



# FIRST QUARTER 2023 FINANCIAL RESULTS

MAY 1, 2023

©2023 Vertex Pharmaceuticals Incorporated



# 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, and statements regarding our (i) expectations, development plans, and timelines for the company's products, product candidates, and pipeline programs, including expectations for five potential launches in five years, multiple clinical-stage programs with launch potential by 2030, anticipated benefits of new products, patient populations, study designs, data availability, anticipated regulatory filings, approvals, and timing thereof, (ii) expectations for continued growth in the number of CF patients treated with our existing therapies, including targeted 2023 global launch of TRIKAFTA/KAFTRIO in patients aged 2-5 and new reimbursement agreements, (iii) 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, (iv) expectations for the benefits of vancacftor triple combination therapy, plans to complete Phase 3 studies in 2023, and expectations for near-term launch, commercial potential and lower royalty burden, (v) 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, and expectations for near-term launch and commercial potential, including expected patient population and expectations regarding providers and payers, (vi) expectations for our pain program, including its potential to treat acute pain without the limitations of opioids, the anticipated timeline to complete Phase 3 pivotal program for VX-548 in acute pain and complete Phase 2 studies of VX-548 in neuropathic pain, and plans for near-term commercial launch in moderate-to-severe acute pain, (vii) our expectations and beliefs regarding our pivotal program for inaxaplin, including its potential to treat the underlying cause of AMKD, plans to complete Phase 2B portion of studies in 2023, our beliefs regarding anticipated results of the study and the potential path to accelerated approval in the U.S., (viii) expectations for the development of our T1D programs, including the patient population, potential curative benefits and safety of VX-880, plans to initiate Part C of the VX-880 Phase 1/2 trial and availability of updated clinical data in 2023, plans to enroll and dose patients with VX-264 in coming months, and expected use of CRISPR/Cas9 gene editing in our hypoimmune program, (ix) plans for continued advancement of VX-634 and VX-864, (x) plans for our DMD and DM1 programs, including expectations to file INDs, and (xi) 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 the company may not be able to submit anticipated regulatory filings on expected timelines, or at all, that our regulatory submissions could be delayed and 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 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, 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 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 Q1 2023 press release dated May 1, 2023.

**STRONG START TO 2023:  
DELIVERING ON OUR  
GOALS FOR EXPANDED  
LEADERSHIP IN CF,  
MULTIPLE NEAR-TERM  
LAUNCHES, IMPORTANT  
CLINICAL MILESTONES,  
AND CONTINUED  
GROWTH**

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

- Serially innovate to bring highly efficacious CFTRm to all eligible patients
- Reach the last ~5,000 patients (ineligible for a CFTRm) with mRNA therapy
- Continue to build unparalleled portfolio of real-world and long-term data

## **Prepare for potential near-term commercial launches**

- Exa-cel in SCD and TDT: completed regulatory submissions in U.S., Europe and U.K.
- Vanzacaftor triple in CF: Phase 3 studies expected to complete by YE 2023
- VX-548 in moderate to severe acute pain: Phase 3 studies expected to complete by late 2023/early 2024

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

- Five launches possible in next five years
- Multiple clinical-stage programs with launch potential by 2030

## **Deliver financial performance**

- Continue to drive revenue growth from treating more CF patients and upcoming launches in new disease areas, starting with exa-cel
- Maintain 2023 financial guidance; specialty model sustains strong operating margins while allowing for significant investments in the pipeline and commercial capabilities



# EXECUTING ON VERTEX BUSINESS MODEL AND R&D STRATEGY WITH RAPID PROGRESS ON A ROBUST PIPELINE

## FIVE POTENTIAL LAUNCHES IN THE NEXT FIVE YEARS



**4** Approved medicines in cystic fibrosis

**8** Programs in mid- or late-stage development

**Near-term commercial opportunities**

- Exa-cel (SCD)
- Exa-cel (TDT)
- Vanzacaftor triple (CF)
- VX-548 (acute pain)

**8** Programs in mid- or late-stage development

**Mid/late-stage clinical pipeline**

- Inaxaplin (AMKD) - Post PoC
- VX-880 (T1D) - Post PoC
- VX-548 (neuropathic pain) – Phase 2
- VX-864 (AATD) – Phase 2

