Third Quarter 2025 Financial Results

November 3, 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 “Updated 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 commercial launches, advancement of mid- and late-stage programs, relevant estimated and increased eligible patient populations, expectations with respect a rapidly advancing clinical portfolio and the status of "five launches over five years (by 2028)," and expectations for revenue contributions from CASGEVY, ALYFTREK, and JOURNAVX, (ii) beliefs regarding Vertex’s CFTR modulators, including with respect to life-transforming potential, continued growth from our portfolio of CF medicines and long-standing goals, (iii) expectations regarding ALYFTREK, including related to commercial launch progress, clinical benefits, targeted populations for initiations and beliefs around patients transitioning to ALYFTREK from TRIKAFTA/KAFTRIO, (iv) expectations regarding the clinical trials evaluating TRIKAFTA in younger children and potential to file for approval with global regulators in H1:2026, (v) expectations for Vertex’s CF pipeline programs, including those related to the potential benefits of VX-828 as the most efficacious CFTR corrector and to the resumed VX-522 study, (vi) expectations with respect to povetacicept, including with respect to therapeutic scope, clinical benefits, pipeline-in-a-product potential, best-in-class potential, and clinical progress and regulatory success for IgAN and pMN, including plans to begin BLA submission by year-end for IgAN and to complete submission in H1:2026 for accelerated approval in the U.S. if the results of interim analysis are supportive, (vii) expectations and commercial outlook for CASGEVY, including global launch momentum and growing numbers of patients through year-end and beyond, and expectations for CASGEVY Phase 3 trials in children, (viii) status and beliefs regarding the commercial launch progress for JOURNAVX, including expectations to increase formal coverage by adding the third largest national PBM, to expand coverage across commercial and government payors through year-end and into 2026, to extend Vertex’s patient support program into 2026, and plans to add 150 additional JOURNAVX representatives in Q1:2026, and expectations around sales volume, revenue, and clinical unmet need, (ix) expectations with respect to the Phase 4 clinical trials of JOURNAVX in acute pain and plans to share the interim analysis at an upcoming medical conference, (x) expectations and beliefs regarding Vertex’s kidney portfolio, the aim for Vertex to be a leader in renal medicine and that Vertex’s renal franchise will become a significant growth driver and value generator over the next several years, (xi) expectations with respect to the completion of dosing in the ongoing Phase 3 clinical trial evaluating zimislecel in T1D, (xii) expectations for VX-407 in ADPKD, (xiii) expectations with respect to inaxaplin in AMKD, including with respect to potential accelerated approval in the U.S., clinical progress of the AMPLIFIED study, including plans to complete enrollment by year-end, (xiv) expectations for the ongoing Phase 3 trial of suzetrigine in DPN, plans to initiate a second trial in November 2025, and plans to complete enrollment in both trials by the end of 2026, (xv) plans to continue progressing the Phase 2 clinical trial of VX-993 study in DPN, and (xvi) plans to continue to advance the Phase 1/2 study of VX-670 in DM1 patients and expectations to complete enrollment and dosing in the MAD portion in H1:2026. 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 Q3:25 and Q4:24 press releases dated November 3, 2025, and February 10, 2025.

Vertex delivered strong Q3:25 results with 11% growth Y/Y and continued pipeline advancement

Expand CF leadership

- Complete studies in **lower age groups** with **approved CFTR medicines**
  - TRIKAFTA 1–2-year-old study completed; mean sweat chloride reduction of more than 70 mmol/L from baseline through week 24, largest reduction with any CFTR modulator in any population to date
- **VX-828** combo (next-gen 3.0 CFTRm regimen): Initiated CF patient cohort
- **VX-522** (CFTR mRNA): Resumed dosing in MAD portion of Ph 1/2 study

Execute new launches and diversify revenue

alyftrek™ casgevy® JOURNAVX™ (suzetrigine)

