VERTEX

THE SCIENCE *of* POSSIBILITY

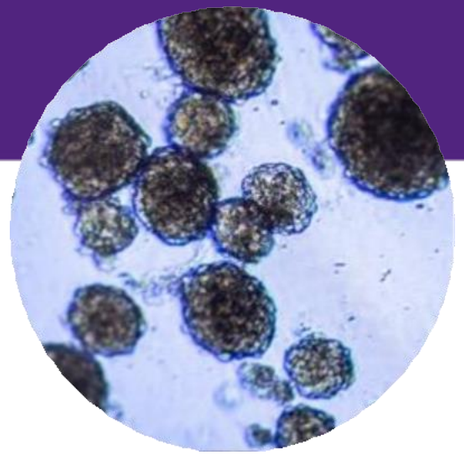
VERTEX OVERVIEW

JANUARY 31, 2023

WE ARE VERTEX

We invest in scientific innovation to create transformative medicines for people with serious diseases with a focus on specialty markets.

Patients are at the heart of everything we do



We strike at the core of serious diseases to change people's lives

We're not afraid to take on the impossible

For the lives we have changed and for those who are still waiting, we will never stop fighting until we discover cures.

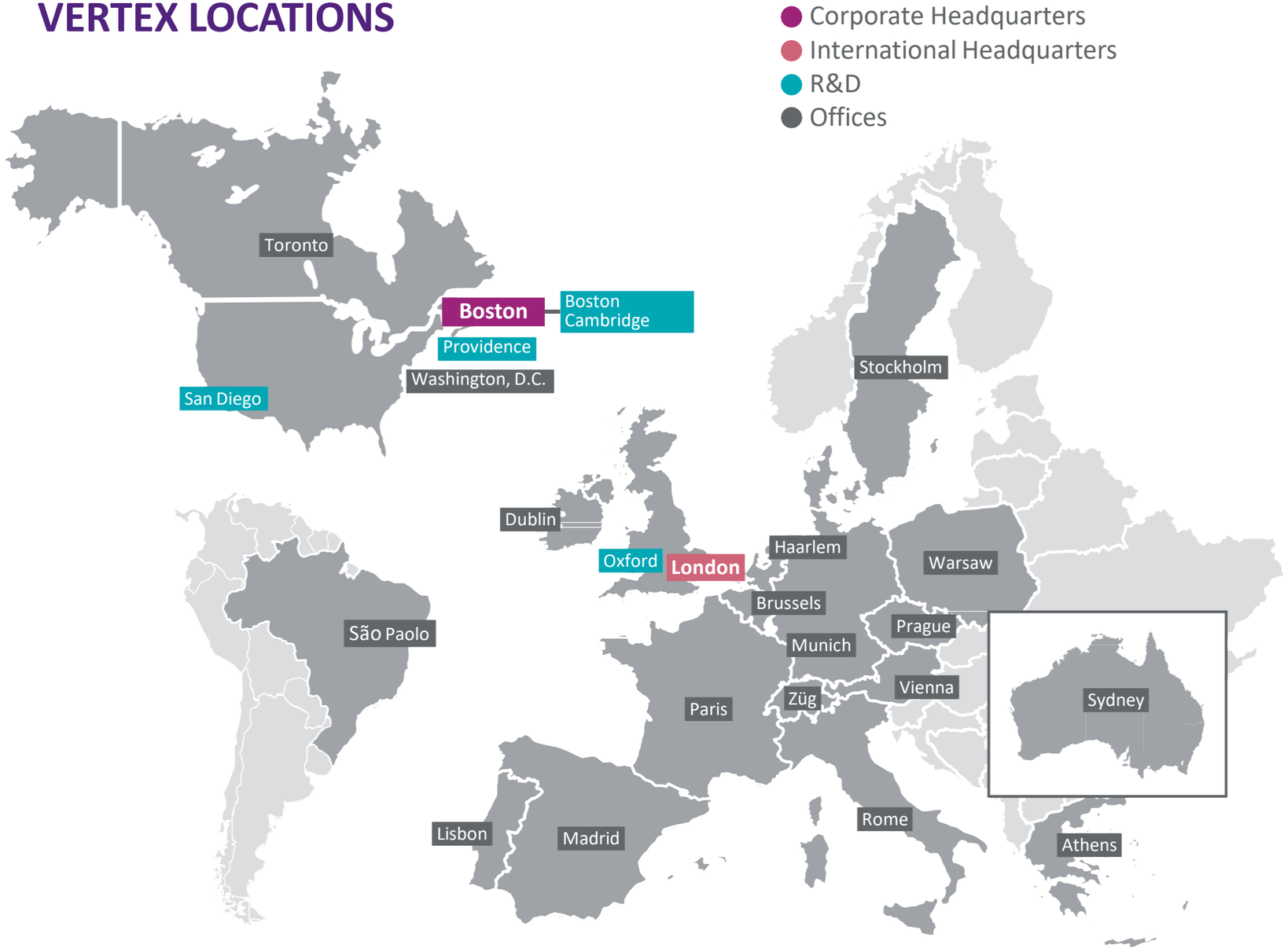
QUICK FACTS

Founded:
1989

Headquarters:
Boston

~4,500
Employees worldwide
(~3,200 in Boston)

