First Quarter 2025 Financial Results

May 5, 2025

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

Duncan McKechnie, SVP, North America Commercial Operations
Chief Commercial Officer (as of July 1, 2025)

Financial Results

Charlie Wagner, Executive Vice President and Chief 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 “Updated full year 2025 financial guidance,” expectations for financial performance in Q1 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 in 2025 and launching in the U.K. later this year, expectations regarding U.S. patients switching to ALYFTREK, and expectations with respect to a lower royalty burden, (iii) expectations for Vertex’s CF 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 enrollment and dosing in the ongoing zimislecel pivotal trial in Q2 2025, and potential global regulatory submissions in the first half of 2026, (v) expectations regarding the therapeutic scope, potential benefits, and target patient population for pove, including its "best-in-class" and "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 accelerated approval in the U.S. in the first half of 2026 if positive, plans to advance pove into pivotal development for pMN, and expectations for the RUBY-3 and RUBY-4 Phase 2 basket studies, (vii) expectations for VX-407 in ADPKD, including regarding advancement to Phase 2 in the second half of 2025, (vii) expectations for CASGEVY, including building global momentum in 2025 and reaching more eligible patients across geographies with regulatory approval and access, and plans to expand manufacturing to support global demand, (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, beliefs regarding momentum with payers and retailers, and expectations regarding JOURNAVX’s addition to the list of medicines covered under the NOPAIN Act, (ix) expectations for the studies of the intravenous and oral formulations of VX-993 in acute pain and DPN, including expectations to complete the ongoing oral study of VX-993 in acute pain this quarter and to share data in the second half of 2025, and expectations to progress additional Nav1.8 and NaV1.7 inhibitors, (x) expectations to complete enrollment in IA cohort of inaxaplin study in 2025 and the potential to file for U.S. accelerated approval, (xi) expectations for the Phase 3 trial of suzetrigine in DPN and plans to advance the pivotal program, and expectations to advance study of suzetrigine in LSR into Phase 3 pending regulatory discussions, and (xii) plans to advance 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 (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. 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 Q1:25 and Q4:24 press releases dated May 5, 2025 and February 10, 2025.

Vertex delivered a strong start to 2025, as we extend leadership in CF, execute multiple launches and advance the pipeline

Expand CF leadership

- **ALYFTREK**: Approved in the U.S. and U.K. for patients with CF ages 6+; strong U.S. launch
- **VX-828** combo (next gen 3.0 CFTRm regimen): on track to initiate clinical trial in CF patients by EoY
- **VX-522** (mRNA): Implemented pause to MAD portion of Ph 1/2 study to assess a tolerability issue

Drive commercial diversification

- **CASGEVY**: Launch gathering momentum across all regions
- **JOURNAVX**: Approved in U.S. for moderate-to-severe acute pain; strong early uptake across the hospital and retail settings
- Preparing for additional launches: 4 programs in pivotal development + 5th to start in 2025 (pMN)

Advance broad and deep clinical-stage pipeline

- **Povetacicept** (IgAN) Phase 3 interim analysis (IA) cohort fully enrolled, potential U.S. filing H1:26
- **Zimislecel** (T1D) Phase 3 dosing to complete in Q2:25, potential global filings in 2026
- **Inaxaplin** (AMKD) Phase 3 IA cohort on track to complete enrollment by end of year
- Rapid progress with earlier stage programs: **VX-993** (oral) acute pain study to complete this quarter and data expected in H2:25
- **VX-407** to advance to Phase 2 POC for ADPKD in H2:25

Deliver strong financial performance

- Q1:25 revenue $2.77B; raised low end of 2025 total revenue guidance to $11.85-$12.0B
- Drive revenue growth: CF as foundation with increasing contributions from CASGEVY, ALYFTREK and JOURNAVX through 2025
- Deliver attractive operating margin while continuing to invest in pipeline; disciplined spend; commitment to specialty model

CFTRm = cystic fibrosis transmembrane conductance regulator modulators; MAD: Multiple Ascending Dose; T1D: type 1 diabetes; IgAN: IgA nephropathy; AMKD: APOL-1 mediated kidney disease; pMN: primary membranous nephropathy.