PoC: proof of concept; SCD: sickle cell disease; TDT: transfusion-dependent beta thalassemia; AMKD: APOL1-mediated kidney disease; T1D: type 1 diabetes; AATD: Alpha-1 Antitrypsin Deficiency



# CONTINUING OUR SERIAL INNOVATION IN CYSTIC FIBROSIS



## Vanzacaftor Triple

- Next-in-class CFTR modulator triple therapy
- Completed enrollment in pivotal program in patients ages 12+ in late 2022, and enrollment in patients ages 6-11 is advancing rapidly. All three studies are expected to complete by YE 2023
- Phase 2 data demonstrate enhanced clinical benefit across all disease manifestations
- 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
- Initiated dosing of CF patients in Single Ascending Dose (SAD) study in Q1:23
- Expect to complete SAD study and initiate Multiple Ascending Dose (MAD) study in 2023
- Program developed in partnership with Moderna



# NEAR-TERM LAUNCH POTENTIAL: EXA-CEL

## COMPLETED ROLLING BLA SUBMISSIONS IN THE U.S. FOR SICKLE CELL DISEASE AND TRANSFUSION-DEPENDENT BETA THALASSEMIA



**Sickle Cell Disease and Beta Thalassemia**  
*Genetic diseases caused by mutation in the beta-globin gene*



- Causal human biology well understood
- Severe, symptomatic diseases

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



- ✓ **The first CRISPR-based gene-editing treatment potentially to be approved**
- ✓ Precise and durable edit to BCL11A gene to increase production of fetal hemoglobin



- ✓ Completed regulatory submissions in the U.S., Europe and U.K.
- ✓ Submissions in U.S. include requests for Priority Review
- ✓ Awaiting assignment of PDUFA date

# NEAR-TERM LAUNCH POTENTIAL: VX-548 FOR MODERATE TO SEVERE ACUTE PAIN

ANTICIPATE COMPLETING THE PHASE 3 PIVOTAL PROGRAM BY LATE 2023/EARLY 2024



## Significant Unmet Needs

- Millions in the U.S. each year suffer from acute pain
- Existing therapies have challenging side effects and/or abuse potential
- Pain often poorly managed and inadequately treated as a result

## Validated Target

- NaV1.8 is genetically and pharmacologically validated
- 5 Proof of Concept studies across VX-150 and VX-548 in major pain types:
  - Acute
  - Peripheral neuropathic (PNP)
  - Musculoskeletal

## Pivotal Program Ongoing

- Phase 3 program similar to Phase 2:
  - Two RCTs: same pain states, duration and endpoints
  - Single-arm study for other types of acute pain
  - Seeking broad, moderate-to-severe, acute pain label

## Near-Term Commercial Opportunity

- Phase 3 enrollment well underway in high-volume procedures
- Short treatment duration facilitates efficient timelines
- Positive interactions with FDA
  - Fast Track and Breakthrough Therapy designations granted