VERTEX LOCATIONS



UNPRECEDENTED RUN OF PROOF-OF-CONCEPT SUCCESSES

MULTIPLE UPCOMING CATALYSTS

6 Programs Advanced Through Phase 2 Proof-of-Concept Studies					
Achieved Proof-of-Concept					Achieved Proof-of-Mechanism
SCD	β-Thal	Pain	AMKD	T1D	AATD
exa-cel	exa-cel	VX-548	VX-147	VX-880	VX-864; VX-634
Approval Submissions *Beginning Late 2022*		Phase 3 *Ongoing*	Phase 3 *Ongoing*	Part B *Ongoing*	*Phase 2 Planned; Phase 1 Ongoing*

STAT

June 2021:

"Can Vertex invent another blockbuster medicine from its own labs, like it's already done with hepatitis C and cystic fibrosis? Or, will it need to get more aggressive reaching outside the company — bigger partnerships or larger acquisitions — to find a solution for the slowdown in projected revenue growth?"

April 2022:

"It's hard not to be impressed with Vertex's R&D output over the past six months or so…Vertex's pipeline is delivering."

INAXAPLIN: FIRST P?TENTIAL MEDICINE TO TARGET THE UNDERLYING CAUSE OF AMKD

APOLI-MEDIATED KIDNEY DISEASE

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

PIVOTAL TRIAL UNDERWAY

- 47.6% reduction in proteinuria in Phase 2 in APOL1-mediated FSGS
- Dose selection portion of Phase 2/3 pivotal trial expected to complete in 2023
- Path to accelerated approval with interim analysis at 48 weeks of treatment
- Final analysis at ”2 years of treatment

RAISING DISEASE AWARENESS

- Education outreach with physicians and patients
- Building trust with historically underserved communities
- Initiatives to increase genetic testing for APOLI

Power rorvvard is a Vertex disease education campaign launched November 2022 IFtpartnership with basketball Hall—of-Famer and kidney health adVDCdte Alonza Mourning, who has AMKD and rzceive‹J a kidney transplant in 2003. ESKO: *End-stage kidney disease; FSGS: Focal segni ental glomerulosclerosis*

OUR VALUES

Our values are our bedrock *and combined with our culture have enabled us to deliver on our mission of creating transformative medicines for serious diseases.*

FEARLESS PURSUIT OF EXCELLENCE

UNCOMPROMISING COMMITMENT TO PATIENTS

INNOVATION IS OUR LIFEBLOOD

“WE” WINS

INVESTING IN OUR COMMUNITIES

BOSTON LEARNING LAB & COMMUNITY PARTNERSHIPS

Boston Learning Lab – est. in 2014

Dedicated space for hands-on STEM learning

*"Doing the lab activity and **learning how to use** different instruments"*

-9th grade student

Class Visit Program

Innovative curriculum & activities available to all BPS high schools

3-hour visit – lab activities & lunch with Vertex employees

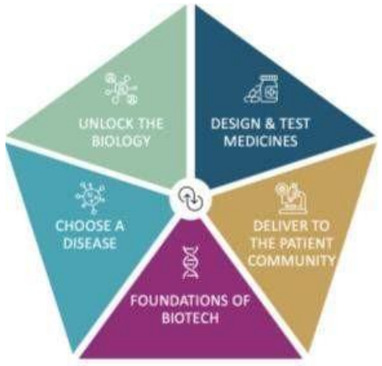
Art-integration (STEAM)

Biology and biochemistry

Business of biotech

Computer science and coding

Engineering



Community Partners & BPS Partner Schools

Proud to invest in our thriving ecosystem

Boston International Newcomers Academy
Boston Day and Evening Academy
John D. O'Bryant School for Mathematics & Science
East Boston High School
Boston Arts Academy
Rafael Hernández K-8 School
PA Shaw Elementary School

*"Being able to **have the opportunity** to see how our superheroes work"*

*"**More experience** with science/STEM"*

-9th grade students

TALENT AND WORKFORCE DEVELOPMENT PROGRAMS

Annual Summer High School Internship

Paid Summer STEM experiences for students

Goals

Explore the **business of biotech**
Strengthen **STEM skills** and knowledge
Cultivate a **professional learning network**

Key Details

342 Boston summer interns employed since 2012
Internship experience includes:

- **Hands-on lab experience** in the Learning Lab
- **1:1 Project with a Vertex manager**
- **1:1 Mentoring by Vertex ERN Members**
- Community enrichment activities
- Q&As with Vertex senior leaders

ISABELLA STEWART GARDNER MUSEUM

Vertex Science Leaders College Scholarship

Economic transformation: From inspiration to a STEM career

17 fully-funded UMass scholarships awarded since 2014
7 students currently receiving the award
6 college graduates
5 program alums working in the STEM field

Bottom Line

VERTEX PARTNERS WITH YEAR UP TO CREATE A BIOTECH CURRICULUM

- In 2020, Vertex committed to a multiyear partnership with Year Up to establish the **first-ever biotechnology curriculum to prepare young adults for future careers in research, development and medicine**.

