




VERTEX

THE SCIENCE *of* POSSIBILITY

# FOURTH QUARTER AND FULL YEAR 2023 FINANCIAL RESULTS

FEBRUARY 5, 2024

# 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, including, without limitation, the information provided regarding and expectations for future financial and operating performance and statements regarding (i) expectations, development plans and timelines for the company's medicines and pipeline programs, including expectations for anticipated near-term commercial launch opportunities in CF and acute pain, expectations for five potential launches in five years, anticipated near-term commercial opportunities in TDT, CF and acute pain, anticipated benefits of new products and relevant patient populations, and plans to broaden and deepen R&D pipeline across modalities, (ii) plans to launch CF medicines in younger age groups globally and to bring additional molecules to market to get CF patients to carrier levels of SwCl, (iii) plans to advance VX-522 to reach the >5,000 CF patients who cannot benefit from a CFTR modulator, and plans to have VX-522 data in late 2024/early 2025, (iv) expectations for CASGEVY, including the potential benefits for patients with SCD and TDT, expectations for CASGEVY commercial launch, expectations for broad access in the US, expectations for initial access in certain ex-US geographies through Early Access Programs and efforts for long-term reimbursement agreements, plans to obtain approvals in additional geographies, and plans to complete dosing in younger age groups, (v) expectations for our pain program, including plans for near-term launch and commercial potential in acute pain, expectations for treatment of acute pain without side effects or addictive properties of opioids, plans to submit regulatory filings for VX-548 in acute pain by mid-2024, plans to advance VX-993 into Phase 2 for acute pain in an oral formulation and to complete IND-enabling studies and file an IND for an intravenous formulation of VX-993 in 2024, plans to engage in meetings with regulators with goal of broad PNP label, plans to advance VX-548 in DPN into pivotal development, plans to enroll and dose VX-548 Phase 2 study in LSR, plans to advance an oral formulation of VX-993 into a Phase 2 study in PNP, and plans to advance NaV 1.7 and NaV1.8 inhibitors, (vi) expectations for our T1D program, including plans to review VX-880 data and resume trial, and expectations for VX-264 studies, (vii) expectations for vanzacaftor triple combination therapy, including the anticipated benefits for patients with CF and plans to file regulatory submissions in multiple geographies in mid-2024, (viii) expectations for inaxaplin, including dose selection and advance into Phase 3 in Q1 2024, (ix) expectations for our ability to reinvest in our pipeline, (ix) expectations for our DM1 program, and (x) plans to file an IND and CTA for VX-407 and initiate first in human trial. While Vertex believes the forward-looking statements contained in this presentation are accurate, these forward-looking statements represent the company's beliefs as of the date of this presentation and there are 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 data from clinical trials, especially if based on a limited number of patients, may not to be indicative of final results, the company's regulatory submissions may be delayed, actual patient populations eligible for our products may be smaller than anticipated, data from the company's development programs may not be available on expected timelines, or at all, support registration or further development of its potential medicines due to safety, efficacy or other reasons, and other risks listed under the heading "Risk Factors" in Vertex's annual report and subsequent quarterly reports filed with the Securities and Exchange Commission at www.sec.gov and available through the company's website at www.vrtx.com. You should not place any undue reliance on these statements, or the 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) intangible asset amortization expense, (iii) gains or losses related to the fair value of the company's strategic investments, (iv) increases or decreases in the fair value of contingent consideration, (v) acquisition-related costs, (vi) an intangible asset impairment charge and (vii) 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 Q4 2023 press release dated February 5, 2024.

# VERTEX DELIVERED EXCELLENT Q4:23 RESULTS AND ESTABLISHED A STRONG FOUNDATION FOR 2024 AND BEYOND

## Expand our leadership and raise the bar in CF

- Increased epidemiology estimates for people living with cystic fibrosis from ~88,000 to ~92,000
  - North America, Europe, Australia
- Shared positive pivotal data for vanzacaftor triple from two head-to-head studies (SKYLINE 102 and 103) in patients with CF ages 12+ and single-arm study (RIDGELINE) in patients ages 6-11
- VX-522: Completed SAD, initiated MAD to reach the >5,000 patients who cannot benefit from CFTRm

## Drive era of diversification with multiple commercial launch opportunities

- CASGEVY: Launching in SCD and TDT in multiple regions; obtain approvals in additional geographies
- VX-548: Shared positive pivotal data in moderate to severe acute pain; on track to file U.S. mid-2024
- Vanzacaftor triple: On track to file regulatory submissions in the U.S., Europe, Canada mid-2024
- Progressing late-stage clinical development programs to achieve five launches in five years (2028) goal

## Broaden and deepen R&D pipeline across modalities

- Advanced multiple programs across multiple modalities
- Driving next wave of innovation into the clinic, starting with DM1 and ADPKD

## Deliver financial performance

- Q4:23 product revenue +9% versus Q4:22; FY 2023 product revenue +11% versus FY 2022
- Continue CF product revenue growth, with incremental sales from launches in new disease areas
- Sustain strong operating margins while continuing to invest in pipeline; commitment to specialty model



