# Second Quarter 2025 Financial Results

August 4, 2025

*Presentation intended for the investment community*

# 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***

*Duncan McKechnie, Executive Vice President and Chief Commercial Officer*

***Financial Results***

*Charlie Wagner, Executive Vice President and Chief Operating & Financial Officer*

# Safe harbor statement & non-GAAP financial measures

This presentation contains forward-looking statements that are subject to risks, uncertainties and other factors. All statements other than statements of historical fact are statements that could be deemed forward-looking statements, including all statements regarding the intent, belief, or current expectation of Vertex and members of the Vertex senior management team. Forward-looking statements are not purely historical and may be accompanied by words such as “anticipates,” “may,” “forecasts,” “expects,” “intends,” “plans,” “potentially,” “believes,” “seeks,” “estimates,” and other words and terms of similar meaning. Such statements include, without limitation, the information provided regarding and expectations for future financial and operating performance, the section captioned “Reiterate full year 2025 financial guidance,” expectations for financial performance in 2025, and statements regarding (i) expectations, development plans and timelines for Vertex’s products and pipeline programs, including beliefs regarding the status of product launches, achievement of key enrollment milestones in 2025, advancement of multiple programs across multiple modalities, significantly expanding the number of patients Vertex serves, relevant estimated patient populations, expectations with respect rapid advancement in Vertex’s clinical portfolio and for "five launches over five years (by 2028)," and expectations for increased revenue contributions from CASGEVY, ALYFTREK, and JOURNAVX in 2025, (ii) expectations regarding ALYFTREK, including those related to ALYFTREK’s clinical benefits and potential to set a new standard of care in CF, for additional potential approvals of ALYFTREK and additional reimbursement agreements, expectations regarding U.S. patients switching to ALYFTREK, and expectations for a lower royalty burden, (iii) expectations for Vertex’s CF pipeline programs, including those related to the potential benefits of VX-828 as a next generation CFTR corrector and the initiation of the VX-828 study in CF patients in 2025, and expectations related to the VX-522 clinical trial, (iv) expectations for Vertex’s T1D programs, including beliefs regarding a potentially curative treatment and treatable patient population, expectations to complete dosing in the ongoing zimislecel pivotal trial, potential global regulatory submissions in 2026, and initial commercial launch expectations, (v) expectations regarding the therapeutic scope, potential benefits, and target patient population for pove, including its "pipeline-in-a-product" potential, expectations for pove’s clinical progress, including with respect to an interim analysis in the Phase 3 RAINIER study and the potential to file for US accelerated approval, plans to advance pove into pivotal development for pMN, and clinical status and expectations for pove as a treatment for gMG and wAIHA, (vi) expectations for VX-407 in ADPKD, including advancement to Phase 2 in 2025, (vii) expectations for CASGEVY, including global launch momentum in 2025 and reaching more eligible patients across geographies with regulatory approval and access, (viii) status and expectations for the U.S. JOURNAVX launch in acute pain, beliefs regarding the commercial potential of JOURNAVX, including expectations for sales volume and revenue, and beliefs regarding momentum with payers and retailers, (ix) expectations for the DPN VX-993 study, and expectations regarding the VX-993 study in acute pain, (x) expectations to complete enrollment in IA cohort of inaxaplin AMPLITUDE study in 2025, the potential to file for U.S. accelerated approval, clinical status of and expectations for the AMPLIFIED study, and expectations for the recently updated AMKD-related diagnostics codes, (xi) expectations for the Phase 3 trials of suzetrigine in DPN, including enrollment completion by the end of 2026, and (xii) plans to complete enrollment and dosing in the MAD portion of the DM1 study. 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, the company may not be able to commercialize its products successfully or in the manner 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. 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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 (loss) (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 (loss) described above and certain discrete items. For full-year 2024, the company’s non-GAAP weighted-average common shares outstanding included the estimated effect of potentially dilutive securities that was not used in the calculation of GAAP diluted weighted-average common shares outstanding because the company incurred a GAAP net loss for the period. 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, AIPR&D and SG&A expenses and effective tax rate on a non-GAAP basis. Unless, otherwise noted, the guidance regarding combined R&D, AIPR&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 Q2:25 and Q4:24 press releases dated August 4, 2025, and February 10, 2025.