Advance mid- and late- stage pipeline

- **Suzetrigine (DPN):** Initiate second DPN Ph 3 this month; complete enrollment of both DPN studies by YE '26
- **Inaxaplin (AMKD):** Completed enrollment in Ph 3 AMPLITUDE IA cohort; on track to complete Ph 2 AMPLIFIED enrollment by YE ‘25
- **Povetacicept (IgAN):** RAINIER Ph 3 fully enrolled; FDA granted Breakthrough Therapy Designation and rolling review of BLA submission; on track to initiate submission before YE ‘25 & complete in H1:26 for potential U.S. accelerated approval
- **Povetacicept (pMN):** Received Fast Track Designation in U.S.; initiated Ph 2/3 pivotal trial
- **VX-407 (ADPKD):** Initiated Ph 2 POC
- **Zimislecel (T1D):** Ph 3 fully enrolled; temporarily postponed completion of dosing pending internal manufacturing analysis

Deliver strong financial performance

- Q3:25 revenue $3.08B; refined 2025 guidance to total revenue $11.9-12.0B, non-GAAP OpEx to $5.0-5.1B, and lowered tax rate guidance to 17%-18% to incorporate several one-time benefits
- Drive revenue growth: CF as foundation, increasing contributions from CASGEVY and 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; 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., European Union, Canada, New Zealand and Switzerland

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
- Best CFTR modulator available for eligible patients: further improvement in CFTR function as measured by sweat chloride and indicated for 31+ additional rare mutations vs. TRIKAFTA
- Also offers convenience of once-daily dosing

Next-generation CFTRm
(N.G 3.0 regimen)

- VX-828 combination therapy:
  - Most efficacious CFTR corrector in the clinic that Vertex has ever studied *in vitro*
  - Initiated cohort in CF patients

VX-522

- CFTR mRNA approach for ~5,000 patients who cannot benefit from CFTRm
- Resumed dosing in MAD portion of Phase 1/2 study

N.G: next-generation; CFTRm: cystic fibrosis transmembrane conductance regulator modulator; MAD: multiple ascending dose.

TRIKAFTA for 12 to <24 months of age pivotal study now complete; largest sweat chloride reduction seen in any population to date

Absolute Change in SwCl (mmol/L) through Week 24

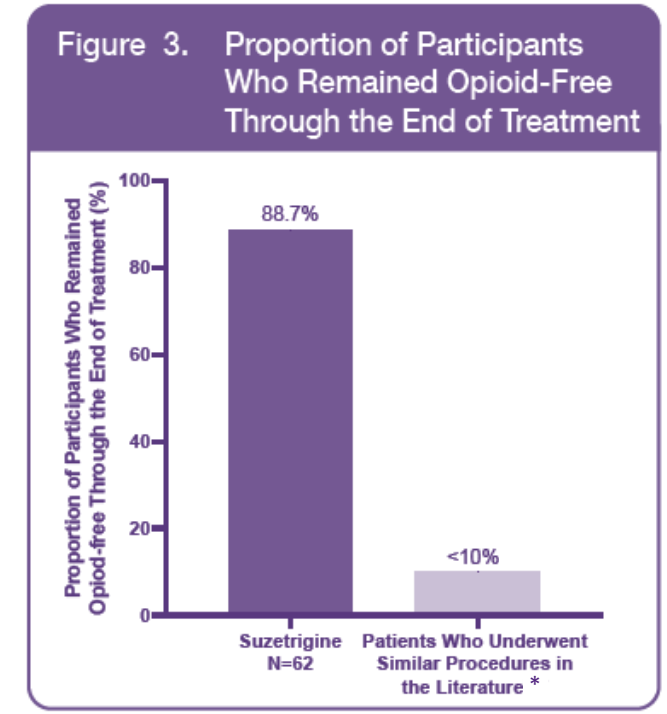
TRIKAFTA	1 – 2-year-olds N=54
Baseline, mean (SD)	99.1 (14.5)
Absolute change through Week 24	
LS mean (SE)	**-71.8 (1.8)**
95% CI	(-75.4, -68.2)
P value	<0.0001

- TRIKAFTA was **generally safe and well-tolerated** in children with CF 12 to <24 months of age
- Treatment with TRIKAFTA resulted in **rapid, robust, and clinically meaningful improvement**:
  - Sweat chloride reduction of -71.8 mmol/L through Week 24 (95% CI: (-75.4, -68.2); *P* < 0.0001)
  - Confirms greater restoration of CFTR function in younger age groups
- **~70% of patients achieved levels of sweat chloride < 30mmol/L "normal" threshold**
- **On track to file for approval with global regulators in H1:2026**