SAD: Single Ascending Dose; MAD: Multiple Ascending Dose portion of Phase 1/2 study; CFTRm = cystic fibrosis transmembrane conductance regulator modulators; SCD: sickle cell disease; TDT: transfusion dependent beta thalassemia

# VANZACAFTOR TRIPLE PIVOTAL PROGRAM RESULTS

# SKYLINE 102, 103 (12+ YEARS): FOLLOWING 4-WEEK RUN-IN WITH TRIKAFTA TO ESTABLISH BASELINE (BL), PATIENTS RANDOMIZED TO TRIKAFTA OR VANZA TRIPLE

## → MET PRIMARY ENDPOINT: NON-INFERIORITY ON PPFEV$_1$ Δ FROM BL

| | SKYLINE 102 | | SKYLINE 103 | |
|---|---|---|---|---|
| | TRIKAFTA N=202 | Vanza Triple N=196 | TRIKAFTA N=289 | Vanza Triple N=284 |
| Baseline ppFEV$_1$; mean (SD) | 67.2 (14.6) | 67.0 (15.3) | 66.4 (14.9) | 67.2 (14.6) |
| Absolute change through Week 24* | | | | |
| LS mean change (SE) | 0.3 (0.3) | 0.5 (0.3) | 0.0 (0.2) | 0.2 (0.3) |
| LS mean difference, 95% CI | - | **0.2** (-0.7, 1.1) | - | **0.2** (-0.5, 0.9) |
| 1-sided *P* for non-inferiority | - | <0.0001 | - | <0.0001 |

*Average of Weeks 16 and 24

**SKYLINE 102:** 398 patients ages 12+ with F/MF mutations; **SKYLINE 103:** 573 patients ages 12+ with F/F, F/G, F/RF, TCR/non-F anchored mutations.

**Trial design**: 4-week screening period → 4-week "run-in" with TRIKAFTA to establish baseline → 52-week treatment period, randomized to TRIKAFTA or Vanza triple → 4-week safety follow up

**Primary endpoint**: Change from baseline in ppFEV$_1$ through Week 24 (average of Weeks 16 and 24); primary analysis – non-inferiority of ppFEV$_1$ (superiority assessed only if lower bound of 95% CI is >0)

**Key secondary endpoints**: 1) change from baseline in SwCl through Week 24; 2) proportion of patients with SwCl <60 mmol/L through Week 24 (pooled across 2 studies); 3) proportion of patients with SwCl <30 mmol/L through Week 24 (pooled across 2 trials). BL: baseline; CI: confidence interval; LS: least squares; ppFEV$_1$: percent predicted forced expiratory volume in 1 second; SD: standard deviation; SE: standard error

# 1ST KEY SECONDARY ENDPOINT: ABSOLUTE CHANGE IN SWEAT CHLORIDE (SwCl) →TREATMENT WITH VANZA TRIPLE WAS SUPERIOR TO TRIKAFTA

| | SKYLINE 102 | | SKYLINE 103 | |
|---|---|---|---|---|
| | TRIKAFTA N=202 | Vanza Triple N=196 | TRIKAFTA N=289 | Vanza Triple N=284 |
| Baseline SwCl; mean (SD) | 54.3 (18.2) | 53.6 (17.0) | 42.1 (17.9) | 43.4 (18.5) |
| **Absolute change through Week 24*** | | | | |
| LS mean change (SE) | 0.9 (0.8) | -7.5 (0.8) | -2.3 (0.7) | -5.1 (0.7) |
| LS mean difference, 95% CI | - | **-8.4** (-10.5, -6.3) | - | **-2.8** (-4.7, -0.9) |
| 2-sided *P* for superiority | - | <0.0001 | - | 0.0034 |

*Average of Weeks 16 and 24

SwCl: sweat chloride, the direct measure of CFTR protein function; SD: standard deviation; LS: least squares; SE: standard error; CI: confidence interval

# 2ND KEY SECONDARY ENDPOINT: PROPORTION PATIENTS SwCl <60 mmol/L →TREATMENT WITH VANZA TRIPLE WAS SUPERIOR TO TRIKAFTA

| | Pooled Endpoint SKYLINE 102 and SKYLINE 103 | |
|---|---|---|
| | TRIKAFTA N=491 | Vanza Triple N=480 |
| Baseline SwCl <60 mmol/L, proportion, % patients | 74% | 76% |
| **SwCl <60 mmol/L through Week 24*** | | |
| Proportion, % patients | 77% | **86%** |
| Odds ratio†, (95% CI) | - | **2.21** (1.55, 3.15) |
| 2-sided *P* for superiority | - | <0.0001 |

*Average of Weeks 16 and 24
†Estimated by GEE model; odds ratio >1 favors vanza triple

SwCl: sweat chloride, the direct measure of CFTR protein function; 60 mmol/L is the diagnostic threshold for CF; CI: confidence interval