- **Year Up's mission is to close the Opportunity Divide** by ensuring that young adults gain the skills, experiences and support that will empower them to reach their potential through careers and higher education.
  - First six months: Learning & Development phase – biotech trained pathway co-developed by Vertex, professional and personal skills developed
  - Last six months: Onsite internship at Vertex to apply skills
  - YU coaches provide ongoing mentoring and support

- After a successful pilot program (**8 out of 10 interns converted to FTEs**), we are expanding our biotech curriculum to include training for cell and gene therapy roles at Vertex.

- **On January 30th, 20 YU students began full-time internships at Vertex:**
  - Material Handler
  - Manufacturing Technician
  - Document Management
  - Manufacturing Associate
  - Process Development Engineering
  - Coordinator, Quality Assurance
  - Coordinator, Clinical Supply Chain
  - Coordinator, Quality Engineering

OUR SUSTAINABILITY EFFORTS MAXIMIZE THE EFFICIENCY OF OUR OPERATIONS, WHILE REDUCING WASTE AND CARBON EMISSIONS

Energy & Carbon Reduction

35%

Reduction from 2014 to 2018

On track to achieve 20% reduction target for 2019-2023

Waste Minimization

42%

Non-Hazardous waste (Regulated and Non-Regulated) sent for recycling or composting in 2021.

Employee Led Green Initiatives

100%

Employee-led Green Teams have led efforts towards green chemistry, re-purposing of gowning and product take-backs.

Green-Certified Facilities

GREEN Rating for Fan Pier and LC1

Rated LEED Gold and our newest Facility LC1 is anticipated to achieve LEED Platinum

THE VERTEX FOUNDATION

ABOUT THE VERTEX FOUNDATION

- Launched in October 2017
- It has 501(c)(3) IRS designation and is incorporated separately from Vertex Pharmaceuticals with a charter, by-laws and governance structure
- Long-term source of charitable giving and an extension of Vertex's corporate giving commitment
- It is fully funded by Vertex Pharmaceuticals

VERTEX | THE VERTEX FOUNDATION

MISSION:

The Vertex Foundation seeks to improve the lives of people with serious diseases and contribute to the communities where Vertex is located through education, innovation and health.

THE VERTEX F?›UNDATION HAS GAANTED *}46M TO N!›INPR‹E›FIT
kiRGAN1&W?iNS IN 41 COUWR1ES 20£7-2022

14TH ANNUAL DAY OF SERVICE

For the first time, more than 50% of employees participated

Supported employees' contributions of time and expertise to **78 nonprofit organizations** in their communities through community, on-site and virtual volunteer projects

1,491 employees (MA)

- **2,972 hours**
- **45** opportunities

26 sites across 20 countries

- 90+ projects completed worldwide
- Czech Republic and Providence sites implemented local projects for the first time

57%

Of all volunteer projects supported Vertex or Vertex Foundation nonprofit partners

VERTEX

THE SCIENCE *of* POSSIBILITY

THIRD QUARTER 2023 FINANCIAL RESULTS

NOVEMBER 6, 2023

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 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) 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

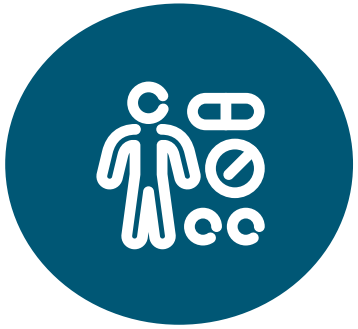
- VX-548 in peripheral neuropathic pain:
  - Phase 2 DPN trial has completed; data by end of 2023
  - Phase 2 LSR trial to initiate by end of 2023
- Inaxaplin in AMKD: completion of enrollment in Phase 2B portion of Phase 2/3 trial this year
- VX-880 in T1D: completed enrollment in Part C of Phase 1/2 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 VANZACAFTOR 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

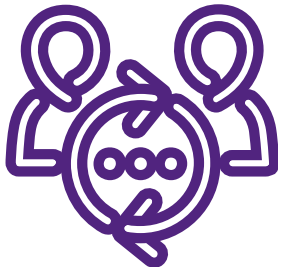
NEAR-TERM LAUNCH POTENTIAL: EXA-CEL

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	• $Na_V1.8$ 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):

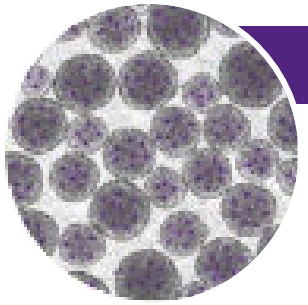
- Completed the Phase 2, 12-week, dose-ranging, proof-of-concept study
- Expect to share results by the end of 2023