Pain program R&D highlights

- **Acute pain:**
- Completed enrollment in two Phase 4 trials evaluating suzetrigine, initiated pre-operatively and as part of multi-modal approaches to acute pain management
- Interim analysis for the first study (following aesthetic and reconstructive procedures) will be shared as a poster at the Annual Congress of Enhanced Recovery and Perioperative Medicine (ASER-PM) later this week
- **Neuropathic pain:**
- First DPN Phase 3 study is well underway
- Second DPN Phase 3 study to initiate this month

Topline results show safety and effectiveness consistent with the pivotal program, with substantial reductions in opioid use



Note: Rescue opioids: opioid analgesics that were taken orally between the end of surgery and the last dose of study drug.
*Literature-based data from different studies: Rose et al. Plastic and Reconstructive Surgery. 2019; Zorrilla et al. The American Journal of Cosmetic Surgery. 2022.

Rapid progress across the kidney portfolio with multiple programs now in mid- and late-stage clinical development

		PATIENTS[1]	RESEARCH	PHASE 1	PHASE 2	PHASE 3	APPROVED	
B cell driven renal diseases	Povetacicept – IgAN[2]	~300K (>750K China)			RAINIER			*Rolling BLA submission for AA to begin YE 2025 Full trial enrolled*
	Povetacicept – pMN[2]	~150K (>300K in China)			OLYMPUS			*Phase 2/3 pivotal trial initiated*
	Additional B cell mediated diseases[3]	TBD						
APOL1-mediated kidney disease (AMKD)	Inaxaplin – Primary AMKD	~150K			AMPLITUDE			*IA cohort enrollment complete*
	Inaxaplin – AMKD with moderate proteinuria or diabetes	~100K		AMPLIFIED				*On track to complete enrollment by YE '25*
Autosomal dominant polycystic kidney disease	VX-407[4]	Up to ~30K			aglow Clinical Study			*Proof-of-concept study underway*
	Serial innovation to reach all ADPKD patients	~300K (incl. 30K)						

1. Estimated patient population in the U.S. and Europe, unless otherwise noted. 2. IgAN and pMN patients continue to be studied in RUBY-3 3. Multiple programs in various phases. 4. Targets a patient population with a subset of variants in the *PKD1* gene.
IgAN: IgA nephropathy; pMN: primary membranous nephropathy.

Povetacicept: Rapid clinical progress and regulatory success across multiple indications

Potential transformative benefit	• **Certain autoimmune diseases are driven by uncontrolled B cells** • Pove specifically engineered for better tissue distribution and to deliver optimized, targeted dual inhibition of the BAFF and APRIL cytokines • BAFF and APRIL play a key role in the pathogenesis of B cell-mediated autoimmune diseases
IgAN: RAINIER Phase 3 trial full enrollment complete	• Pove 80mg vs placebo on top of standard of care ✓ Completed interim analysis cohort enrollment in Q2:25 ✓ FDA granted Breakthrough Therapy Designation and rolling review of BLA filing ✓ Completed studies to launch with at-home administration: monthly, low volume, via sub-Q autoinjector ✓ Completed full enrollment (n=~600) in ~15 months • **BLA submission to begin by YE:2025; if IA is positive, complete submission in H1:2026 for potential U.S. accelerated approval**
pMN: OLYMPUS Phase 2/3 trial now underway	• **Pivotal trial in pMN underway**, second renal indication • Granted Fast Track Designation in the U.S. • ~150K patients in U.S. and EU, ~500K globally • No approved therapies that treat the underlying cause of this disease