# INAXAPLIN: THE FIRST POTENTIAL MEDICINE TO TREAT THE UNDERLYING CAUSE OF APOL1-MEDIATED KIDNEY DISEASE (AMKD)

## RECENT *NEJM* ARTICLES UNDERSCORE SIGNIFICANCE OF INAXAPLIN DATA

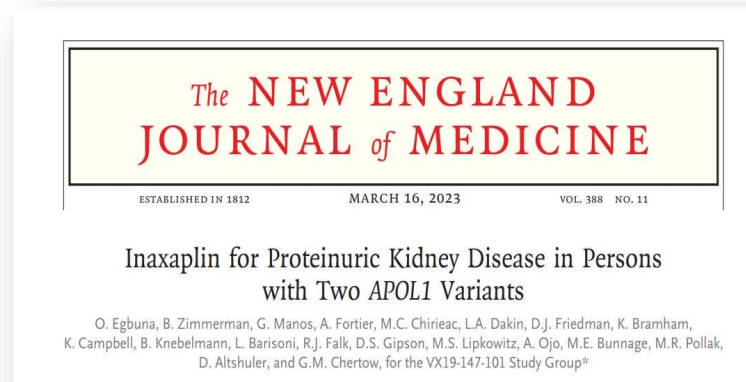


100,000

patients in the  
U.S. and Europe

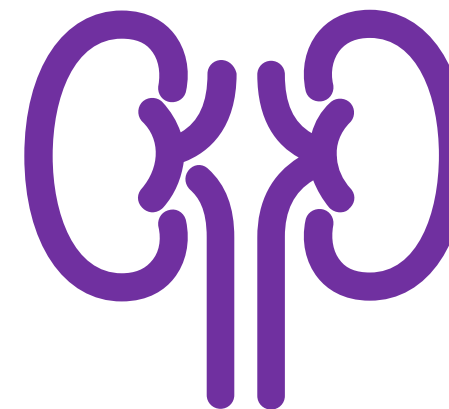
### APOL1-MEDIATED KIDNEY DISEASE

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



### FIRST PUBLICATION FOR INAXAPLIN

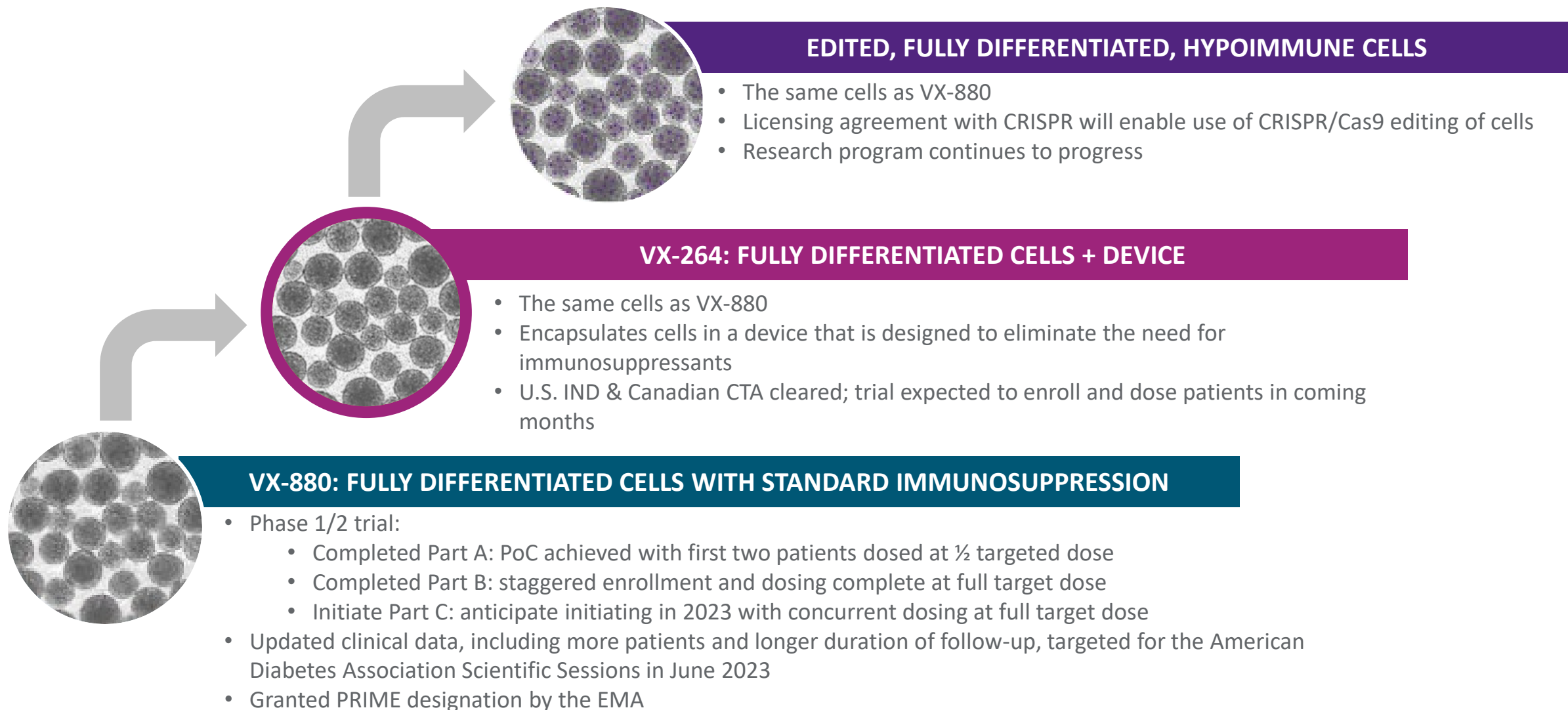
- Phase 2 and preclinical study results of inaxaplin published in *NEJM*
- *NEJM* published the article, an editorial, and a “Science Behind the Study” feature, underscoring the importance of inaxaplin results and AMKD