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

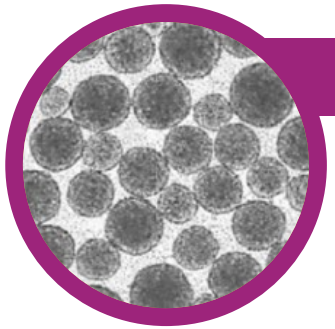
TYPE 1 DIABETES: ADVANCING POTENTIALLY CURATIVE TREATMENTS FOR ~2.5M PATIENTS IN NORTH AMERICA & EUROPE

PART C FULLY ENROLLED IN VX-880 TRIAL



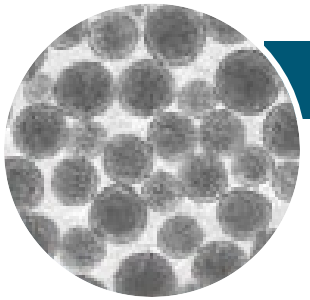
EDITED, FULLY DIFFERENTIATED, HYPOIMMUNE CELLS

- The same cells as VX-880
- Research program continues to progress



VX-264: FULLY DIFFERENTIATED CELLS + DEVICE

- The same cells as VX-880
- Encapsulates cells in a device that is designed to eliminate the need for immunosuppressants
- Part A of Phase 1/2 trial enrolling and dosing (partial dose with staggered enrollment)



VX-880: FULLY DIFFERENTIATED CELLS WITH STANDARD IMMUNOSUPPRESSION

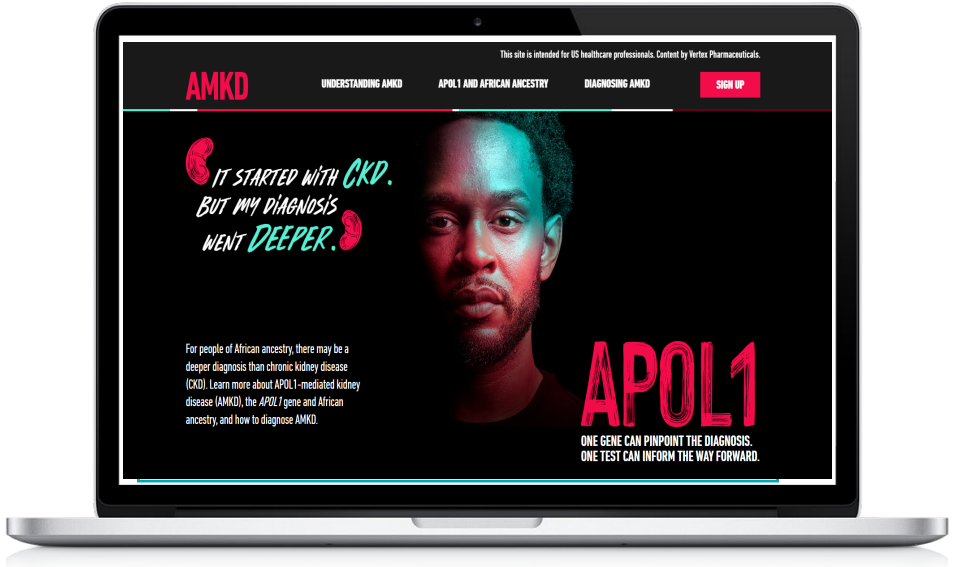
- Phase 1/2 trial:
  - ✓ Part A and Part B complete
    - ✓ Presented positive updated clinical data at EASD in October 2023
  - ✓ Part C fully enrolled

VCTX-211, a hypoimmune program that originated under ViaCyte, has finished enrollment and dosing in Group 1 of the Phase 1/2 trial.

EASD: European Association for the Study of Diabetes

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

Select, Next Wave Research-stage Programs	Phase 1 in Healthy Volunteers	Phase (1)/2 in Patients	Pivotal Development	Regulatory Submissions Completed	Launched
Vertex hypoimmune cells Type 1 diabetes	**Follow-on programs:** • CF • Pain • AMKD • AATD	**VX-880** Type 1 diabetes *PoC achieved*	**VX-548** Acute Pain	**Exa-cel** Sickle Cell Disease	trikafta™
Huntington's		**VX-264 cells + device** Type 1 diabetes	**Vanzacaftor triple** Cystic Fibrosis	**Exa-cel** TD Beta Thalassemia	symdeko™
ADPKD		**VCTX-211 (ViaCyte) hypoimmune cells** Type 1 diabetes	**Inaxaplin** AMKD		ORKAMBI®
Exa-cel Improved conditioning		**VX-548** Peripheral Neuropathic Pain - DPN			kalydeco®
Na_V 1.7 Pain		**VX-548** Peripheral Neuropathic Pain - LSR*			
DMD		**VX-522**** CFTR mRNA			
DM1					