Expanding CF leadership: ALYFTREK approved in U.S. & U.K. and Positive CHMP Opinion in EU

Vertex CFTR modulators have the potential to transform the lives of nearly 95% of patients with CF

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
- Label includes additional 31 rare mutations beyond TRIKAFTA
- Potential approvals in 2025: EU, Australia, New Zealand, Canada, Switzerland

Next-generation CFTRm

N.G 3.0 regimen

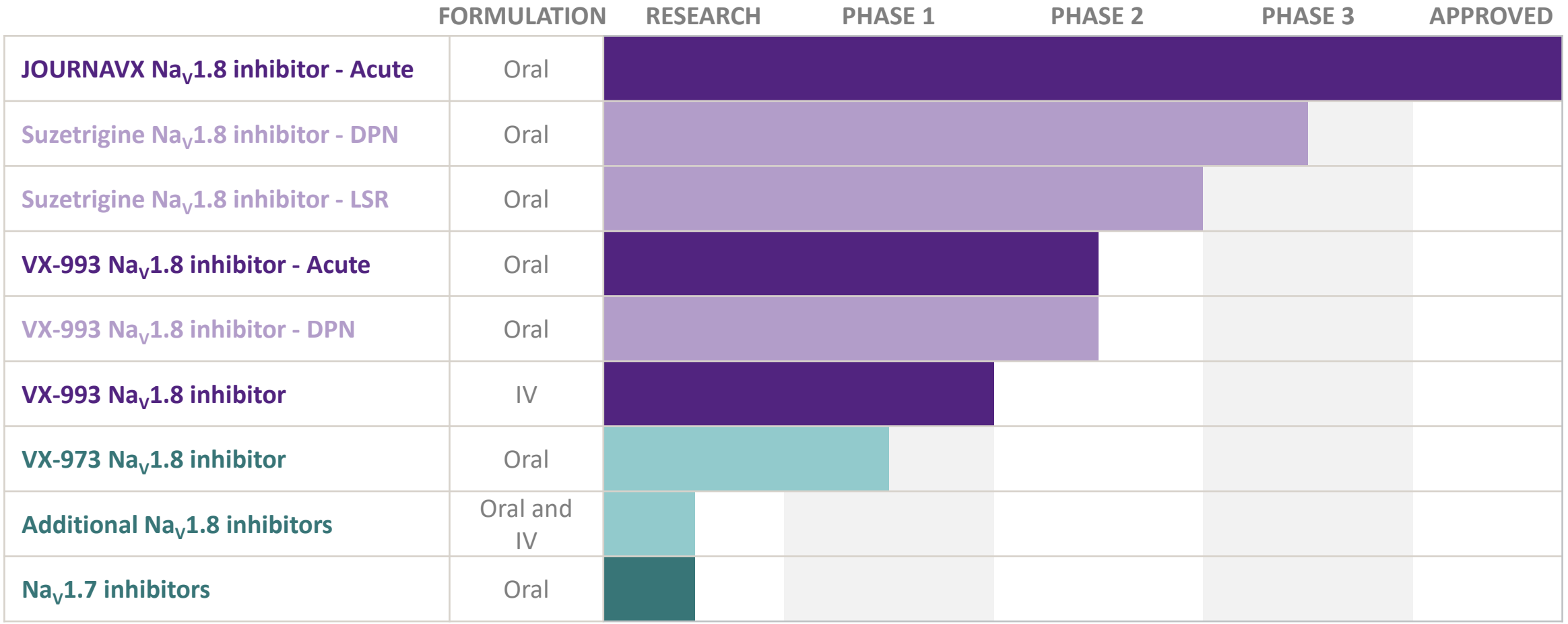
- VX-828 combination therapy:
  - Most efficacious CFTR corrector Vertex has ever studied *in vitro* in HBE assays
  - Expect to initiate study in CF patients in 2025

VX-522

- mRNA approach for >5,000 patients who cannot benefit from CFTRm
- Temporary pause implemented to MAD portion of Phase 1/2 study to assess a tolerability issue

NG: next generation; CFTR: cystic fibrosis transmembrane conductance regulator; HBE: human bronchial epithelial cells; MAD: multiple ascending dose.