# 3RD KEY SECONDARY ENDPOINT: PROPORTION PATIENTS SwCl <30 mmol/L →TREATMENT WITH VANZA TRIPLE WAS SUPERIOR TO TRIKAFTA

| | Pooled Endpoint SKYLINE 102 and SKYLINE 103 | |
|---|---|---|
| | TRIKAFTA N=491 | Vanza Triple N=480 |
| Baseline SwCl <30 mmol/L, proportion, % patients | 21% | 19% |
| **SwCl <30 mmol/L through Week 24*** | | |
| Proportion, % patients | 23% | **31%** |
| Odds Ratio†, 95% CI | - | **2.87** (2.00, 4.12) |
| 2-sided *P* for superiority | - | <0.0001 |

*Average of Weeks 16 and 24
†Estimated by GEE model; odds ratio >1 favors vanza triple

SwCl: sweat chloride, the direct measure of CFTR protein function; <30 mmol/L is the carrier level threshold for CF; CI: confidence interval

# RIDGELINE (6-11 YEARS) STUDY: FOLLOWING 4-WEEK RUN-IN WITH TRIKAFTA TO ESTABLISH BASELINE, PATIENTS TREATED WITH VANZA TRIPLE; 95% OF CHILDREN ACHIEVED SwCl <60 mmol/L AND 53% ACHIEVED CARRIER LEVELS OF SwCl WITH VANZA TRIPLE

| SwCl <60 mmol/L | RIDGELINE |
|---|---|
| | Vanza Triple N=78 |
| Baseline SwCl, proportion, % children | 84% |
| **SwCl <60 mmol/L through Week 24*** | |
| Proportion, % children | **95%** |
| 95% CI | (0.87, 0.99) |

*Average of weeks 16 and 24

| SwCl <30 mmol/L | RIDGELINE |
|---|---|
| | Vanza Triple N=78 |
| Baseline SwCl, proportion, % children | 39% |
| **SwCl <30 mmol/L through Week 24*** | |
| Proportion, % children | **53%** |
| 95% CI | (0.41, 0.64) |

*Average of weeks 16 and 24

**RIDGELINE** : 78 children ages 6-11 years with at least one TCR mutation (including F508del)

**Study design: Single arm** 4-week screening period → 4-week "run-in" with TRIKAFTA → 24-week vanza triple treatment period→ 4-week safety follow up

**Primary endpoint:** Safety and tolerability

**Secondary efficacy endpoints included:** Change from baseline in SwCl through Week 24 and change from baseline in $ppFEV_1$ through Week 24, proportion of children with SwCl<60 mmol/L and <30 mmol/L through Week 24

SwCl: sweat chloride, the direct measure of CFTR protein function; 60 mmol/L is the diagnostic threshold for CF, <30 mmol/L is the carrier level threshold for CF. CI: confidence interval

# COMMON TEAES (≥10% IN ANY TREATMENT GROUP) (POOLED) WERE CONSISTENT WITH UNDERLYING CF AND ACROSS TREATMENT GROUPS

| | SKYLINE 102 AND 103 | | *445-102/105 52 wks* |
|---|---|---|---|
| | TRIKAFTA N=491 n (%) | Vanza Triple N=480 n (%) | *TRIKAFTA N=403* |
| Subjects with any TEAEs | 469 (95.5) | 459 (95.6) | *399 (99.0)* |
| Infective PEx | 158 (32.2) | 133 (27.7) | *151 (37.5)* |
| Cough | 101 (20.6) | 108 (22.5) | *129 (32.0)* |
| COVID-19 | 127 (25.9) | 107 (22.3) | *0* |
| Nasopharyngitis | 95 (19.3) | 102 (21.3) | *77 (19.1)* |
| Headache | 63 (12.8) | 76 (15.8) | *87 (21.6)* |
| Upper Respiratory Tract Infection | 67 (13.6) | 72 (15.0) | *71 (17.6)* |
| Oropharyngeal Pain | 60 (12.2) | 69 (14.4) | *76 (18.9)* |
| Diarrhoea | 59 (12.0) | 58 (12.1) | *55 (13.6)* |
| Influenza | 26 (5.3) | 52 (10.8) | *35 (8.7)* |
| Pyrexia | 50 (10.2) | 52 (10.8) | *55 (13.6)* |
| Fatigue | 46 (9.4) | 51 (10.6) | *42 (10.4)* |
| Nasal Congestion | 47 (9.6) | 48 (10.0) | *59 (14.6)* |
| Sputum Increased | 50 (10.2) | 45 (9.4) | *87 (21.6)* |





CF: cystic fibrosis; PEx: pulmonary exacerbation of cystic fibrosis; TEAE: Treatment-emergent adverse event

# EXPANDING LEADERSHIP IN CF AND RAISING THE BAR WITH SERIAL INNOVATION

**Vanzacaftor triple combination**

- Delivered positive results in all three Phase 3 studies:
  - SKYLINE 102 and 103 studies in ages 12+
  - RIDGELINE study in ages 6+
- On track to file in U.S., Europe, Canada by mid-2024 for ages 6+