ADPKD: Autosomal Dominant Polycystic Kidney Disease; DM1: Myotonic Dystrophy Type 1; DPN: diabetic peripheral neuropathy; FIH: First In Human; LSR: painful lumbosacral radiculopathy.
**Trial to initiate by YE 2023. **Phase 1, single ascending dose study in patients with CF.*

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

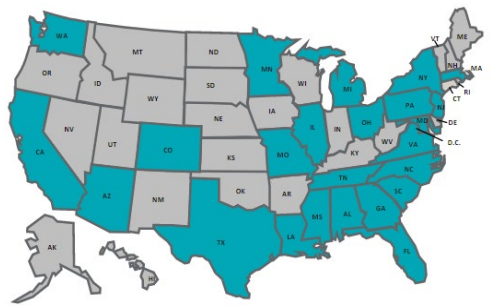
Note: estimated CF patient population and population breakdown as of January 2023
*Cystic Fibrosis Foundation Patient Registry 2021 Annual Data Report

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

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

Additional opportunity

~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.

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

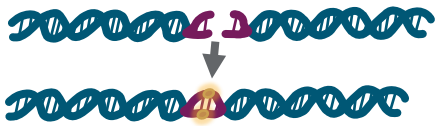
GOAL TO DELIVER TRANSFORMATIVE PATIENT OUTCOMES WITH THE POSSIBILITY OF A LIFETIME OF BENEFIT

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

ATC: Authorized Treatment Center

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

80
MILLION PATIENTS
every year in the U.S.

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

10
MILLION PATIENTS
every year in the U.S.

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

IDNs = integrated delivery networks.

Q3 2023 FINANCIAL HIGHLIGHTS

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

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 **approvals in EU and U.K.** in ages 2-5 years by end of 2023
Received approval from Health Canada for TRIKAFTA in ages 2 to 5	**Secure reimbursement in Canada**
Fully enrolled vanzacaftor/tezacaftor/deutivacaftor Phase 3 studies (ages 6-11 and 12+)	**Complete all Phase 3 studies (6+)** by end of 2023; **data in early 2024**
Enrolling and dosing SAD study for VX-522 CFTR mRNA in CF patients	**Complete SAD portion and initiate MAD portion of the study by end of 2023**
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**	**SCD PDUFA: December 8, 2023; TDT PDUFA: March 30, 2024** **Completion of UK and EU regulatory reviews** **Regulatory review in the Kingdom of Saudi Arabia**
Phase 3 program for VX-548 in acute pain nearing completion; Ph 3 abdominoplasty study completed	**Complete all Phase 3 studies** by end of 2023; **data in early 2024**
Completed Phase 2 dose-ranging study for VX-548 in diabetic peripheral neuropathy	**Share data in late 2023**
Expect to initiate Phase 2 PNP study for VX-548 in lumbosacral radiculopathy	**Initiate trial by end of 2023**
Enrolling and dosing pivotal trial of inaxaplin in broad AMKD population	**Complete enrollment of Phase 2B portion** 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; **Part C fully enrolled**	**Complete dosing in Part C**
Enrolling and dosing patients in Phase 1/2 trial for VX-264, the cells + device program	**Continue to enroll and dose Phase 1/2 trial**
Discontinued Phase 2 trial for VX-864 in patients with AATD FIH trials for **VX-634 and VX-668 continue to enroll and dose healthy volunteers**	**Complete VX-634 and VX-668 studies**
Pursue additional *in vitro* and animal studies for **gene-editing therapy for DMD**	Ongoing preclinical research

