA in children ages 2-5 years
  - Outside the U.S., strong KAFTRIO growth in patients ages 6 years and older following approval, reimbursement and launch across multiple countries
- 2. More people with CF, living longer**
  - Median predicted age of survival is ~65 years\*
- 3. Raising the bar**
  - Vanzacaftor triple: all pivotal studies in CF patients ages 12+ and 6-11 years expected to complete by the end of 2023
- 4. Advancing therapies for all patients**
  - Ongoing VX-522 CFTR mRNA Phase 1 (SAD/MAD) trial in CF patients who cannot benefit from CFTR modulators

Note: estimated CF patient population and population breakdown as of January 2023

\*Cystic Fibrosis Foundation Patient Registry 2021 Annual Data Report

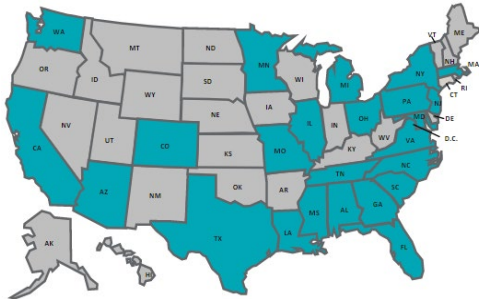
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# EXA-CEL MARKET REPRESENTS A POTENTIAL MULTI- $\$$ B OPPORTUNITY



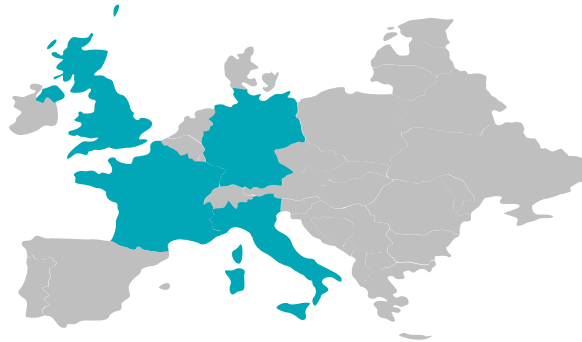
32,000 eligible patients with severe disease in the U.S. and Europe

~24 States with ~90% of SCD/TDT Patients



- On track with our globally-enabled supply network and launch preparations with Authorized Treatment Centers and payors.

4 Countries in Europe with ~75% of SCD/TDT Patients



- Italy has highest prevalence of eligible TDT patients; France and UK have majority of eligible SCD patients.
- On track with our globally-enabled supply network and launch preparations with Authorized Treatment Centers and payors.

Additional opportunity

The Kingdom of Saudi Arabia



- Exa-cel represents first-ever investigational therapy granted Breakthrough Designation by KSA.
- Vertex team engaging with Saudi health authorities and working on the processes to support ATC activation, access and reimbursement.



# 2024 WILL BE A FOUNDATIONAL YEAR FOR EXA-CEL

GOAL TO DELIVER TRANSFORMATIVE PATIENT OUTCOMES WITH THE POSSIBILITY OF A LIFETIME OF BENEFIT

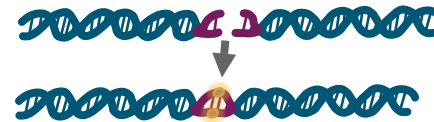
*Each stage can take several months*

## Stage 1: Patient referral & preparation



- Patient referred to transplant physician at ATC
- Testing and full work-up

## Stage 2: Cell collection & manufacturing



- Mobilization to move blood stem cells from the bone marrow into the peripheral blood, where cells are collected through apheresis
- SCD patients typically need 2 months of RBC transfusions, and ~2 rounds of apheresis
- Cells sent to manufacturing facilities for editing and testing

## Stage 3: Treatment



- Myeloablative conditioning
- Infusion of edited cells
- Engraftment
- Post-infusion care

# VX-548 HAS POTENTIAL TO PLAY A KEY ROLE IN ACUTE AND PERIPHERAL NEUROPATHIC PAIN MARKETS



ACUTE PAIN AND PNP ARE EACH MULTI-\$B MARKETS TODAY



Acute pain

- More than 2/3 of patients receive acute pain treatment driven by an institution
- Hospital-driven prescribing concentrated across ~2,000 hospitals and 200 IDNs



Peripheral neuropathic pain

- Lumbosacral radiculopathy (LSR) represents >40% of all PNP patients while DPN represents ~20% of all PNP patients
- Specialists play a critical role in treating PNP

Acute and peripheral neuropathic pain fit the Vertex specialty model and have significant unmet need