Vertex is committed to long-term leadership in pain with a broad and deep pipeline



DPN: diabetic peripheral neuropathy; LSR: lumbosacral radiculopathy; IV: intravenous.

Zimislecel: Pivotal trial will complete enrollment and dosing in Q2:25, with global regulatory submissions planned for 2026

Patient population

- Initial launch targets ~60,000 severe T1D patients in U.S. and Europe

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.

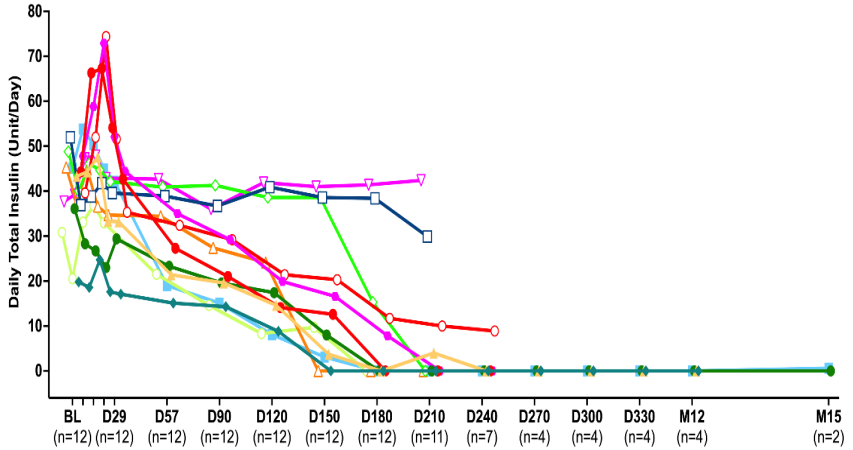
Updated clinical data expected at ADA in June

- Longer duration of follow-up from 12 participants who received full dose as a single infusion in Phase 1/2 portion

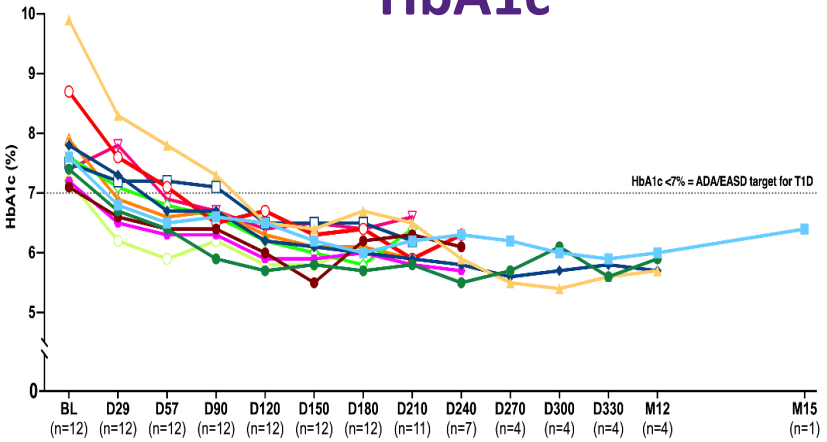
Alternative approaches in research stage

- Novel immunoprotective devices
- Alternative immunosuppression regimens
- Hypoimmune approach

Total Daily Insulin



HbA1c



EASD 2024

Data presented on 12 patients who completed Day 180 visit:

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

11 had **elimination or reduction of exogenous insulin use***

9 were **no longer using exogenous insulin***

*Although prohibited by protocol, two patients had steroid use in the peri-infusion period. One participant had one dose of steroids on the day of zimislecel infusion and did reduce (43%), but not eliminate, exogenous insulin. One participant received four doses of steroids in the peri-infusion period and saw a 12% increase in their use of exogenous insulin.