VERTEX

THE SCIENCE *of* POSSIBILITY

THIRD QUARTER 2023 FINANCIAL RESULTS

NOVEMBER 6, 2023

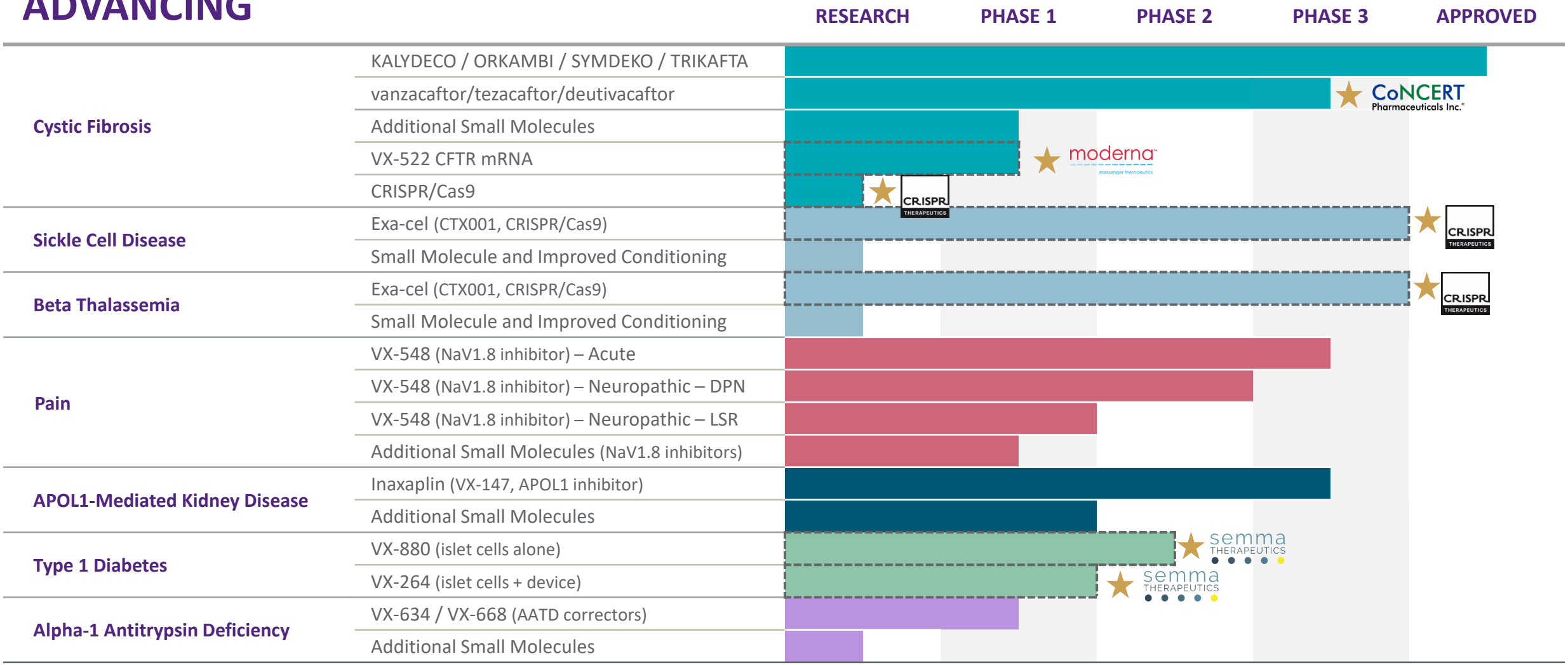
APPENDIX

GAAP TO NON-GAAP FINANCIAL INFORMATION

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

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

Vertex Receives CHMP Positive Opinion for the First CRISPR/Cas9 Gene-Edited Therapy, CASGEVY™ (exagamglogene autotemcel), for the Treatment of Sickle Cell Disease and Transfusion-Dependent Beta Thalassemia

December 15, 2023

- If approved by the European Commission, patients 12 years of age and older with severe sickle cell disease or transfusion-dependent beta thalassemia, for whom hematopoietic stem cell transplantation is appropriate and a human leukocyte antigen matched related donor is not available, would be eligible for treatment -

- Approval decision from the European Commission is expected in Q1 2024 -

BOSTON--(BUSINESS WIRE)--Dec. 15, 2023-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) announced today that the European Medicines Agency's (EMA's) Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion for the conditional approval of CASGEVY ™(exagamglogene autotemcel [exa-cel]), a CRISPR/Cas9 gene-edited therapy, for the treatment of severe sickle cell disease (SCD) and transfusion-dependent beta thalassemia (TDT).

If approved, exa-cel would be the only genetic therapy for patients in the European Union who are 12 years of age and older with either severe SCD with recurrent vaso-occlusive crises (VOCs) or TDT, for whom hematopoietic stem cell (HSC) transplantation is appropriate and a human leukocyte antigen matched related HSC donor is not available. An approval decision by the European Commission is expected in February 2024.

"This positive opinion is yet another important regulatory milestone underscoring the potentially transformative benefit of CASGEVY for eligible patients with sickle cell and transfusion-dependent beta thalassemia," said Nia Tatsis, Ph.D., Executive Vice President and Chief Regulatory and Quality Officer at Vertex.

"There is an urgent need for new potentially curative treatments in beta thalassemia and sickle cell disease, as people with these diseases still have a shorter life expectancy than the general population and an impaired quality of life," said Franco Locatelli, M.D., Ph.D., Principal investigator in the CLIMB-111 and CLIMB-121 studies, Professor of Pediatrics at the Catholic University of the Sacred Heart, Rome, and Director of the Department of Pediatric Hematology and Oncology at the Bambino Gesù Children's Hospital. "As an investigator, I have witnessed first-hand the transformative impact exa-cel can have on patients' lives and I eagerly await the approval in the European Union."

About Sickle Cell Disease (SCD)

SCD is a debilitating, progressive, life shortening genetic disease. SCD patients report health-related quality of life scores well below the general population and significant health care resource utilization. SCD affects the red blood cells, which are essential for carrying oxygen to all organs and tissues of the body. SCD causes severe pain, organ damage and shortened life span due to misshapen or "sickled" red blood cells. The clinical hallmark of SCD is vaso-occlusive crises (VOCs), which are caused by blockages of blood vessels by sickled red blood cells and result in severe and debilitating pain that can happen anywhere in the body at any time. SCD requires lifelong treatment and significant use of health care resources, and ultimately results in reduced life expectancy, decreased quality of life and reduced lifetime earnings and productivity. In Europe, the mean age of death for patients living with SCD is around 40 years. Stem cell transplant from a matched donor is a curative option but is only available to a small fraction of people living with SCD because of the lack of available donors.