**VX-522: mRNA approach for >5,000 patients who cannot benefit from CFTR modulators**

- Completed enrollment in single ascending dose (SAD) portion of the study, initiated the multiple ascending dose (MAD) portion
- MAD portion of the study is now enrolling and dosing patients

# CASGEVY (EXA-CEL): BEGINNING OF NEW ERA OF DIVERSIFICATION

casgevy™
(exagamglogene autotemcel)

***The first precise, durable, CRISPR/Cas9 gene-edited therapy, delivering a potential one-time functional cure for patients with SCD and TDT***

## *Rapid pace of global approvals:*

- Approved for eligible patients ages 12+ with sickle cell disease or transfusion-dependent beta thalassemia by
  - ✓ **MHRA**
  - ✓ **FDA**
  - ✓ **BFDA**
  - ✓ **SFDA**
- Received CHMP positive opinion for sickle cell disease and transfusion-dependent beta thalassemia in EU



MHRA: Medicines and Healthcare Products Regulatory Agency (Great Britain); BFDA: Bahrain FDA, SFDA: Saudi Arabia FDA

CRISPR/Cas9 precisely targets the erythroid-specific enhancer region of the BC11A gene.

# VX-548 ACUTE PAIN
# PIVOTAL PROGRAM RESULTS

# VX-548 FOR ACUTE PAIN: TREATMENT WITH VX-548 SHOWED STAT SIG PAIN RELIEF COMPARED TO PLACEBO IN BOTH RANDOMIZED CONTROLLED TRIALS

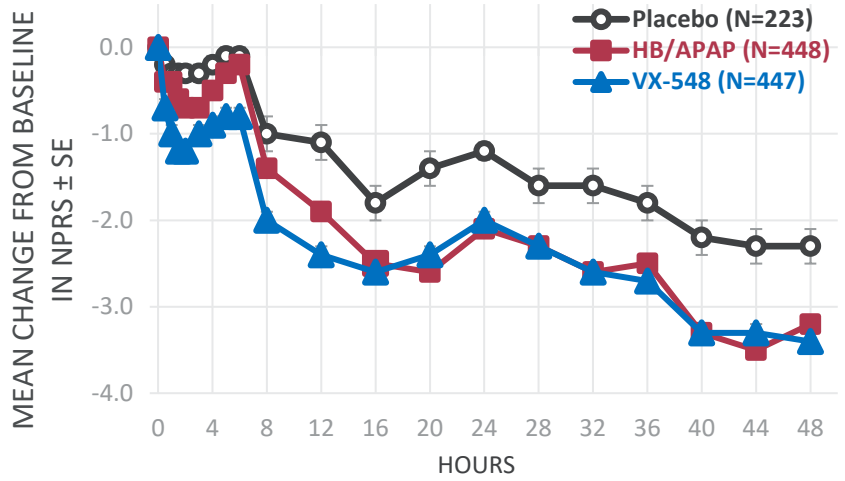
## Primary endpoint: SPID48 VX-548 vs. placebo

| | 548-105 ABDOMINOPLASTY | | 548-104 BUNIONECTOMY | |
|---|---|---|---|---|
| | PLACEBO<br>N=223 | VX-548<br>100 mg, 50 mg q12h<br>N=447 | PLACEBO<br>N=216 | VX-548<br>100 mg, 50 mg q12h<br>N=426 |
| SPID48 LS mean (SE) | 70.1<br>(6.1) | 118.4<br>(4.3) | 70.6<br>(6.3) | 99.9<br>(4.5) |
| SPID48 LS mean difference from placebo | | **48.4** | | **29.3** |
| 95% CI | | (33.6, 63.1) | | (14.0, 44.6) |
| *P* value vs. placebo | | <0.0001 | | 0.0002 |

SPID48 = time-weighted sum of the pain intensity difference (SPID) from 0 to 48 hours; LS = least squares; SE = standard error; CI = confidence interval; q12h = every 12 hours