# Vertex delivered strong Q2:25 results across the board

## Deliver launch excellence and revenue diversification

alyftrek™ casgevy® JOURNAVX™ (suzetrigine)

## Expand CF leadership

- Complete studies in **lower age groups** with **approved CFTR medicines**
- **VX-828** combo (next gen 3.0 CFTRm regimen): on track to initiate CF patient cohort by YE 2025
- **VX-522** (mRNA): IDMC endorsed re-start of MAD portion of Phase 1/2 study; working to resume dosing in near term

## Advance broad and deep mid- and late- stage pipeline

- **Suzetrigine (DPN)** Phase 3 well underway; advance a second DPN Phase 3 shortly with goal to complete enrollment in both DPN studies by YE 2026
- **Zimislecel (T1D)** Phase 3 dosing to complete soon; on track for global filings in 2026
- **Inaxaplin (AMKD)** Phase 3 IA cohort on track to complete enrollment by YE 2025
- **Povetacicept (IgAN)** Phase 3 IA cohort fully enrolled; potential U.S. filing for AA H1:26; full study enrollment on track for completion by YE 2025
- **Povetacicept (pMN)** Phase 3 pivotal trial to begin later this year
- **VX-407 (ADPKD)** Phase 2 POC to begin in Q3:2025

## Deliver strong financial performance

- Q2:25 revenue $2.96B; reiterated 2025 total revenue guidance of $11.85-$12.0B
- Drive revenue growth: CF as foundation, increasing contributions from CASGEVY, ALYFTREK & JOURNAVX
- Deliver attractive operating margin while continuing to invest in pipeline

DPN: diabetic peripheral neuropathy; T1D: type 1 diabetes; AMKD: APOL-1 mediated kidney disease; IA: interim analysis; IgAN: IgA nephropathy; AA: accelerated approval; pMN: primary membranous nephropathy; ADPKD: autosomal dominant polycystic kidney disease; POC: proof of concept.

# Expanding CF leadership: ALYFTREK now approved in U.S., U.K., EU and Canada

***Vertex CFTR modulators have the potential to transform the lives of ~95% of patients with CF in our core markets***

| kalydeco | ORKAMBI | symdeko | trikafta |
|---|---|---|---|
| Patients 1 month and older | Patients 1 year and older | Patients 6 years and older | N.G 1.0 regimen, ages 2+ |

**alyftrek™**
N.G 2.0 regimen, ages 6+

- Serial innovation: fifth CF launch since 2012; potential to set new standard of CF care
- OUS reimbursement: secured in England, Germany, and Denmark, adding Ireland shortly; working with Canadian and other EU reimbursement bodies to secure access
- Potential additional approvals in 2025: Australia, New Zealand, Switzerland

**Next-generation CFTRm**
N.G 3.0 regimen

- VX-828 combination therapy:
  - Most efficacious CFTR corrector Vertex has ever studied *in vitro* that is in clinic
  - Completing healthy volunteer study; expect to initiate cohort in CF patients by YE 2025

**VX-522**

- mRNA approach for ~5,000 patients who cannot benefit from CFTRm
- Revised protocol to address tolerability issues
- IDMC endorsed re-start of MAD portion of Phase 1/2 study; working to resume dosing in near term

NG: next generation; CFTRm: cystic fibrosis transmembrane conductance regulator modulator; IDMC: independent data monitoring committee; MAD: multiple ascending dose.

# VX-993 Phase 2 Study in acute pain post bunionectomy powered to detect higher clinical efficacy than previously demonstrated with $Na_V1.8$ pathway

***VX-993 did not yield statistically significant improvement on primary endpoint***

- VX-993 was safe and well-tolerated with no related SAEs; overall profile consistent with placebo
- Placebo effect was well controlled and desired VX-993 exposures were achieved
- On efficacy, as measured by SPID48:
  - treatment with VX-993 after bunionectomy surgery did not meet the primary endpoint
  - treatment effect similar at the mid- and high-doses and numerically better versus placebo