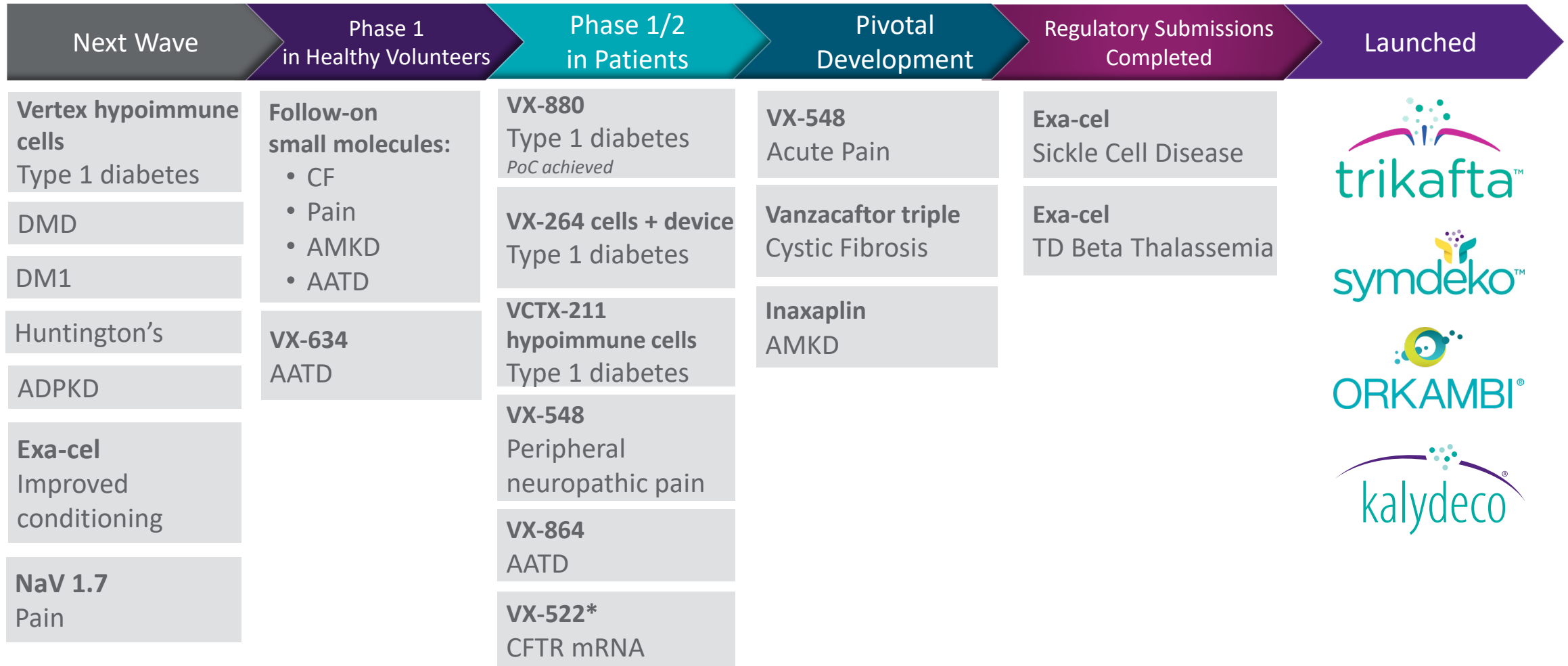
### PIVOTAL TRIAL UNDERWAY

- On track to complete dose selection portion of Phase 2/3 pivotal trial in 2023
- Path to accelerated approval with interim analysis at 48 weeks of treatment
- Final analysis at ~2 years of treatment

# TYPE 1 DIABETES: ADVANCING FULLY DIFFERENTIATED CELLS AS CURATIVE TREATMENTS FOR ~2.5 MILLION PATIENTS IN NORTH AMERICA AND EUROPE



# CLINICAL PORTFOLIO IS BROAD, DIVERSE AND RAPIDLY ADVANCING; RESEARCH PIPELINE PROGRESSING TO DELIVER NEXT WAVE OF INNOVATION



# SUSTAINING AND EXPANDING LEADERSHIP IN CF WITH SERIAL INNOVATION

RECENTLY RECEIVED FDA APPROVAL FOR TRIKAFTA IN PATIENTS AGES 2-5 YEARS IN THE U.S.