# REDUCTION IN ACUTE PAIN WITH VX-548 WAS RAPID, SUSTAINED AND CLINICALLY MEANINGFUL IN BOTH TRIALS

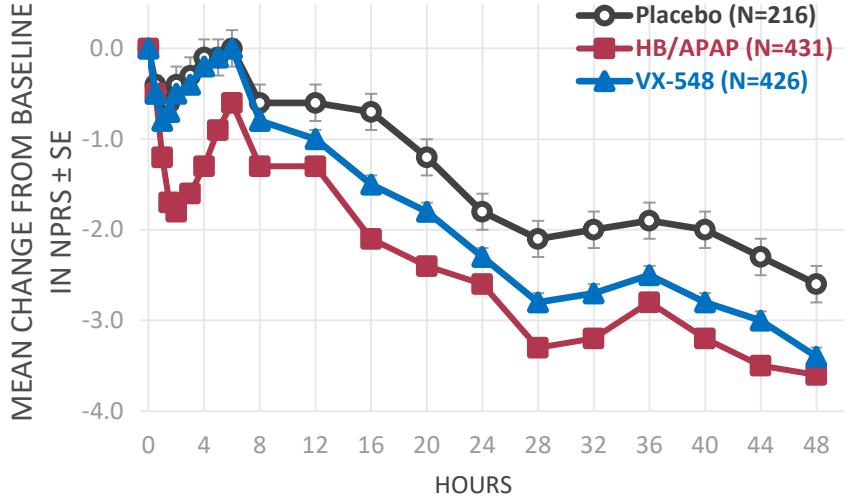
## 548-105 ABDOMINOPLASTY




## 548-105 ABDOMINOPLASTY

| | PLACEBO N=223 | HB/APAP 5 mg / 325 mg q6h N=448 | VX-548 100 mg, 50 mg q12h N=447 |
|---|---|---|---|
| Baseline NPRS, mean | 7.5 | 7.4 | 7.3 |
| Change from baseline in NPRS, mean | -2.3 | -3.2 | **-3.4** |
| % reduction from baseline in mean NPRS | 31% | 43% | **47%** |

## 548-104 BUNIONECTOMY




## 548-104 BUNIONECTOMY

| | PLACEBO N=216 | HB/APAP 5 mg / 325 mg q6h N=431 | VX-548 100 mg, 50 mg q12h N=426 |
|---|---|---|---|
| Baseline NPRS, mean | 6.8 | 6.8 | 6.7 |
| Change from baseline in NPRS, mean | -2.6 | -3.6 | **-3.4** |
| % reduction from baseline in mean NPRS | 38% | 53% | **51%** |



NPRS = numeric pain rating scale; SE = standard error; HB/APAP = hydrocodone bitartrate/ acetaminophen; q6h = every 6 hours; q12h = every 12 hours

# VX-548 WAS SAFE AND WELL TOLERATED IN THESE TRIALS WITH >2,400 PATIENTS WITH MODERATE TO SEVERE ACUTE PAIN

Results support broad moderate to severe acute pain label

**VX-548**

- Across all three studies, the majority of AEs with VX-548 were mild or moderate in severity
- Across all three studies, there were no SAEs related to VX-548
- In general, AEs in the two RCTs were consistent with the post-surgical setting
- In the two RCTs, the incidence of AEs in VX-548 arms was lower than placebo

RCT = randomized controlled trial

# NEXT STEPS FOR OUR PAIN PROGRAM

**Acute Pain**

- Results from pivotal program support a broad moderate-to-severe acute pain label
- On track to file NDA in the U.S. by mid-2024
- Advance VX-993 into Phase 2 study in acute pain – oral formulation
- Initiate VX-993 Phase 1 study in acute pain – intravenous formulation

**Peripheral Neuropathic Pain**

- Engage in VX-548 End-of-Phase 2 meeting with regulators; goal is broad PNP label
- Advance VX-548 into pivotal development in diabetic peripheral neuropathy
- Continue to enroll and dose VX-548 Phase 2 study in lumbosacral radiculopathy
- Advance VX-993 into Phase 2 study in peripheral neuropathic pain - oral formulation

**Research**

- Advance $Na_V1.7$ inhibitors, alone or in combination
- Advance follow-on $Na_V1.8$ inhibitors

# CLINICAL PORTFOLIO IS BROAD, DIVERSE AND RAPIDLY ADVANCING

## STRONG PROGRESS TOWARDS OUR GOAL OF FIVE LAUNCHES OVER FIVE YEARS (2028)

| Select, Next Wave<br>Research-stage Programs | Phase 1<br>in Healthy Volunteers | Phase (1)/2<br>in Patients | Pivotal Development | Regulatory Submissions Completed or Underway | Approved |
|---|---|---|---|---|---|
| **Hypoimmune cells**<br>Type 1 diabetes | **Follow-on molecules:**<br>• CF<br>• Pain<br>• AMKD<br>• AATD | **VX-880**<br>Type 1 diabetes | **Inaxaplin**<br>AMKD | **Exa-cel additional geographies**[4]<br>SCD & TDT | trikafta® |
| **Small molecule**<br>Huntington's | | **VX-264 cells + device**<br>Type 1 diabetes | **VX-548**[3]<br>Peripheral Neuropathic Pain - DPN | **VX-548**[5]<br>Acute Pain | symdeko® |
| **Improved conditioning**<br>CASGEVY – SCD & TDT | | **VX-548**<br>Peripheral Neuropathic Pain - LSR | | **Vanzacaftor triple**[5]<br>Cystic Fibrosis | ORKAMBI® |
| **NaV1.7 inhibitor**<br>Pain | | **VX-522**<br>CFTR mRNA | | | kalydeco® |
| **VX-407**[1]<br>ADPKD | | **VX-670**[2]<br>DM1 | | | casgevy™ (exagamglogene autotemcel) |

ADPKD: autosomal dominant polycystic kidney disease; DM1: myotonic dystrophy type 1; DPN: diabetic peripheral neuropathy; LSR: painful lumbosacral radiculopathy.
[1]Anticipate first-in-human clinical trial to initiate H1:24. [2]CTAs cleared in Canada and UK. Trial initiated and enrolling in Canada. On clinical hold in the U.S.
[3]Anticipated to begin in 2024. [4]Under regulatory review for SCD and TDT in EU, Switzerland. [5]Regulatory submissions planned for mid-2024.