**VX-993 BUNIONECTOMY**

| Treatment Groups | Placebo N = 71 | High-Dose VX-993 (180 mg first dose/90 mg every 12 hours) n = 71 | Mid-dose VX-993 (70 mg first dose/35 mg every 12 hours) n = 77 | Low-dose VX-993 (10 mg first dose/5 mg every 12 hours) n = 73 | Hydrocodone bitartrate /acetaminophen reference arm (5 mg/325 mg every 6 hours) n = 75 |
|---|---|---|---|---|---|
| Mean SPID48 | 50.2 | 74.5 | 71.5 | 54.0 | 94.4 |
| Mean SPID48 difference from placebo (95% CI) | -- | 24.3 (-6.3, 54.9) | 21.2 (-8.7, 51.2) | 3.7 (-26.7,34.1) | 44.2 (14.0, 74.4) |
| p-value vs placebo | | 0.1190 | 0.1643 | 0.8094 | 0.0043 |

367 patients were enrolled; All p-values are based on individual comparisons to placebo; SAE: serious adverse event; CI: confidence interval.

# T1D: Zimislecel Phase 3 study dosing to complete soon

***Global regulatory submissions planned for 2026***

**Patient population**

- Initial launch targets ~60,000 severe T1D patients*

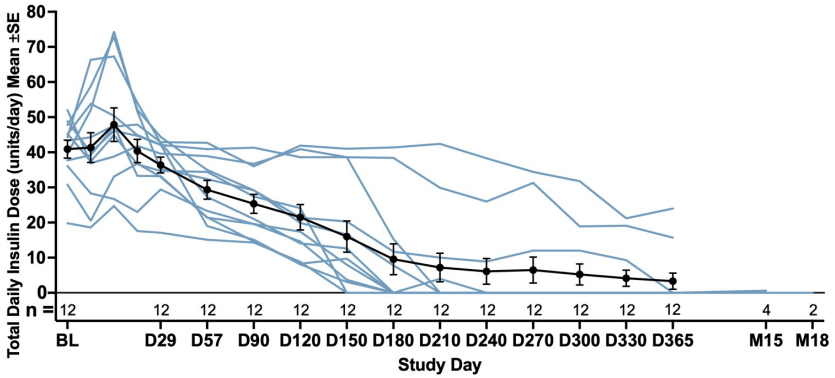
**Multiple global regulatory designations**

- RMAT and Fast Track in the U.S.
- PRIME in the EU
- Innovation Passport under the Innovative Licensing and Access Pathway in the U.K.

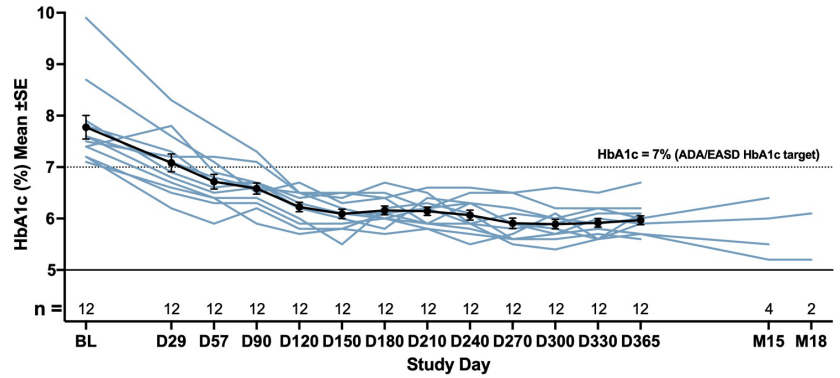
**Alternative approaches in research stage**

- Improved immunosuppression
- Hypoimmune islet cells
- Novel encapsulation to protect the islet cells

## Total Daily Insulin




## HbA1c




## ADA 2025

Data presented on 12 patients from the Phase 1/2 portion, who have at least 1 year of follow-up:

**12** achieved a **reduction in HbA1c to <7%**

**12** had **reduction of exogenous insulin use****

**10** were **insulin free at Month 12**

**12** achieved Phase 1/2 **primary endpoint of elimination of SHEs with HbA1c <7%**

*Based on clinical trial population.

**1 had 70% reduction and received 1 dose of steroids (protocol prohibited) for a rash on the day of zimislecel infusion; 1 had 36% reduction and received 4 doses of steroids (protocol prohibited) in the peri-infusion period.