**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

- Targeting 2023 TRIKAFTA/KAFTRIO global launch in patients ages 2-5 years
- New reimbursement agreements for younger patients in Europe, Australia and New Zealand

### 2. More people with CF, living longer

- 33.5-year increase in the median projected survival of people with CF with TRIKAFTA therapy versus standard of care\*

### 3. Raising the bar

- Vanzacaftor triple: pivotal studies in CF patients ages 12+ and 6-11 years expected to complete by YE 2023

### 4. Advancing therapies for all patients

- Ongoing VX-522 CFTR mRNA Phase 1 trial in CF patients who cannot benefit from CFTR modulators

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

\*Modeled data published in the *Journal of Cystic Fibrosis*.



# NEAR-TERM LAUNCH POTENTIAL: EXA-CEL

## LAUNCH PREPAREDNESS WORK FOCUSES ON KEY STAKEHOLDERS

### Patients



- Initial launch will focus on ~32,000 most severe patients
- More than a quarter of surveyed SCD and TDT patients strongly believe genetic therapy is right choice for them<sup>1</sup>



Patient identified;  
cells collected



Cells are  
edited



Patient  
receives  
edited cells

### Providers



ATC

- Clear recognition of different genetic therapy approaches
- 70% of providers prefer a gene-edited approach over other gene therapy mechanisms<sup>1</sup>
- ~50 U.S. centers are actively engaged in process to become an ATC
- All 25 targeted European centers are in process to become an ATC

### Payers



- Commercial payers (~35% of U.S. payer mix<sup>2</sup>): working to ensure broad access to care; Vertex is confident in recognition of exa-cel's value to patients
- Government payers (Medicaid ~45% of U.S. payer mix<sup>2</sup>):
  - Partnering with state Medicaid agencies to ensure broad access
  - Cell and Gene Therapy Access Model: demonstration project to be administered by CMS to accelerate and enhance access

1: Source: Vertex market research, April-June 2022; 2: Source: DRG claims analysis



# Q1 2023 FINANCIAL HIGHLIGHTS

<i>(\$ in millions except where noted or per share data and percentages)</i>	<b>Q1 22</b>	<b>FY 22</b>	<b>Q1 23</b>
Total CF product revenues	<u>\$2.10B</u>	<u>\$8.93B</u>	<u>\$2.37B</u>
TRIKAFTA/KAFTRIO	1.76B	7.69B	<b>2.10B</b>
Other CF products	336	1.24B	<b>278</b>
Combined non-GAAP R&D, acquired IPR&D and SG&A expenses	<u>687</u>	<u>3.07B</u>	<u>1.21B</u>
Non-GAAP operating income	1.17B	4.79B	<b>902</b>
Non-GAAP operating margin %	56%	54%	<b>38%</b>
Non-GAAP net income	907	3.86B	<b>794</b>
Non-GAAP net income per share – diluted	\$3.52	\$14.88	<b>\$3.05</b>
Cash, cash equivalents & total marketable securities (period-end)	\$8.2B	\$10.9B	<b>\$11.5B</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 Q1 2023 press release dated May 1, 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.

# STRATEGIC COLLABORATIONS AUGMENT OUR INTERNAL INNOVATION

## TRANSACTIONS COMPLETED IN Q1:23



*Discovery and development of intracellular Endosomal Escape Vehicle (EEV™) therapeutics for myotonic dystrophy type 1 (DM1).*



*Research collaboration for new tRNA-based therapies for patients with Duchenne muscular dystrophy (DMD) caused by nonsense mutations.*



*Accelerate development of hypimmune gene-edited therapies for T1D.*



*Multi-target license and option agreement to use ImmunoGen's ADC technology for gentler conditioning agents for genetic therapies.*

Q1 results include \$347M of acquired IPR&D charges

# REITERATE FULL YEAR 2023 FINANCIAL GUIDANCE

	Current FY 2023 Guidance	FY 2023 Commentary
Total CF Product Revenue	\$9.55 - \$9.7B	Continued performance of TRIKAFTA in ages 6+, approval and launch of TRIKAFTA in ages 2-5
Combined GAAP R&D, Acquired IPR&D and SG&A Expenses	\$4.35 - \$4.6B	No change to full year total operating expense outlook; now includes ~\$400 million of upfronts and milestones from completed BD transactions
Combined Non-GAAP R&D, Acquired IPR&D and SG&A Expenses	\$3.9 - \$4.0B	
Non-GAAP Effective Tax Rate	21%-22%	