About Transfusion-Dependent Beta Thalassemia (TDT)

TDT is a serious, life-threatening genetic disease. TDT patients report health-related quality of life scores below the general population and significant health care resource utilization. TDT requires frequent blood transfusions and iron chelation therapy throughout a person's life. Due to anemia, patients living with TDT may experience fatigue and shortness of breath, and infants may develop failure to thrive, jaundice and feeding problems. Complications of TDT can also include an enlarged spleen, liver and/or heart, misshapen bones and delayed puberty. TDT requires lifelong treatment and significant use of health care resources, and ultimately results in reduced life expectancy, decreased quality of life and reduced lifetime earnings and productivity. In Europe, the mean age of death for patients living with TDT is 50-55 years. Stem cell transplant from a matched donor is a curative option but is only available to a small fraction of people living with TDT because of the lack of available donors.

About CASGEVY™ (exagamglogene autotemcel [exa-cel])

CASGEVY™ is a non-viral *ex vivo* CRISPR/Cas9 gene-edited cell therapy for eligible patients with SCD or TDT, in which a patient's own hematopoietic stem and progenitor cells are edited at the erythroid specific enhancer region of the *BCL11A* gene through a precise double-strand break. This edit results in the production of high levels of fetal hemoglobin (HbF; hemoglobin F) in red blood cells. HbF is the form of the oxygen-carrying hemoglobin that is naturally present during fetal development, which then switches to the adult form of hemoglobin after birth. CASGEVY has been shown to reduce or eliminate VOCs for patients with SCD and alleviate transfusion requirements for patients with TDT.

The use of CASGEVY in the European Union remains investigational.

CASGEVY is approved in the U.S. to treat people aged 12 years and older with SCD who have recurrent VOCs. CASGEVY was granted a conditional marketing authorization in Great Britain by the U.K. Medicines and Healthcare products Regulatory Agency for patients 12 years of age and older with SCD characterized by recurrent VOCs or TDT, for whom hematopoietic stem cell transplantation is appropriate and a human leukocyte antigen matched related hematopoietic stem cell donor is not available. CASGEVY is currently under review by the Saudi Food and Drug Authority for both SCD and TDT and the U.S. Food and Drug Administration for TDT.

About Conditional Marketing Authorizations (CMAs)

CMAs are for medicines that fulfil a significant unmet medical need such as being for serious and life-threatening diseases, where no satisfactory treatment methods are available or where the medicine offers a major therapeutic advantage. A CMA is granted where comprehensive clinical data is not yet complete, but the benefit of the medicine to address a significant unmet need outweighs the need for data that will become available in the future. CMAs are valid for one year and renewable annually with ongoing regulatory review of data.

U.S. INDICATIONS AND IMPORTANT SAFETY INFORMATION FOR CASGEVY (exagamglogene autotemcel)

WHAT IS CASGEVY?

CASGEVY is a one-time therapy used to treat people aged 12 years and older with sickle cell disease (SCD) who have frequent vaso-occlusive crises or VOCs.

CASGEVY is made specifically for each patient, using the patient's own edited blood stem cells, and increases the production of a special type of hemoglobin called hemoglobin F (fetal hemoglobin or HbF). Having more HbF increases overall hemoglobin levels and has been shown to improve the production and function of red blood cells. This can eliminate VOCs in people with SCD.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about CASGEVY?
After treatment with CASGEVY, you will have fewer blood cells for a while until CASGEVY takes hold (engrafts) into your bone marrow. This includes low levels of platelets (cells that usually help the blood to clot) and white blood cells (cells that usually fight infections). Your doctor will monitor this and give you treatment as required. The doctor will tell you when blood cell levels return to safe levels.

- **Tell your healthcare provider right away** if you experience any of the following, which could be signs of low levels of platelet cells:
    - severe headache
    - abnormal bruising
    - prolonged bleeding
    - bleeding without injury such as nosebleeds; bleeding from gums; blood in your urine, stool, or vomit; or coughing up blood

- **Tell your healthcare provider right away** if you experience any of the following, which could be signs of low levels of white blood cells:
    - fever
    - chills
    - infections

You may experience side effects associated with other medicines administered as part of the treatment regimen with CASGEVY. Talk to your physician regarding those possible side effects. Your healthcare provider may give you other medicines to treat your side effects.

How will I receive CASGEVY?
Your healthcare provider will give you other medicines, including a conditioning medicine, as part of your treatment with CASGEVY. It's important to talk to your healthcare provider about the risks and benefits of all medicines involved in your treatment.

After receiving the conditioning medicine, it may not be possible for you to become pregnant or father a child. You should discuss options for fertility preservation with your healthcare provider before treatment.