# Povetacicept: Delivering on the promise of a pipeline-in-a-product

***Assessment of patient impact, treatment landscape and commercial opportunity leads to focus on IgAN, pMN, gMG and wAIHA***

| | |
|---|---|
| **Potential transformative benefit** | • **Certain autoimmune diseases are driven by uncontrolled B cells**<br>• Pove specifically engineered as small format protein to provide B cell control through optimized, targeted, dual inhibition of the BAFF and APRIL cytokines, which both play a key role in pathogenesis of B cell-mediated autoimmune diseases |
| **IgAN: RAINIER Phase 3 trial well underway** | • **Pove 80mg vs placebo** on top of standard of care (n= ~480)<br>✓ Enrollment of **IA cohort complete:** If IA is positive, plan to file for accelerated approval in the U.S. in H1:26<br>✓ On track to complete enrollment of full study by the end of 2025 |
| **pMN: Phase 2/3 trial initiating shortly** | • Advancing into **pivotal development in pMN later this year**<br>• Phase 2/3 adaptive study vs. standard of care<br>• Primary endpoint: complete clinical remission at 72 weeks of treatment |
| **Delivering on pipeline-in-a-product potential** | • Prioritized opportunities for pove: IgAN, pMN, gMG, wAIHA<br>• **Myasthenia Gravis (gMG):** ~175,000 patients in North America and Europe<br>• **Warm Autoimmune Hemolytic Anemia (wAIHA):** ~35,000 patients in North America and Europe<br>• De-prioritized other indications |

BAFF: B-cell activating factor; APRIL: A Proliferation-Inducing Ligand; IA: Interim Analysis; pMN: primary membranous nephropathy.

# AMKD: Progress across the board as AMPLITUDE on track to complete interim analysis enrollment by YE 2025

***New ICD-10 codes for AMKD, a significant achievement for the kidney disease community***

## Ongoing inaxaplin trials

AMPLITUDE

Primary AMKD: Phase 2/3 pivotal trial **on track to complete enrollment of the interim analysis cohort by YE 2025**

AMPLIFIED

AMKD with comorbidities: Phase 2 proof-of-concept study enrolling and dosing; **on track to complete enrollment of the study by YE 2025**

## ICD-10 codes

- **The U.S. CMS recently updated diagnostics codes, known as ICD-10-CM codes, to include new codes for AMKD**
- New codes will make AMKD patients visible in the healthcare system both for diagnosis and potential treatment

| N07.B | Z84.11 |
|---|---|
| AMKD | Family history of AMKD |

AMKD: APOL1-mediated kidney disease; CMS: Center for Medicare and Medicaid.

# VX-407: First-in-class PC1 corrector for ADPKD advancing to Phase 2 in Q3:2025

- **~300,000** people in the U.S. & Europe diagnosed with ADPKD
- No treatments address the underlying cause of disease

**VX-407**

- First-in-class, small molecule protein-folding corrector
- Designed to target the underlying cause of ADPKD in patients with a subset of variants in the *PKD1* gene
  - Estimated up to ~30,000 patients (up to ~10% of overall ADPKD patient population)