# INDUSTRY LEADING CULTURE OF INNOVATION AND INCLUSION WILL SUSTAIN LONG-TERM SUCCESS



## Improve the Lives of People With Serious Diseases

### Majority

of business operating expenses invested in R&D (GAAP)

### 3 out of 5

employees work in R&D roles

### 8

programs in mid- or late-stage clinical development

### 60+

countries where our cystic fibrosis medicines are reimbursed or accessible



## Foster an Ethical Culture That Embraces Innovation, Inclusion, Diversity and Equity

### 51%

of new hires are from underrepresented ethnic and racial groups (U.S.)

### 7 out of 11

Board directors are women and/or from underrepresented ethnic and racial groups

### 100%

of employees completed annual code of conduct training

### 16

Best Places to Work awards in the U.S.



## Carefully Manage Our Operations and Environmental Footprint

### 21.4%

reduction in absolute GHG emissions since 2018

### 83%

green-certified square footage in our buildings<sup>1</sup>

### 100%

renewable electricity at our London and Oxford facilities

### B

Score on 2022 CDP Climate Change survey for addressing environmental impacts of our business and ensuring good environmental management (global average score is C)



## Make a Positive Impact in the Communities Where We Are Located

### \$35+ million

in charitable giving by Vertex and the Vertex Foundation

### 57%

of employees volunteered during annual global Day of Service

### 1,895








nonprofit organizations supported through Employee Matching Gift Program

### ~700

students participated in global early career or STEAM education programs

<sup>1</sup>—Including Leiden Center for Cell and Genetic Therapies, which is expected to receive green certification in 2023.

# STRONG START TO 2023 SETS UP CADENCE OF CLINICAL CATALYSTS

Recent Highlights	
	<p>Received FDA approval in U.S. for TRIKAFTA in patients with CF ages 2 to 5</p> <p>Fully enrolled vanzacaftor/tezacaftor/deutivacaftor Phase 3 studies (ages 12+)</p> <p>Initiated SAD study for VX-522 CFTR mRNA in CF patients</p>
	Completed regulatory filings for SCD and TDT in U.S., Europe and U.K.
	<p>All Phase 3 trials underway for VX-548 in acute pain</p> <p>Continue to enroll and dose Phase 2 dose-ranging study of VX-548 in neuropathic pain</p>
	Initiated pivotal development of inaxaplin in broad AMKD population
	<p>Completed enrollment and dosing of Part B for VX-880 in type 1 diabetes</p> <p>Secured PRIME designation</p> <p>IND and CTA cleared in U.S. and Canada for VX-264, the cells + device program in type 1 diabetes</p>
	Dosing Phase 2 trial for VX-864 in patients with AATD and FIH trial for VX-634
	IND-enabling studies ongoing for DMD and DM1



Anticipated Key Milestones in 2023
TRIKAFTA/KAFTRIO <b>global launch</b> in patients ages 2-5 years
<b>Complete Phase 3 studies</b> , including pediatric study
<b>Complete SAD study and initiate MAD study</b>
<p><b>Await PDUFA date assignment in the U.S.</b></p> <p><b>Continue commercial launch preparedness efforts</b></p>
<b>Complete Phase 3 trials late 2023/early 2024</b>
<b>Complete Phase 2 trial late 2023/early 2024</b>
<b>Complete Phase 2B (dose-ranging) portion</b> of Phase 2/3 pivotal study
<p><b>Initiate Part C</b> (concurrent dosing)</p> <p><b>Present updated clinical data at ADA</b> in June</p>
<b>Initiate Phase 1/2 trial</b> in near term
<p><b>VX-864: Complete Phase 2 enrollment</b></p> <p><b>VX-634: Complete FIH study</b></p>
<b>File INDs</b>