# EXPANDING LEADERSHIP IN CF AND RAISING THE BAR WITH SERIAL INNOVATION

**~92,000**
patients with CF*

**~20,000**
eligible patients not on CFTR modulators

## DURABLE GROWTH DRIVERS

- ✓ Treating younger patients
- ✓ Patients living longer
- ✓ Serial CFTRm innovation
- ✓ mRNA for last >5,000 patients

**Cystic Fibrosis Approvals**

kalydeco® symdeko® ORKAMBI® trikafta®

**Vanzacaftor triple**

- Anticipate filing in U.S., Europe, Canada by mid-2024 for ages 6+
  - New option for ~6,000 patients who discontinued CFTRm therapy
  - Opportunity for TRIKAFTA patients who seek even lower levels of sweat chloride

**VX-522 mRNA**

- For the last >5,000 patients who cannot benefit from CFTR modulators

**Best-in-class medicines**

**Goal:** carrier levels of CFTR function

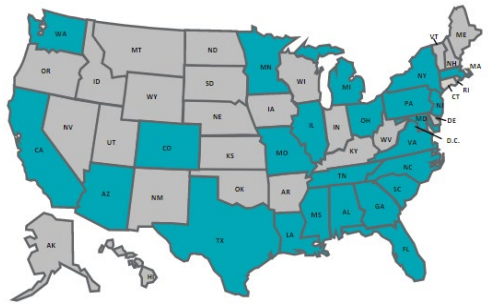
*Patient populations include North America, Europe, and Australia.

# CASGEVY REPRESENTS A POTENTIAL MULTI-$B OPPORTUNITY FOR VERTEX

## 2024 A FOUNDATIONAL YEAR; STRONG PROGRESS ACROSS ALL REGIONS WITH PAYERS, PATIENTS, PHYSICIANS

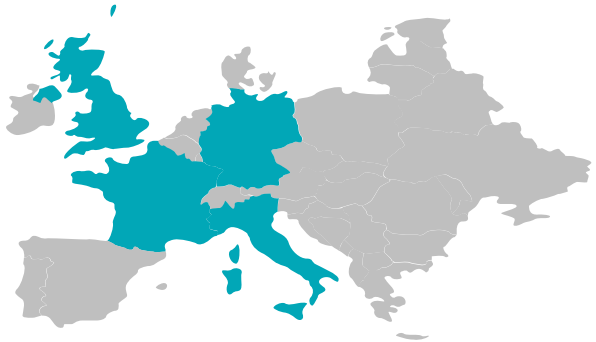
**35,000 eligible patients with severe disease in the U.S. and Europe**

### ~24 States in U.S. with ~90% of SCD/TDT Patients



- 12 ATCs activated in the U.S.
- Case-by-case reimbursement initially
- ~80% of Commercial/~60% of Medicaid SCD lives with pathway to reimbursement
  - States with additional ~25% of Medicaid lives actively progressing reimbursement methodology
- CMMI Cell & Gene Therapy (CGT) Access Model provides for CMS to negotiate CGT OBAs for states' SCD patients*

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



- 3 ATCs activated in EU
- Secured Early Access Program in France for TDT; pursuing submission for SCD
- In the U.K., engaged in Highly Specialized Technology (HST) process with NICE
- Ongoing discussions in other countries

**Additional opportunities**

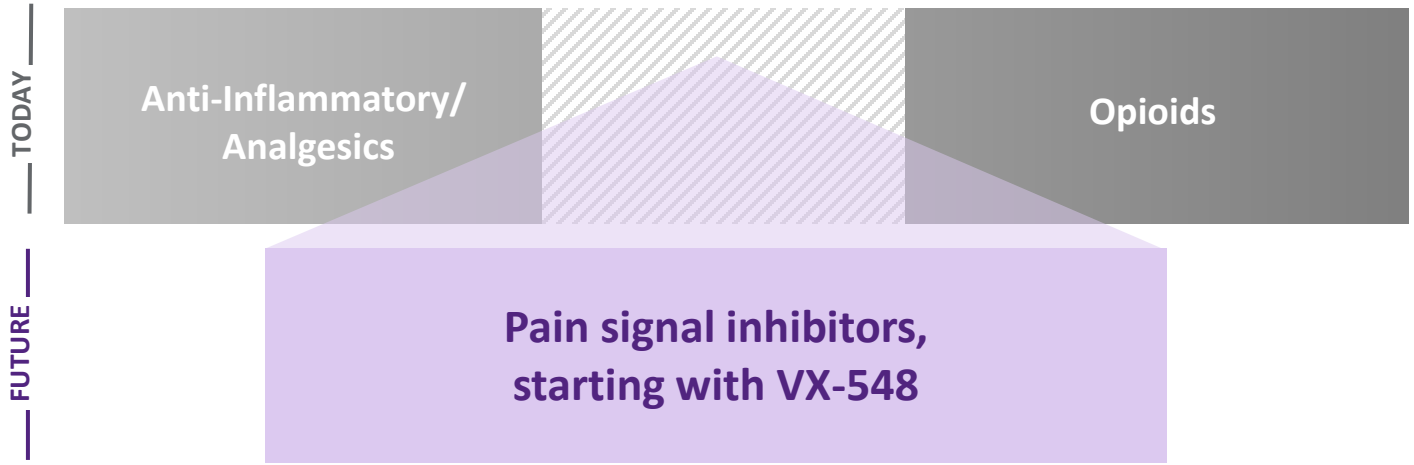
### Bahrain and the Kingdom of Saudi Arabia