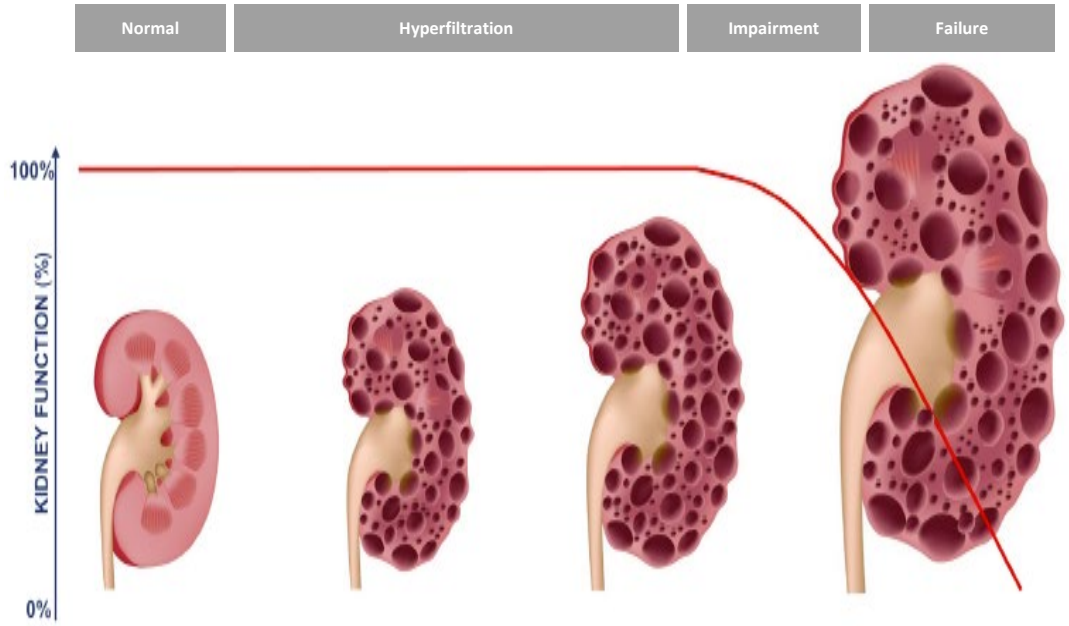
**Phase 2, proof-of-concept study to begin in Q3:2025**

- Ph 1 in HVs: PK and safety supportive of advancement
- Phase 2: 52-week, single arm study (n=~24)

ADPKD: autosomal dominant polycystic kidney disease; HV: healthy volunteers.



## Over time, kidney cysts lead to kidney function (eGFR) decline and kidney failure




Goal: Target the underlying cause of ADPKD by restoring PC1 protein function, thereby reducing total kidney volume and preventing progression to kidney failure

# Clinical portfolio is broad, diverse, and rapidly advancing
# On track to meet goal of 5 launches over 5 years (by 2028)

| Select, Next Wave<br>Research-stage Programs | Phase 1<br>in Healthy Volunteers | Phase (1)/2<br>in Patients | Pivotal Development | Approved |
|---|---|---|---|---|
| **Improved conditioning**<br>CASGEVY – SCD & TDT | **Follow-on molecules:**<br>• CF<br>• Pain<br>• AMKD | **VX-993**<br>Acute pain - completed | **Zimislecel**<br>Type 1 diabetes | JOURNAVX™ (suzetrigine) |
| **$Na_V1.7$ inhibitor**<br>Pain | **VX-993**<br>Acute pain (Intravenous) | **VX-993**<br>PNP - DPN | **Povetacicept**<br>IgA nephropathy | alyftrek™ |
| **Islet cells + alt. IS**<br>**Islet cells + device**<br>**Hypoimmune islet cells**<br>Type 1 diabetes | **VX-828**<br>Cystic fibrosis | **VX-522**<br>CFTR mRNA | **Povetacicept****<br>pMN | casgevy® |
| **Small molecule**<br>Huntington's disease | | **VX-670**<br>DM1 | **Suzetrigine**<br>DPN | trikafta® |
| | | **Povetacicept, RUBY-3**<br>IgAN, pMN, LN, AAV | **Inaxaplin**<br>AMKD | symdeko® |
| | | **Povetacicept, RUBY-4**<br>wAIHA, ITP, CAD | | ORKAMBI® |
| | | **VX-407***<br>ADPKD | | kalydeco® |

*Expect to begin in Q3:2025; **Expect to begin later this year.

SCD: sickle cell disease; TDT: transfusion-dependent beta thalassemia; alt. IS: alternative immunosuppression; CF: cystic fibrosis; AMKD: APOL-1 mediated kidney disease; ADPKD: autosomal dominant polycystic kidney disease; PNP: peripheral neuropathic pain; DPN: diabetic peripheral neuropathy; CFTR mRNA: cystic fibrosis transmembrane conductance regulator messenger RNA; DM1: myotonic dystrophy type 1; pMN: primary membranous nephropathy; wAIHA: warm autoimmune hemolytic anemia.