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

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 Ongoing & planned	Approved
Improved conditioning CASGEVY – SCD & TDT	**Follow-on molecules:** • CF • Pain • AMKD	**VX-993** DPN	**Zimislecel** Type 1 diabetes	JOURNAVX™ (suzetrigine)
$Na_V1.7$ inhibitor Pain		**VX-522** CFTR mRNA	**Povetacicept** IgA nephropathy	alyftrek™
Islet cells + alt. IS **Islet cells + device** **Hypoimmune islet cells** Type 1 diabetes		**VX-670** DM1	**Povetacicept** pMN	casgevy®
Small molecule Huntington's disease		**Povetacicept** gMG, wAIHA*	**Suzetrigine**** DPN	trikafta®
		VX-407 ADPKD	**Inaxaplin** AMKD	symdeko®
		VX-828 Cystic fibrosis		ORKAMBI®
				kalydeco®

*Next potential indications for povetacicept. Other RUBY-3 and RUBY-4 indications have been deprioritized.
**Second pivotal DPN trial to begin this month (Nov).
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; DPN: diabetic peripheral neuropathy; CFTR mRNA: cystic fibrosis transmembrane conductance regulator messenger RNA; DM1: myotonic dystrophy type 1; pMN: primary membranous nephropathy; gMG: generalized myasthenia gravis; wAIHA: warm autoimmune hemolytic anemia.

ALYFTREK: Approved for ages 6+ in U.S., U.K., EU, Canada, New Zealand and Switzerland

U.S. launch progressing well across all patient groups;
OUS early launch off to a strong start in multiple markets

INITIATE

- Newly eligible patients
- Discontinued patients

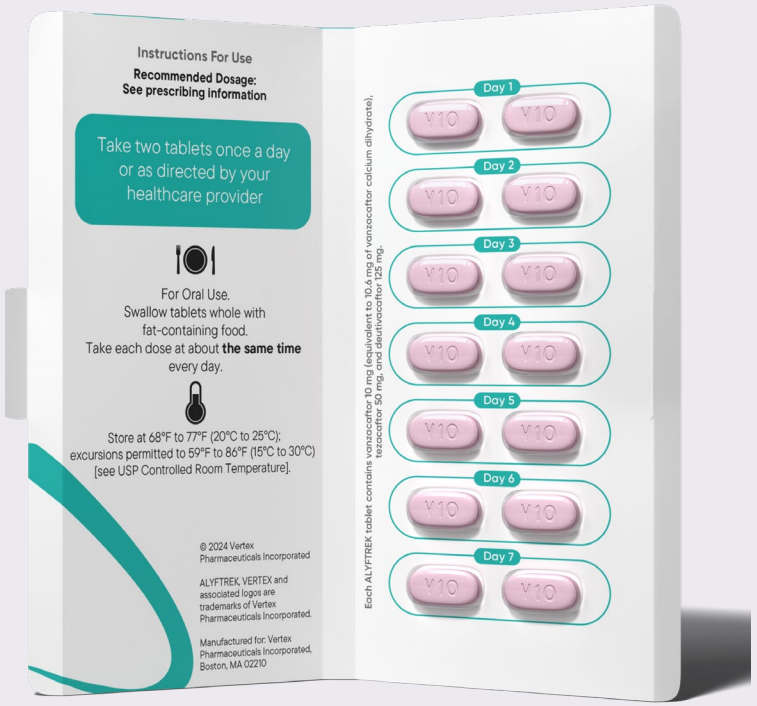
- Rapid uptake in patients naïve to CFTR modulators
- Vast majority of previously untreated patients in U.S. have initiated ALYFTREK

TRANSITION

- Current TRIKAFTA/KAFTRIO patients
  - Improved CFTR function
  - More convenient dosing

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

alyftrek™
(vanzacaftor/tezacaftor/deutivacaftor)