- 1 ATC activated in KSA
- Continue to work with local healthcare authorities to serve large number of patients in the region
- Established local presence



 ATC = Authorized Treatment Center; OBAs = Outcomes-Based Arrangements *Begins 2025; optional for both states and manufacturers

# VX-548 IN ACUTE PAIN FILLS THE "GAP"/UNMET NEED FOR ~80 MILLION PATIENTS; LAUNCH PREP UNDERWAY




- **Acute pain is a multi-$B market today** (despite ~100% generic)
  - 80M U.S. patients receive Rx for mod-severe acute pain annually
    - Over 1 billion calendar days of treatment
- **Yet limitations of existing treatment options leave significant unmet need**
  - Medicines with good safety/tolerability but limited efficacy
  - Opioids: therapeutic efficacy but undesirable SEs and addiction potential
- **Significant opportunity for VX-548, a non-opioid pain signal inhibitor**
  - Phase 3 results demonstrate compelling combination of efficacy and safety to fill existing gap in the treatment of moderate to severe acute pain

## Actively planning for a potential near-term launch

- **Specialty market due to concentration of prescribing**
  - Focus on ~2,000 hospitals/institutions writing majority of acute pain Rx's
- **Stakeholders recognize high unmet need**
  - Society, hospital guidelines limit opioid use
- **Federal and state legislative tailwinds**
  - Recently introduced:
    - Bipartisan "Alternatives to Prevent Addiction in the Nation Act"
  - Effective 2025:
    - "NO PAIN Act" add-on payment
  - Multiple states with pending legislation to
    - Require education on non-opioids
    - Remove financial barriers to use non-opioids

# Q4 AND FULL YEAR 2023 FINANCIAL HIGHLIGHTS

| *($ in millions except where noted or per share data and percentages)* | Q4 22 | FY 22 | Q1 23 | Q2 23 | Q3 23 | Q4 23 | FY 23 |
|---|---|---|---|---|---|---|---|
| Total CF product revenues | $2.30B | **$8.93B** | $2.37B | $2.49B | $2.48B | $2.52B | **$9.87B** |
| TRIKAFTA/KAFTRIO | 2.02B | **7.69B** | 2.10B | 2.24B | 2.27B | 2.33B | **8.94B** |
| Other CF product revenues | 281 | **1.24B** | 278 | 253 | 209 | 184 | **925** |
| Combined non-GAAP R&D, acquired IPR&D and SG&A expenses | 872 | **3.07B** | 1.21B | 1.04B | 993 | 1.00B | **4.24B** |
| Non-GAAP operating income | 1.15B | **4.79B** | 902 | 1.15B | 1.17B | 1.15B | **4.37B** |
| Non-GAAP operating margin % | 50% | **54%** | 38% | 46% | 47% | 46% | **44%** |
| Non-GAAP net income | 978 | **3.86B** | 794 | 1.01B | 1.06B | 1.10B | **3.97B** |
| Non-GAAP net income per share - diluted | $3.76 | **$14.88** | $3.05 | $3.89 | $4.08 | $4.20 | **$15.23** |
| Cash, cash equivalents & total marketable securities (period-end) | $10.9B | **$10.9B** | $11.5B | $12.6B | $13.6B | $13.7B | **$13.7B** |

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 Q4 2023 press release dated February 5, 2024. 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.

# 2024 FINANCIAL GUIDANCE

| | FY 2023 Actuals | FY 2024 Guidance | FY 2024 Commentary |
|---|---|---|---|
| Total Product Revenue | $9.87B | $10.55 - $10.75B | Includes expectations for continued growth in CF as well as the launch of CASGEVY in approved indications and geographies |
| Combined GAAP R&D, Acquired IPR&D and SG&A Expenses | $4.83B | $4.9 - $5.1B | Includes expectations for continued investment in our multiple mid and late-stage clinical development programs, commercial and manufacturing capabilities, and approximately $125 million of upfront and milestone payments. |
| Combined Non-GAAP R&D, Acquired IPR&D and SG&A Expenses | $4.24B | $4.3 - $4.4B | |
| Non-GAAP Effective Tax Rate | 19.4% | 20%-21% | |