# ALYFTREK: Approved for ages 6+ in U.S., U.K., EU & Canada

***U.S. launch well underway & now launching in England, Germany and Denmark, with Ireland soon to follow***

## INITIATE

- Patients who discontinued prior CFTRm
- Newly eligible patients with ultra-rare mutations

- Rapid uptake in those who are naïve to CFTR modulators and newly eligible, as well as discontinued patients

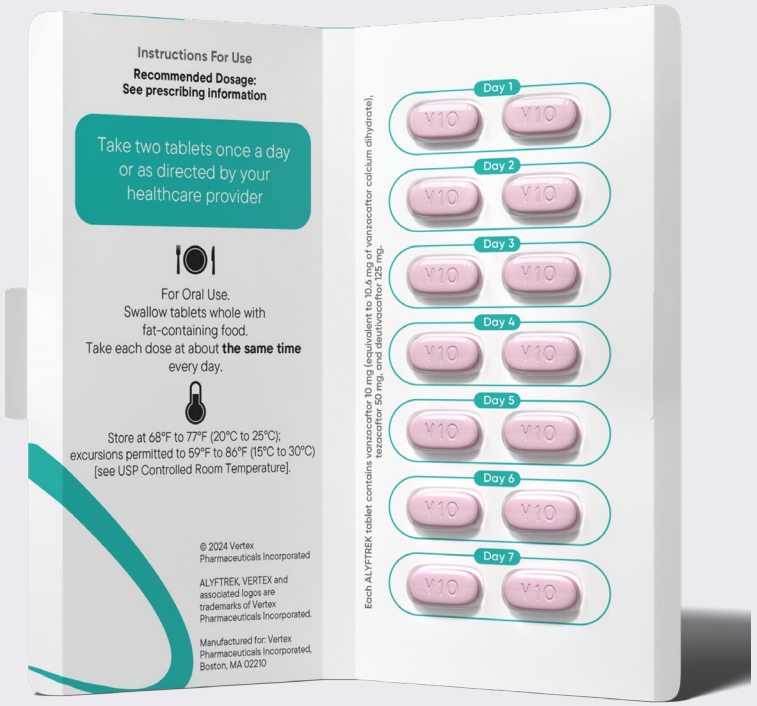
## TRANSITION

- Current TRIKAFTA/KAFTRIO patients over time given
  - more convenient dosing
  - improved CFTR function

- Expect majority of TRIKAFTA patients to switch to ALYFTREK over time given multiple benefits

alyftrek™

(vanzacaftor/tezacaftor/deutivacaftor)




**ALYFTREK: A highly efficacious, once-daily CFTR modulator delivering equivalent improvement in lung function* and greater CFTR function** vs. TRIKAFTA**

*Lung function as measured by improvements in ppFEV1 vs. TRIKAFTA.
**CFTR function as measured by improvements in sweat chloride vs. TRIKAFTA.

# CASGEVY: Launch building momentum in all regions


- Now approved in U.S., UK, EU, Kingdom of Saudi Arabia, Qatar, Bahrain, Canada, Switzerland, and United Arab Emirates

- U.S.: Commercial – broad access secured; Medicaid – single case agreements + CMMI Demonstration Project
- OUS: Reimbursed access in multiple countries and working to secure access in additional countries with regulatory approval

- ✓ Reached ATC goal of >75 ATCs activated globally
- ✓ ~250 patients referred to ATCs; ~115 patients have had first cell collections,* including 35 first cell collections in Q2
- ✓ 29 total patients infused,* including 16 CASGEVY infusions in Q2

*Since launch through end of Q2:2025.
ATC: authorized treatment center.

# JOURNAVX: Ongoing launch delivering strong reception across the board


## Rapid progress with payers*

- **~150 million covered lives with reimbursed access to JOURNAVX**
- Formal coverage gained with 2 out of 3 large national pharmacy benefit managers (PBMs)
- 16 state Medicaid plans providing access to JOURNAVX, without prior authorization or step edit requirements

## Advancing Broad Hospital Access

- National agreements in place with two of the largest group purchasing organizations (GPOs) in the U.S.
- >50 of targeted 150 large healthcare systems and >500 individual hospitals of targeted 2,000 institutions have added JOURNAVX to formularies, protocols or order sets

## Encouraging prescribing patterns

- **>110,000 prescriptions successfully filled (as of mid-July)**
- Excellent breadth of usage across a wide range inpatient and outpatient settings, pain conditions, and physician specialties, in line with the broad label

*Payer/coverage statistics as of mid-July; ~150 million covered lives reflect both commercial and government payers.