# Q3 2023 FINANCIAL HIGHLIGHTS

<i>(\$ in millions except where noted or per share data and percentages)</i>	<b>Q3 22</b>	<b>FY 22</b>	<b>Q3 23</b>
Total CF product revenues	<u>\$2.33B</u>	<u>\$8.93B</u>	<u>\$2.48B</u>
TRIKAFTA/KAFTRIO	2.01B	7.69B	<b>2.27B</b>
Other CF products	324	1.24B	<b>209</b>
Combined non-GAAP R&D, acquired IPR&D and SG&A expenses	<u>758</u>	<u>3.07B</u>	<u>993</u>
Non-GAAP operating income	1.29B	4.79B	<b>1.17B</b>
Non-GAAP operating margin %	55%	54%	<b>47%</b>
Non-GAAP net income	1.04B	3.86B	<b>1.06B</b>
Non-GAAP net income per share – diluted	\$4.01	\$14.88	<b>\$4.08</b>
Cash, cash equivalents & total marketable securities (period-end)	\$9.8B	\$10.9B	<b>\$13.6B</b>








Notes: An explanation of non-GAAP financial measures and reconciliation of combined non-GAAP R&D, Acquired IPR&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 2023 press release dated November 6, 2023. 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.

# RAISING FULL YEAR 2023 PRODUCT REVENUE GUIDANCE

	Current FY 2023 Guidance	Previous FY 2023 Guidance	Commentary
Total CF Product Revenues	~\$9.85B	\$9.7 - \$9.8B	Includes expectations in the U.S. for continued performance of TRIKAFTA in ages 6+ and the launch of TRIKAFTA in the 2-5 age group, as well as the continued uptake of TRIKAFTA/KAFTRIO in multiple countries internationally.
Combined GAAP R&D, Acquired IPR&D and SG&A Expenses	Unchanged	\$4.55 - \$4.8B	
Combined Non-GAAP R&D, Acquired IPR&D and SG&A Expenses	Unchanged	\$4.1 - \$4.2B	
Non-GAAP Effective Tax Rate	20% to 21%	21% to 22%	



# MULTIPLE CATALYSTS THROUGH EARLY 2024

Recent Highlights		Anticipated Key Milestones	
	Received positive CHMP opinion in patients with CF ages 2 to 5	→	TRIKAFTA/KAFTRIO <b>approvals in EU and U.K.</b> in ages 2-5 years by end of 2023
	Received approval from Health Canada for TRIKAFTA in ages 2 to 5	→	<b>Secure reimbursement in Canada</b>
	Fully enrolled vanzacaftor/tezacaftor/deutivacaftor Phase 3 studies (ages 6-11 and 12+)	→	<b>Complete all Phase 3 studies (6+)</b> by end of 2023; <b>data in early 2024</b>
	Enrolling and dosing SAD study for VX-522 CFTR mRNA in CF patients	→	<b>Complete SAD portion and initiate MAD portion of the study by end of 2023</b>
	Completed FDA advisory committee meeting for exa-cel in SCD Regulatory reviews in EU and U.K. well underway Submitted MAA to the Kingdom of Saudi Arabia	→	<b>SCD PDUFA: December 8, 2023; TDT PDUFA: March 30, 2024</b> <b>Completion of UK and EU regulatory reviews</b> <b>Regulatory review in the Kingdom of Saudi Arabia</b>
	Phase 3 program for VX-548 in acute pain nearing completion; Ph 3 abdominoplasty study completed	→	<b>Complete all Phase 3 studies</b> by end of 2023; <b>data in early 2024</b>
	Completed Phase 2 dose-ranging study for VX-548 in diabetic peripheral neuropathy	→	<b>Share data in late 2023</b>
	Expect to initiate Phase 2 PNP study for VX-548 in lumbosacral radiculopathy	→	<b>Initiate trial by end of 2023</b>
	Enrolling and dosing pivotal trial of inaxaplin in broad AMKD population	→	<b>Complete enrollment of Phase 2B portion</b> of Phase 2/3 pivotal study by end of 2023; select dose and advance to Phase 3 portion in first quarter of 2024
	Presented updated positive clinical data at EASD in type 1 diabetes; <b>Part C fully enrolled</b>	→	<b>Complete dosing in Part C</b>
	Enrolling and dosing patients in Phase 1/2 trial for VX-264, the cells + device program	→	<b>Continue to enroll and dose Phase 1/2 trial</b>
	Discontinued Phase 2 trial for VX-864 in patients with AATD FIH trials for <b>VX-634 and VX-668 continue to enroll and dose healthy volunteers</b>	→	<b>Complete VX-634 and VX-668 studies</b>
	Pursue additional <i>in vitro</i> and animal studies for <b>gene-editing therapy for DMD</b>	→	Ongoing preclinical research