# MULTIPLE CATALYSTS THROUGHOUT 2024 AND BEYOND

| RECENT HIGHLIGHTS | ANTICIPATED KEY MILESTONES |
|---|---|
| • **Received approvals for TRIKAFTA in EU, U.K. and Canada** in patients with CF ages 2 to 5<br>• **Reported positive Phase 3 results with the vanzacaftor triple combo therapy** in patients ages 6+<br>• **VX-522 CFTR mRNA study: completed dosing SAD, initiated MAD portion and dosing patients** | • **Advance launch of TRIKAFTA/KAFTRIO OUS** in ages 2-5 years<br>• **Prepare for vanza triple filings and potential launch** in U.S., EU, Canada<br>• **Complete MAD portion** of the VX-522 study; data late 2024/early 2025 |
| • **Received approval for CASGEVY in U.S., U.K., Bahrain and KSA for TDT and SCD**<br>• **Received CHMP positive recommendation** for exa-cel in SCD and TDT in EU<br>• **Regulatory reviews ongoing** in Switzerland for SCD and TDT<br>• **Enrollment completed in global Phase 3 studies** in patients with SCD or TDT **ages 5 to 11** | • **Launch CASGEVY in U.S., U.K., Bahrain and KSA**<br>• **Secure additional global regulatory approvals:**<br>  • **EU and Switzerland (SCD and TDT)**<br>• **Complete dosing in younger age group** |
| • **VX-548: Reported positive Phase 3 results in acute pain**<br>• **VX-548: Reported positive Phase 2 results in diabetic peripheral neuropathy (DPN)**<br>• **VX-548: Initiated Phase 2 study in lumbosacral radiculopathy (LSR)**<br>• **VX-993: Completed Phase 1 study (oral); IND-enabling studies ongoing (IV)** | • **VX-548: Prepare for filing and potential launch in the U.S. in acute pain**<br>• **VX-548: DPN End-of-Phase 2 meeting Q1:24**; initiate pivotal trial<br>• **VX-548: LSR trial – continue enrollment and dosing**<br>• **VX-993: initiate acute pain Phase 2 study (oral); submit IND (IV)**<br>• **VX-993: initiate neuropathic pain Phase 2 study (oral)** |
| • **Completed enrollment in Phase 2B portion of Phase 2/3 pivotal trial of inaxaplin in AMKD** | • Select dose and **advance to Phase 3 portion** of study in Q1:24 |
| • **VX-880: Phase 1/2 trial fully enrolled** (Parts A, B, C) for T1D<br>• **VX-264** (the "cells + device" program)**: Completed Part A of Phase 1/2 trial and initiated Part B** | • **VX-880**: Review Phase 1/2 data, **resume trial**<br>• **VX-264: Enroll and dose patients in Part B** |
| • **CTAs cleared in Canada and U.K. for VX-670 in DM1; study initiated in Canada** | • **Enroll and dose VX-670 Phase 1/2 study** in DM1 patients |
| • **Completed IND-enabling studies for VX-407 in ADPKD** | • **File IND and CTA; initiate first-in-human trial** |



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# FOURTH QUARTER AND FULL YEAR 2023 FINANCIAL RESULTS

FEBRUARY 5, 2024

# APPENDIX

## *GAAP TO NON-GAAP FINANCIAL INFORMATION*

| *($ in millions except as noted, per share data and percentages)* | Q4 22 | FY 22 | Q1 23 | Q2 23 | Q3 23 | Q4 23 | FY 23 |
|---|---|---|---|---|---|---|---|
| **Combined R&D, Acquired IPR&D, and SG&A** | | | | | | | |
| GAAP | 984 | **3.60B** | 1.33B | 1.16B | 1.13B | 1.21B | **4.83B** |
| Non-GAAP | 872 | **3.07B** | 1.21B | 1.04B | 993 | 1.00B | **4.24B** |
| **Operating income** | | | | | | | |
| GAAP | 1.03B | **4.31B** | 779 | 1.03B | 1.04B | 989 | **3.83B** |
| Non-GAAP | 1.15B | **4.79B** | 902 | 1.15B | 1.17B | 1.15B | **4.37B** |
| **Operating Margin %:** | | | | | | | |
| GAAP | 45% | **48%** | 33% | 41% | 42% | 39% | **39%** |
| Non-GAAP | 50% | **54%** | 38% | 46% | 47% | 46% | **44%** |
| **Net income** | | | | | | | |
| GAAP | 819 | **3.32B** | 700 | 916 | 1.04B | 969 | **3.62B** |
| Non-GAAP | 978 | **3.86B** | 794 | 1.01B | 1.06B | 1.10B | **3.97B** |
| **Net income per share - diluted** | | | | | | | |
| GAAP | $3.15 | **$12.82** | $2.69 | $3.52 | $3.97 | $3.71 | **$13.89** |
| Non-GAAP | $3.76 | **$14.88** | $3.05 | $3.89 | $4.08 | $4.20 | **$15.23** |

Note: An explanation of non-GAAP financial measures and reconciliations 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 Q4 2023 press release dated February 5, 2024.