Kidney: Broad pipeline of potentially transformative medicines in multiple serious renal diseases

		PATIENTS[1]	RESEARCH	PHASE 1	PHASE 2	PHASE 3	APPROVED
B cell mediated renal diseases	Povetacicept – IgAN[2]	~300K (>750K China)				RAINIER ★	*Enrollment complete in IA cohort*
	Povetacicept – pMN	~150K					*Moving to pivotal Development H2:25*
	Povetacicept – LN	~225K			RUBY-3		
	Povetacicept – AAV	~225K			RUBY-3		
APOL1 mediated kidney disease (AMKD)	Inaxaplin – Primary AMKD	~150K				AMPLITUDE	
	Inaxaplin – AMKD with comorbidities[3]	~100K			AMPLIFIED APOL-1 Mediated Kidney Disease Study		
	Additional APOL1 inhibitors[4]	~250K (150K+100K)					
Autosomal dominant polycystic kidney disease	VX-407[5]	Up to ~30K					
	Additional ADPKD serial innovation	~300K (incl. 30K)					

1. Estimated patient population in the U.S. and Europe, unless otherwise noted. 2. IgAN patients continue to be studied in RUBY-3 3. AMPLIFIED Phase 2 trial began January 2025. 4. Multiple programs in various phases. 5. Targets a patient population with a subset of variants in the *PKD1* gene.
IgAN: IgA nephropathy; pMN: primary membranous nephropathy; LN: lupus nephritis; AAV: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides.

Povetacicept: IgAN - completed enrollment of interim analysis cohort in global Phase 3 study; pMN - advancing to pivotal development

Best-in-class potential

Strong preclinical profile:

- Dual antagonist of BAFF/APRIL cytokines with high affinity and potency

Compelling RUBY-3 data (ASN 2024):

- Reduced UPCR mean ~66% at 48 weeks; stable renal function (eGFR)
- 63% achieved clinical remission*

Convenient dosing:

- Once every four weeks, at home
- Subcutaneous
- Small volume

RAINIER Phase 3 trial in IgAN

RAINIER™

- **Pove 80mg vs placebo** on top of standard of care (n= ~480)

✓ Completed enrollment of the **interim analysis (IA) cohort:**

- If IA is positive, potential to file for accelerated approval in the U.S. in H1:26

Phase 2/3 trial in pMN

- Reached agreement with FDA to advance into **pivotal development for pMN**
  - Single Phase 2/3 adaptive study vs. standard of care
  - Primary endpoint: complete clinical remission at 72 weeks of treatment

*Defined as UPCR (urine protein creatinine ratio) < 0.5 g/g, negative hematuria, and stable renal function.
BAFF: B-cell activating factor; APRIL: A Proliferation-Inducing Ligand; eGFR: estimated glomerular filtration rate; pMN: primary membranous nephropathy.

VX-407: First-in-class PC1 corrector for ADPKD advancing to Phase 2 in H2 2025

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

VX-407

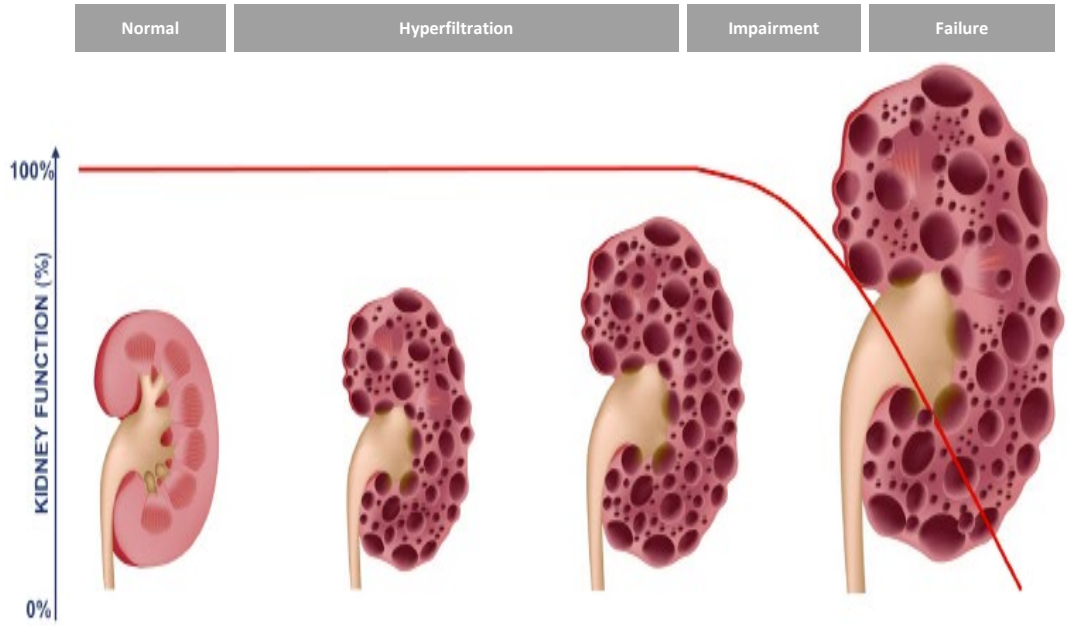
- First-in-class, small molecule protein-folding corrector
- Designed to target the underlying cause of ADPKD in patients with a subset of variants in the *PKD1* gene
  - Estimated up to ~30,000 patients (~10% of overall ADPKD patient population)