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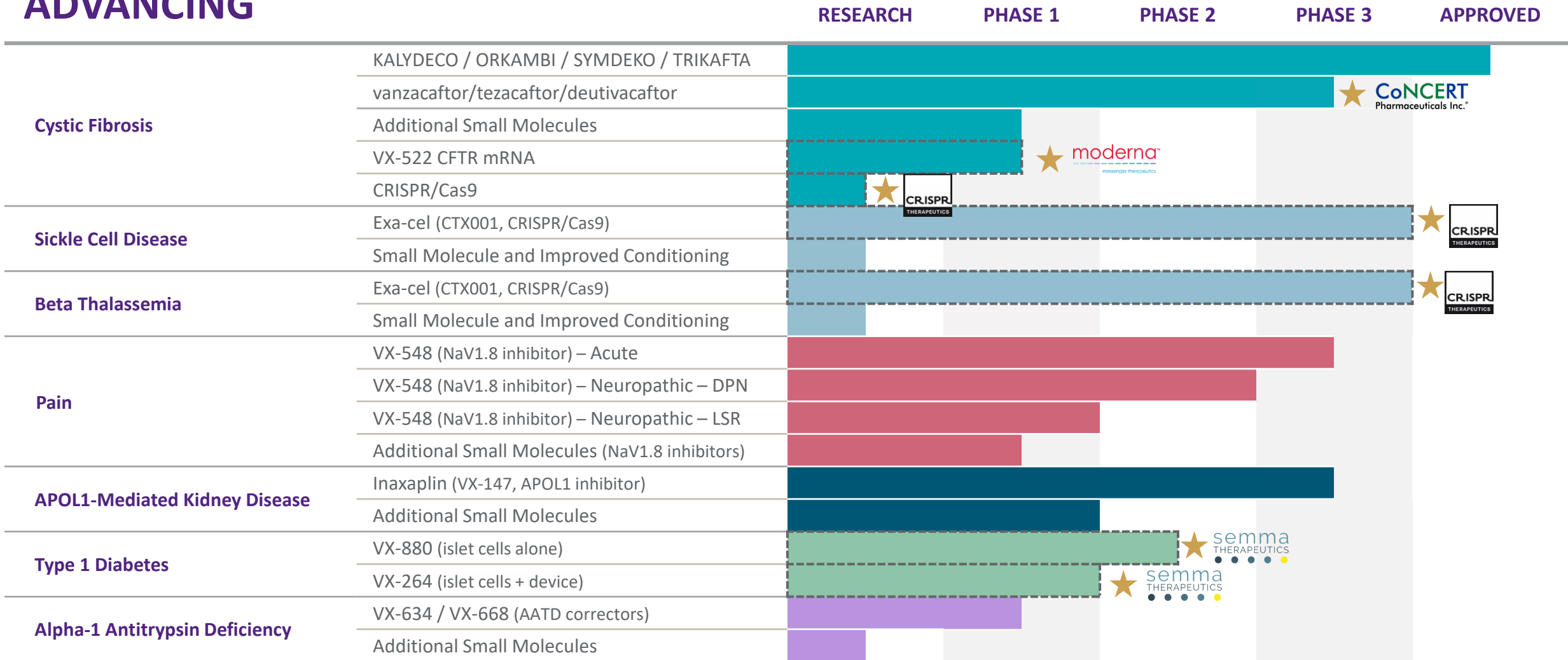
# APPENDIX

## GAAP TO NON-GAAP FINANCIAL INFORMATION

<i>(\$ in millions except as noted, per share data and percentages)</i>	<b>Q3 22</b>	<b>FY 22</b>	<b>Q3 23</b>
<b>Combined R&amp;D, Acquired IPR&amp;D and SG&amp;A</b>			
GAAP	921	3.60B	<b>1.13B</b>
Non-GAAP	758	3.07B	<b>993</b>
<b>Operating income</b>			
GAAP	1.13B	4.31B	<b>1.04B</b>
Non-GAAP	1.29B	4.79B	<b>1.17B</b>
<b>Operating Margin %:</b>			
GAAP	48%	48%	<b>42%</b>
Non-GAAP	55%	54%	<b>47%</b>
<b>Net income</b>			
GAAP	931	3.32B	<b>1.04B</b>
Non-GAAP	1.04B	3.86B	<b>1.06B</b>
<b>Net income per share - diluted</b>			
GAAP	\$3.59	\$12.82	<b>\$3.97</b>
Non-GAAP	\$4.01	\$14.88	<b>\$4.08</b>

Note: An explanation of non-GAAP financial measures and reconciliation of combined non-GAAP R&D, Acquired IPR&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 2023 press release dated November 6, 2023.

# R&D STRATEGY DESIGNED TO DELIVER SERIAL INNOVATION WITH HIGH PROBABILITY OF SUCCESS; CLINICAL-STAGE PIPELINE IS BROAD, DEEP AND ADVANCING



Cell therapy or nucleic acid therapy (mRNA, gene editing) ★ Complementary BD