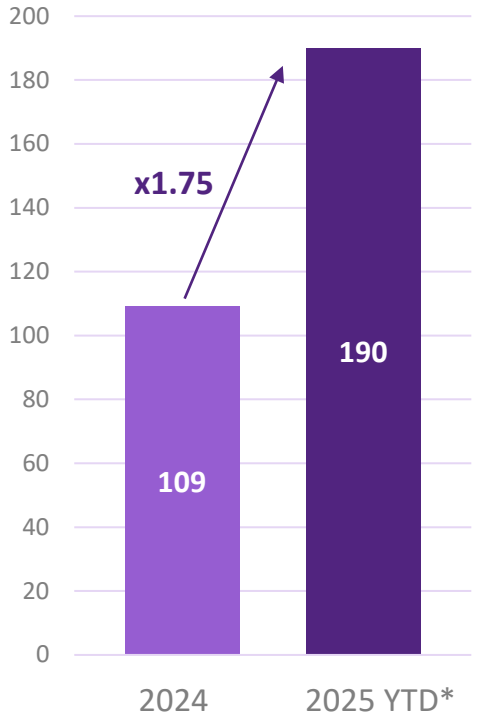
ALYFTREK: A highly efficacious, once-daily CFTR modulator delivering equivalent improvement in lung function* and greater CFTR function vs. TRIKAFTA**

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

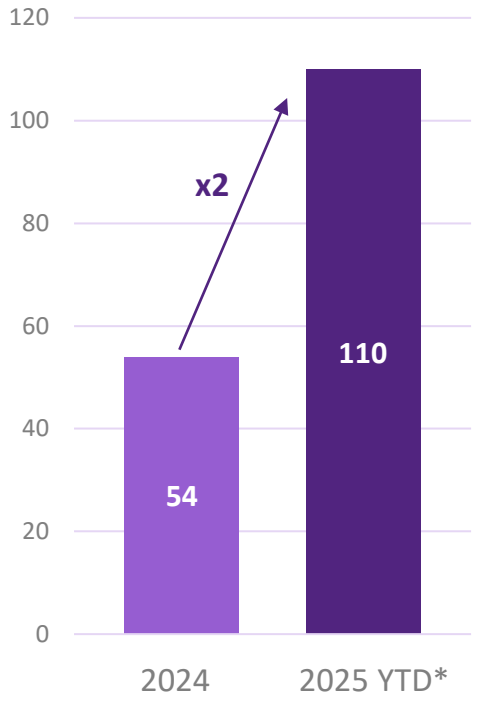
CASGEVY momentum continues to build

Expect $100M+ in CASGEVY revenue for FY 2025

Patients Initiated



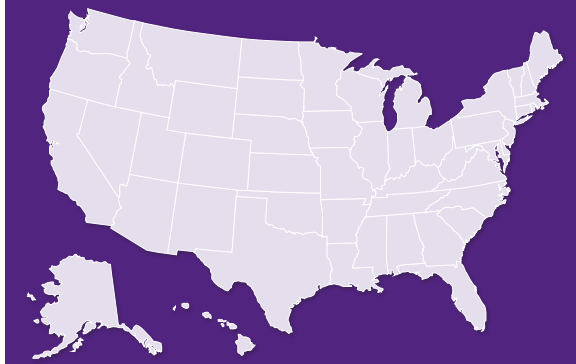
1st Cell Collections



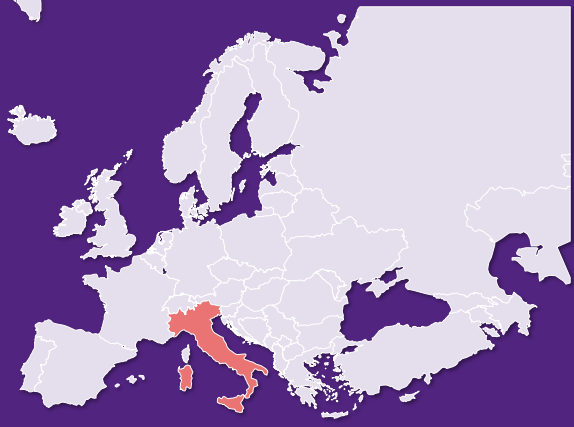
39 patients have completed treatment with CASGEVY since launch, including 10 patients in Q3:2025

*As of September 30, 2025

Infusions occurring in all regions for both sickle cell disease and transfusion dependent beta thalassemia; at least one ATC in each region has initiated 20 or more patients

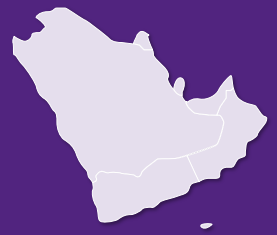


United States



United Kingdom & Europe

National Reimbursement Oct 2025



Middle East (Gulf Cooperation Council)