# Q2 2025 financial highlights

| *($ in millions except where noted or per share data and percentages)* | Q2:24 | FY:24 | **Q2:25** |
|---|---|---|---|
| TRIKAFTA/KAFTRIO | 2.45B | 10.24B | **2.55B** |
| ALYFTREK | – | – | **157** |
| Other product revenues* | 196 | 782 | **236** |
| Product revenues, net | $2.65B | $11.02B | **$2.94B** |
| Other revenues | – | – | **21** |
| Total revenues | $2.65B | $11.02B | **$2.96B** |
| Combined non-GAAP, Acquired IPR&D and SG&A expenses | 5.43B | 8.82B | **1.24B** |
| Non-GAAP operating income (loss) | (3.15)B | 696 | **1.33B** |
| Non-GAAP operating margin % | (119)% | 6% | **45%** |
| Non-GAAP net income (loss) | (3.31)B | 111 | **1.17B** |
| Non-GAAP net income (loss) per share – diluted | $(12.83) | $0.42 | **$4.52** |
| Cash, cash equivalents & total marketable securities (period-end) | $10.2B | $11.2B | **$12.0B** |

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 (loss), non-GAAP net income (loss) and non-GAAP net income (loss) per share – diluted to corresponding GAAP measures are included in the company's Q2:25 and Q4:24 press releases dated August 4, 2025, and February 10, 2025. 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. *Q2:25 includes $30 million CASGEVY revenues and $12M JOURNAVX revenues. FY:24 includes $10M CASGEVY revenues.

# Reiterate full year 2025 financial guidance

| | Current FY 2025 Guidance | Commentary |
|---|---|---|
| Total Revenue | $11.85 - $12.0B | Includes expectations for continued growth in CF, including the launch of ALYFTREK globally; continued uptake of CASGEVY in multiple regions; and early contributions from the U.S. launch of JOURNAVX. |
| Combined GAAP R&D, Acquired IPR&D and SG&A Expenses* | $5.55 - $5.7B | Includes expectations for continued investment in multiple mid- and late-stage clinical development programs and commercial capabilities, and AIPR&D expenses of approximately $100 million. |
| Combined Non-GAAP R&D, Acquired IPR&D and SG&A Expenses* | $4.9 - $5.0B | |
| Non-GAAP Effective Tax Rate | 20.5% - 21.5% | |

*The difference between the combined GAAP R&D, AIPR&D and SG&A expenses and the combined non-GAAP R&D, AIPR&D and SG&A expenses guidance relates primarily to $650 million to $700 million of stock-based compensation expense.

# ANTICIPATED KEY MILESTONES

| | |
|---|---|
| **ALYFTREK (CF)** | **Continued U.S. launch; launch in UK, EU, and Canada once reimbursement secured and achieve regulatory approvals in other geographies;** complete Phase 3 studies in younger age groups |
| **VX-522 (CF)** | Resume dosing in the MAD portion of the Phase 1/2 study in near term |
| **Next-generation 3.0 (CF)** | **VX-828 (next-generation CFTR corrector) combo on track to initiate CF patient cohort by YE 2025** |
| **CASGEVY (SCD/TDT)** | • **Reach more eligible 12+ year-old patients** across geographies<br>• Complete dosing in Phase 3 trial in 5–11-year-olds in H2:2025 |
| **Suzetrigine (pain)** | • **Acute: JOURNAVX – Continued U.S. launch**<br>• **PNP - DPN:** Enroll and dose ongoing Phase 3 pivotal trial; **begin second DPN Phase 3 shortly; complete enrollment of both studies by YE 2026** |
| **VX-993 (pain)** | • **DPN: Continue to progress Phase 2 study** (DPN; oral) |
| **Zimislecel/VX-880 (T1D)** | • **Enrollment and dosing in pivotal trial to complete soon;** planning for **global regulatory submissions in 2026** |
| **Inaxaplin (AMKD)** | • **AMPLITUDE: Complete enrollment in IA cohort by YE 2025**; following 48 weeks of treatment; potential to file for U.S. accelerated approval<br>• **AMPLIFIED**: Complete enrollment of study by YE 2025 |
| **Povetacicept (IgAN, pMN)** | • **IgAN: Completed enrollment in IA cohort**; following 36 weeks of treatment, potential to file for U.S. accelerated approval in H1:2026; expect to complete enrollment in full cohort by YE 2025<br>• **pMN: Initiate Phase 2/3 pivotal trial later this year**<br>• **Other: Prioritize gMG and wAIHA as next potential indications** |
| **VX-407 (ADPKD)** | **Begin Phase 2 proof-of-concept study in ADPKD patients in Q3:2025** |
| **VX-670 (DM1)** | **Continue to advance Phase 1/2 study in DM1 patients**; on track to complete enrollment and dosing of MAD in H1:2026 |