Phase 2, proof-of-concept study to begin in H2 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 Research-stage Programs	Phase 1 in Healthy Volunteers	Phase (1)/2 in Patients	Pivotal Development	Approved
Improved conditioning CASGEVY – SCD & TDT	**Follow-on molecules:** • CF • Pain • AMKD	**Suzetrigine** LSR	**Zimislecel** Type 1 diabetes	JOURNAVX™ (suzetrigine)
$Na_V1.7$ inhibitor Pain	**VX-993** Acute pain (Intravenous)	**VX-993** Acute pain	**Povetacicept** IgA nephropathy	alyftrek™
Islet cells + alt. IS **Islet cells + device** **Hypoimmune islet cells** Type 1 diabetes	**VX-828** Cystic fibrosis	**VX-993** PNP - DPN	**Povetacicept*** pMN	casgevy®
Small molecule Huntington's disease		**VX-522** CFTR mRNA	**Suzetrigine** DPN	trikafta®
		VX-670 DM1	**Inaxaplin** AMKD	symdeko®
		Povetacicept, RUBY-3 LN, AAV		ORKAMBI®
		Povetacicept, RUBY-4 ITP, AIHA, CAD		kalydeco®
		VX-407* ADPKD		

*Expect to begin in H2 2025.

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; LSR: lumbosacral radiculopathy; 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; LN: lupus nephritis; AAV: ANCA-associated vasculitides; ITP: idiopathic thrombocytopenia; AIHA: warm autoimmune hemolytic anemia; CAD: cold agglutin disease.

ALYFTREK: Approved for ages 6+ in U.S. and U.K; Uptake across all eligible patient groups in U.S.

Reimbursement discussions underway in UK
Potential approvals in EU and other geographies in 2025

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

INITIATE

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

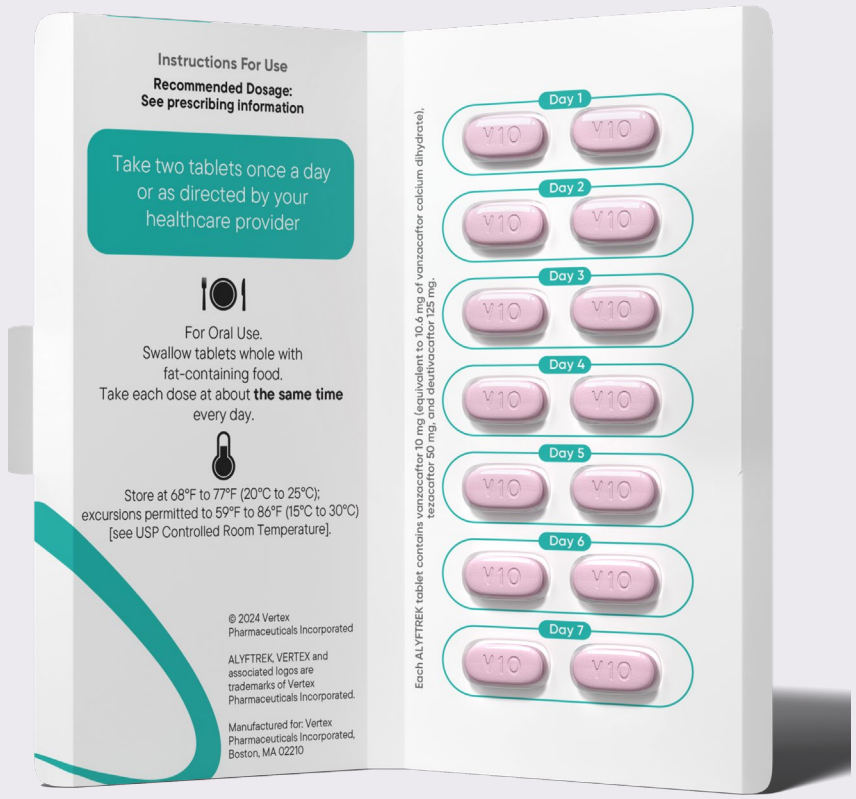
TRANSITION

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

Launch Progress:

- Enthusiastic feedback from physicians and patients
- Prescriptions off to a strong start across all patient types

alyftrek™
(vanzacaftor/tezacaftor/deutivacaftor)



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

CASGEVY: Launch gathering momentum in all regions

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

>65 ATCs activated and ~90 patients have had first cell collections*
8 CASGEVY infusions in Q1 2025

Payer Highlights

U.S.
Commercial – continue to secure access; **Medicaid** – single case agreements and first-ever CMMI Demonstration Project launched: *Cell & Gene Therapy Access Model*

OUS
Reimbursed access in multiple countries: England, Wales, Denmark, Austria, Luxembourg, KSA, Bahrain, UAE**

Expanding manufacturing to support global demand

*From launch through May 1, 2025. **Majority of Emirates.
ATC: authorized treatment center; CMMI: Center for Medicare and Medicaid Innovation.

JOURNAVX: FDA approved Jan 30, 2025
Strong early launch signals

Wide availability, strong early uptake

- **Retail pharmacy stocking:** JOURNAVX was broadly available at ~33,000 retail locations by mid-March
- **>20,000 prescriptions** filled through April 18th

Rapid progress with payers

- **~94 million covered lives with access to JOURNAVX** (as of May 1)
  - Coverage across commercial and government plans
- **~42 million with unrestricted access: no prior authorizations/step edits**

Compelling data support policy tailwinds

- **Health economics research presented at AAPM**: Replacing 25% acute pain opioid Rx's with non-opioids could deliver $4.5B annual savings
- **Federal legislation: NOPAIN Act** effective on Jan. 1; expect JOURNAVX to be added near-term to list of medicines covered
- **~35 states** have enacted or proposed **legislation to support use of non-opioids**

AAPM: American Academy of Pain Medicine.

Q1 2025 financial highlights

($ in millions except where noted or per share data and percentages)	Q1:24	FY:24	Q1:25
Total revenue	$2.69B	$11.02B	**$2.77B**
TRIKAFTA/KAFTRIO	2.48B	10.24B	**2.54B**
ALYFTREK	-	-	**54**
Other product revenue*	207	782	**171**
Combined non-GAAP, Acquired IPR&D and SG&A expenses	1.02B	8.82B	**1.23B**
Non-GAAP operating income	1.34B	696	**1.18B**
Non-GAAP operating margin %	50%	6%	**43%**
Non-GAAP net income	1.24B	111	**1.05B**
Non-GAAP net income per share – diluted	$4.76	$0.42	**$4.06**
Cash, cash equivalents & total marketable securities (period-end)	$14.6B	$11.2B	**$11.4B**

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, non-GAAP net income and non-GAAP net income per share – diluted to corresponding GAAP measures are included in the company's Q1:25 and Q4:24 press releases dated May 5, 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. *Q1:25 includes $14 million CASGEVY revenues and an insignificant amount from JOURNAVX. FY:24 includes $10M CASGEVY revenues.

Updated full year 2025 financial guidance

	Current FY 2025 Guidance	Previous FY 2025 Guidance	Commentary
Total Revenue	$11.85 - $12.0B	$11.75 - $12.0B	Includes expectations for continued growth in CF, including the launch of ALYFTREK; continued uptake of CASGEVY; and a contribution from the launch of JOURNAVX, primarily in the second half of 2025
Combined GAAP R&D, Acquired IPR&D and SG&A Expenses	Unchanged	$5.55 - $5.7B	Reflects investment in our multiple mid- and late-stage clinical development programs and ramp of commercial capabilities; ranges include approximately $100 million in currently anticipated IPR&D expenses
Combined Non-GAAP R&D, Acquired IPR&D and SG&A Expenses	Unchanged	$4.9 - $5.0B	
Non-GAAP Effective Tax Rate	Unchanged	20.5%-21.5%	

*Note that GAAP 2025 operating income, net income, and EPS will reflect an intangible asset impairment charge of $379M recorded in Q1:25 associated with VX-264 (the "cells plus device" program) in patients with type 1 diabetes (T1D), which will not be advancing further in clinical development.