# FIRST QUARTER 2023 FINANCIAL RESULTS

MAY 1, 2023

©2023 Vertex Pharmaceuticals Incorporated



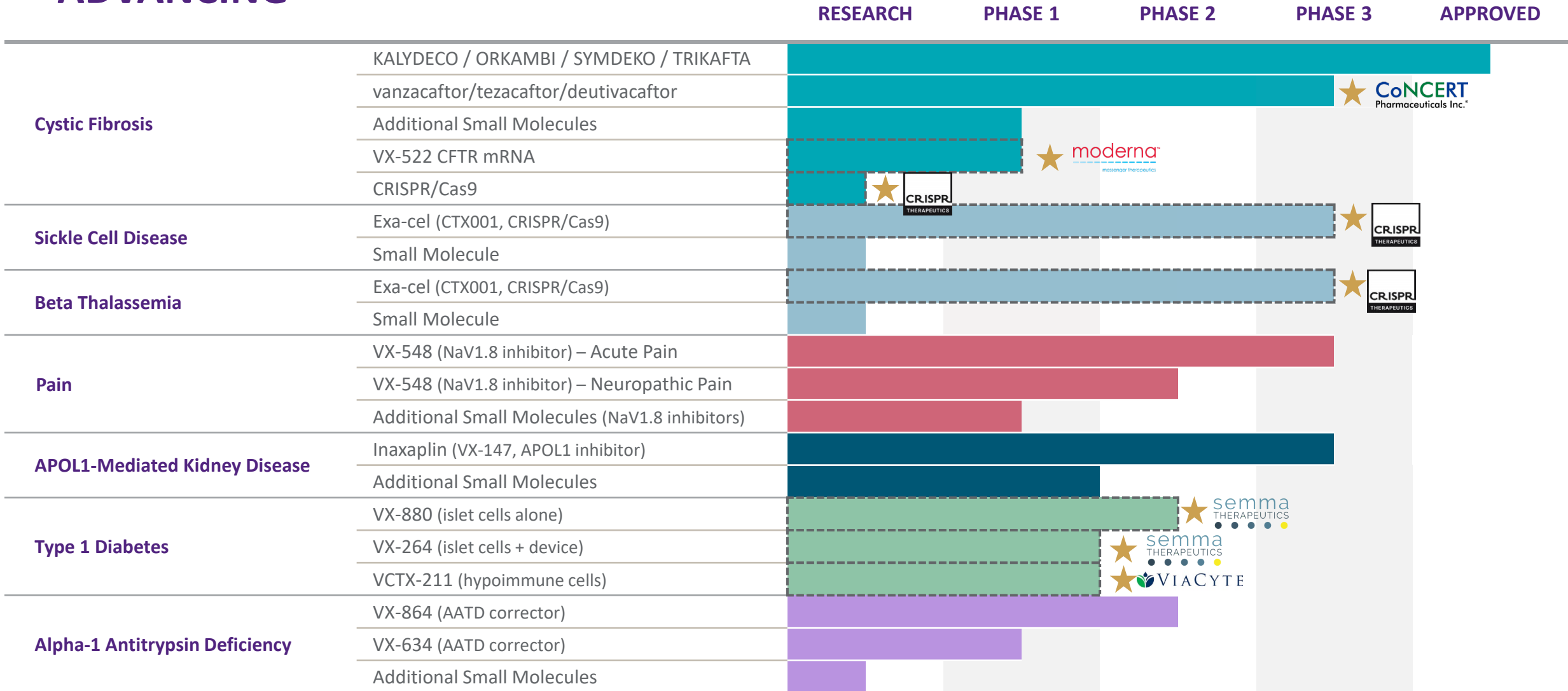
# APPENDIX

## GAAP TO NON-GAAP FINANCIAL INFORMATION

<i>(\$ in millions except as noted, per share data and percentages)</i>	<b>Q1 22</b>	<b>FY 22</b>	<b>Q1 23</b>
<b>Combined R&amp;D, Acquired IPR&amp;D and SG&amp;A</b>			
GAAP	818	3.60B	<b>1.33B</b>
Non-GAAP	687	3.07B	<b>1.21B</b>
<b>Operating income</b>			
GAAP	1.04B	4.31B	<b>779</b>
Non-GAAP	1.17B	4.79B	<b>902</b>
<b>Operating Margin %:</b>			
GAAP	50%	48%	<b>33%</b>
Non-GAAP	56%	54%	<b>38%</b>
<b>Net income</b>			
GAAP	762	3.32B	<b>700</b>
Non-GAAP	907	3.86B	<b>794</b>
<b>Net income per share - diluted</b>			
GAAP	\$2.96	\$12.82	<b>\$2.69</b>
Non-GAAP	\$3.52	\$14.88	<b>\$3.05</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 Q1 2023 press release dated May 1, 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