STEP 1: Before CASGEVY treatment, a doctor will give you a mobilization medicine. This medicine moves blood stem cells from your bone marrow into the blood stream. The blood stem cells are then collected in a machine that separates the different blood cells (this is called apheresis). This entire process may happen more than once. Each time, it can take up to one week.

During this step, rescue cells are also collected and stored at the hospital. These are your existing blood stem cells and are kept untreated just in case there is a problem in the treatment process. If CASGEVY cannot be given after the conditioning medicine, or if the modified blood stem cells do not take hold (engraft) in the body, these rescue cells will be given back to you. If you are given rescue cells, you will not have any treatment benefit from CASGEVY.

STEP 2: After they are collected, your blood stem cells will be sent to the manufacturing site where they are used to make CASGEVY. It may take up to 6 months from the time your cells are collected to manufacture and test CASGEVY before it is sent back to your healthcare provider.

STEP 3: Shortly before your stem cell transplant, your healthcare provider will give you a conditioning medicine for a few days in hospital. This will prepare you for treatment by clearing cells from the bone marrow, so they can be replaced with the modified cells in CASGEVY. After you are given this medicine, your blood cell levels will fall to very low levels. You will stay in the hospital for this step and remain in the hospital until after the infusion with CASGEVY.

STEP 4: One or more vials of CASGEVY will be given into a vein (intravenous infusion) over a short period of time.

After the CASGEVY infusion, you will stay in hospital so that your healthcare provider can closely monitor your recovery. This can take 4-6 weeks, but times can vary. Your healthcare provider will decide when you can go home.

What should I avoid after receiving CASGEVY?

- Do not donate blood, organs, tissues, or cells at any time in the future

What are the possible or reasonably likely side effects of CASGEVY?

The most common side effects of CASGEVY include:

- Low levels of platelet cells, which may reduce the ability of blood to clot and may cause bleeding
- Low levels of white blood cells, which may make you more susceptible to infection

Your healthcare provider will test your blood to check for low levels of blood cells (including platelets and white blood cells). Tell your healthcare provider right away if you get any of the following symptoms:

- fever
- chills
- infections
- severe headache
- abnormal bruising
- prolonged bleeding
- bleeding without injury such as nosebleeds; bleeding from gums; blood in your urine, stool, or vomit; or coughing up blood

These are not all the possible side effects of CASGEVY. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of CASGEVY

Talk to your healthcare provider about any health concerns.

Please see full Prescribing Information including Patient Information for CASGEVY.

About Vertex

Vertex is a global biotechnology company that invests in scientific innovation to create transformative medicines for people with serious diseases. The company has approved medicines that treat the underlying cause of multiple chronic, life-shortening genetic diseases — cystic fibrosis, sickle cell disease and transfusion-dependent beta thalassemia — and continues to advance clinical and research programs in these diseases.Vertex also has a robust clinical pipeline of investigational therapies across a range of modalities in other serious diseases where it has deep insight into causal human biology, including APOL1-mediated kidney disease, acute and neuropathic pain, type 1 diabetes and alpha-1 antitrypsin deficiency.

Vertex was founded in 1989 and has its global headquarters in Boston, with international headquarters in London. Additionally, the company has research and development sites and commercial offices in North America, Europe, Australia and Latin America. Vertex is consistently recognized as one of the industry's top places to work, including 14 consecutive years on Science magazine's Top Employers list and one of Fortune’s 100 Best Companies to Work For. For company updates and to learn more about Vertex's history of innovation, visit www.vrtx.com or follow us on LinkedIn, Facebook, Instagram, YouTube and Twitter/X.

(VRTX-GEN)

Vertex Special Note Regarding Forward-Looking Statements

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements made by Nia Tatsis, Ph.D., and Franco Locatelli, M.D., Ph.D., in this press release and statements regarding our expectations for regulatory approval for CASGEVY ™, including anticipated timing of approval, the anticipated population eligible for treatment, our expectation that, if approved, CASGEVY will be the only genetic therapy available for eligible patients in the European Union, and our beliefs regarding the benefits of our genetic therapy. While Vertex believes the forward-looking statements contained in this press release are accurate, these forward-looking statements represent the company's beliefs only as of the date of this press release 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 regulatory authorities may not approve CASGEVY on a timely basis or at all, and other risks listed under the heading “Risk Factors” in Vertex's annual report and in subsequent filings filed with the Securities and Exchange Commission and available through the company's website at www.vrtx.com and www.sec.gov. You should not place undue reliance on these statements. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

View source version on businesswire.com: https://www.businesswire.com/news/home/20231214351567/en/

Vertex Pharmaceuticals Incorporated

Investors:

InvestorInfo@vrtx.com
or
Manisha Pai, +1 617-961-1899

Media:

mediainfo@vrtx.com

or
International: +44 20 3204 5275
or
U.S.: 617-341-6992
or
Heather Nichols: +1 617-839-3607

Source: Vertex Pharmaceuticals Incorporated