Multiple catalysts throughout 2025

	ANTICIPATED KEY MILESTONES
ALYFTREK (CF)	**Drive U.S. launch, secure reimbursement in U.K. and secure regulatory approvals in EU and other geographies**
VX-522 (CF)	Temporary pause implemented to **assess a tolerability issue**
Next-generation 3.0 (CF)	**VX-828 (next-generation CFTR corrector) combo on track to initiate CF patient trial this year**
CASGEVY (SCD/TDT)	• **Reach more eligible 12+ year-old patients** across geographies • Work to **expand label** to younger age groups
Suzetrigine (pain)	• **Acute: JOURNAVX approved** 1/30/25 for moderate to severe acute pain; **U.S. launch underway** • **PNP - DPN: Enroll and dose** ongoing Phase 3 pivotal trial; **Advance LSR to Phase 3, pending regulatory discussions**
VX-993 (pain)	• **Acute: Complete Phase 2 study (BUN; oral) in Q2:2025, share results in H2:2025** • **PNP - DPN: Continue to progress Phase 2 study** (DPN; oral)
Zimislecel/VX-880 (T1D)	• **Complete enrollment and dosing in pivotal trial Q2:25;** potential **for global regulatory submissions in 2026**, after patients achieve insulin independence and reach 1 year of insulin-free follow-up
Inaxaplin (AMKD)	• **Complete enrollment in IA cohort in 2025; following 48 weeks of treatment;** potential to file for U.S. accelerated approval
Povetacicept (IgAN, etc.)	• **IgAN: Completed enrollment in IA cohort**; following 36 weeks of treatment, potential to file for U.S. accelerated approval in H1:2026 • **pMN: Initiate Phase 2/3 pivotal trial in H2:2025** • **Other autoimmune renal/cytopenia indications:** results from additional cohorts in RUBY-3/RUBY-4 Phase 2 basket studies in 2025
VX-407 (ADPKD)	**Begin Phase 2 proof-of-concept study in ADPKD patients in H2:2025**
VX-670 (DM1)	**Advance MAD portion of Phase 1/2 study in DM1 patients**, which will evaluate both safety and efficacy

First Quarter 2025 Financial Results

May 5, 2025

Appendix A

GAAP to non-GAAP Financial Information

($ in millions except as noted, per share data and percentages)	Q1:24	FY:24	Q1:25
Combined R&D, Acquired IPR&D and SG&A			
GAAP	1.21B	9.72B	**1.40B**
Non-GAAP	1.02B	8.82B	**1.23B**
Operating income			
GAAP	1.14B	(233)	**630**
Non-GAAP	1.34B	696	**1.18B**
Operating Margin %:			
GAAP	42%	(2)%	**23%**
Non-GAAP	50%	6%	**43%**
Net income			
GAAP	1.10B	(536)	**646**
Non-GAAP	1.24B	111	**1.05B**
Net income per share – diluted			
GAAP	$4.21	$(2.08)	**$2.49**
Non-GAAP	$4.76	$0.42	**$4.06**
Shares used in diluted per share calculations			
GAAP	261.1	257.9	**259.5**
Non-GAAP	261.1	260.9	**259.5**

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, non-GAAP net income and non-GAAP net income per share – diluted to corresponding GAAP measures are included in the company's Q1:25 and Q4:24 press releases dated May 5, 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)	Peripheral neuropathic pain	Suzetrigine	Small molecule NaV1.8 inhibitor	>10M
	AMKD	Inaxaplin	Small molecule inhibitor	~250,000
	T1D	Zimislecel Other approaches	Cell and gene therapy	~ 60,000 w/initial filing* ~3.8M
	IgA nephropathy	Povetacicept	Fusion protein	~300K U.S./Europe >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***

*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 ~10%) of the overall patient population.