# Second Quarter 2025 Financial Results

August 4, 2025

*Presentation intended for the investment community*

# Appendix A

## *GAAP to non-GAAP Financial Information*

| *($ in millions except as noted, per share data and percentages)* | Q2:24 | FY:24 | Q2:25 |
|---|---|---|---|
| **Combined R&D, Acquired IPR&D and SG&A** | | | |
| GAAP | 5.79B | 9.72B | **1.41B** |
| Non-GAAP | 5.43B | 8.82B | **1.24B** |
| **Operating income (loss)** | | | |
| GAAP | (3.51)B | (233) | **1.15B** |
| Non-GAAP | (3.15)B | 696 | **1.33B** |
| **Operating Margin %:** | | | |
| GAAP | (133)% | (2)% | **39%** |
| Non-GAAP | (119)% | 6% | **45%** |
| **Net income (loss)** | | | |
| GAAP | (3.59)B | (536) | **1.03B** |
| Non-GAAP | (3.31)B | 111 | **1.17B** |
| **Net income (loss) per share – diluted** | | | |
| GAAP | $(13.92) | $(2.08) | **$3.99** |
| Non-GAAP | $(12.83) | $0.42 | **$4.52** |
| **Shares used in diluted per share calculations** | | | |
| GAAP | 258.1 | 257.9 | **258.9** |
| Non-GAAP | 258.1 | 260.9 | **258.9** |

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 (loss), non-GAAP net income (loss) and non-GAAP net income (loss) per share – diluted to corresponding GAAP measures are included in the company's Q2:25 and Q4:24 press releases dated August 4, 2025 and February 10, 2025.

# Vertex targeted disease area epidemiology estimates

| | DISEASE STATE | ASSET | APPROACH/MODALITY | PATIENT OPPORTUNITY |
|---|---|---|---|---|
| **COMMERCIALIZED** | Cystic fibrosis | 5 approved, incl. ALYFTREK | Small molecules | ~109,000 |
| | Sickle cell disease + TDT | CASGEVY | Cell and gene therapy | ~60,000 severe |
| | Acute Pain | JOURNAVX | Small molecule NaV1.8 inhibitor | ~80M |
| **IN PIVOTAL STUDIES (in progress or near-term)** | Diabetic peripheral neuropathy | Suzetrigine | Small molecule NaV1.8 inhibitor | >2M |
| | AMKD | Inaxaplin | Small molecule inhibitor | ~250,000 |
| | T1D | Zimislecel<br>Other approaches | Cell and gene therapy | ~60,000 w/initial filing*<br>~3.8M |
| | IgA nephropathy | Povetacicept | Fusion protein | ~300K U.S./Europe<br>>750K China |
| | pMN | Povetacicept | Fusion protein | ~150,000 |
| **PIPELINE** | DM1 | VX-670 | Oligonucleotide with cyclic peptide | ~110,000 |
| | CF | VX-522 | mRNA | ~5,000** |
| | ADPKD | VX-407 | Small molecule corrector | ~300,000*** |
| | gMG | Povetacicept | Fusion protein | ~175,000 |
| | wAIHA | Povetacicept | Fusion protein | ~35,000 |

*Zimislecel initial program seeks first approval for ~60,000 patients; Vertex will seek to serve the full ~125,000 patient population with severe T1D over time.
**VX-522 targets a patient population that does not make any CFTR protein and is a subset of the ~109,000 overall CF patient population.
*** VX-407 targets a patient population with a subset of variants in the *PKD1* gene, estimated at up to ~30,000 (or up to ~10%) of the overall patient population.