JOURNAVX: Ongoing launch delivering strong reception across the board

JOURNAVX™
(suzetrigine)

Rapid progress with payers*

- **~170 million covered lives with reimbursed access to JOURNAVX**
- Formal coverage gained with 2 out of 3 large national pharmacy benefit managers (PBMs)
- 19 state Medicaid plans passed legislation to support access to non-opioids including JOURNAVX, without prior authorization or step edit requirement

Advancing hospital access

- ~90 of the targeted 150 large healthcare systems and >750 individual hospitals of the targeted 2,000 institutions have added JOURNAVX to formularies, protocols or order sets

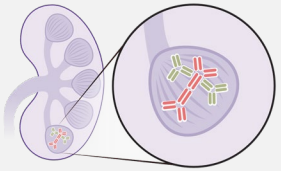
Broad adoption of JOURNAVX

- Wide range of physicians using JOURNAVX in broad range of acute pain types and care settings
- Promotionally responsive to representative calls and digital engagement of HCPs
- **>300,000 prescriptions successfully filled to date** (through mid-October)

*Payer/coverage statistics as of mid-October; ~170 million covered lives reflect both commercial and government payers.

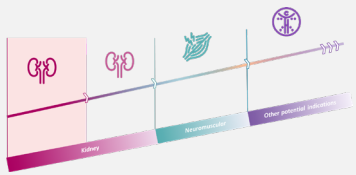
Povetacicept is a dual BAFF + APRIL inhibitor with best-in-class potential

Engineered for high tissue distribution, target affinity and potency



In clinical data to date, pove has an excellent benefit:risk profile with substantial reductions in Gd-IgA1, hematuria and proteinuria

Differentiated dosing: every four weeks at home
subcutaneous auto-injector
small volume (<0.5 mL)



Pipeline-in-a-product potential for optimal B cell control in multiple B cell-mediated autoimmune diseases

2 renal diseases in pivotal development: IgAN, pMN

Q3 2025 financial highlights

($ in millions except where noted or per share data and percentages)	Q3:24	FY:24	**Q3:25**
TRIKAFTA/KAFTRIO	2.59B	10.24B	**2.65B**
ALYFTREK	–	–	**247**
Other product revenues*	187	782	**176**
Total revenues	$2.77B	$11.02B	**$3.08B**
Combined non-GAAP, Acquired IPR&D and SG&A expenses	1.08B	8.82B	**1.28B**
Non-GAAP operating income	1.31B	696	**1.38B**
Non-GAAP operating margin %	47%	6%	**45%**
Non-GAAP net income	1.14B	111	**1.24B**
Non-GAAP net income per share – diluted	$4.38	$0.42	**$4.80**
Cash, cash equivalents & total marketable securities (period-end)	$11.2B	$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, non-GAAP net income and non-GAAP net income per share – diluted to corresponding GAAP measures are included in the company's Q3:25 and Q4:24 press releases dated November 3, 2025, and February 10, 2025, respectively. 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. *Q3:25 includes $17 million CASGEVY revenues and $20M JOURNAVX revenues. Q3:24 and FY:24 includes $2M and $10M CASGEVY revenues, respectively.

Updated full year 2025 financial guidance

	Current FY 2025 Guidance	Previous FY 2025 Guidance	Commentary
Total Revenue	$11.9 - 12.0B	$11.85 - $12.0B	Full year revenue guidance assumes continued growth in CF, including the global launch of ALYFTREK; continued uptake of CASGEVY; and early contributions from the U.S. launch of JOURNAVX.
Combined GAAP R&D, Acquired IPR&D and SG&A Expenses	$5.65 - 5.8B	$5.55 - $5.7B	Revised outlook accounts for acceleration of povetacicept programs and increased investments in sales and marketing initiatives for JOURNAVX. Full year outlook continues to include ~$100M of AIPR&D expenses.
Combined Non-GAAP R&D, Acquired IPR&D and SG&A Expenses	$5.0 - 5.1B	$4.9 - $5.0B	
Non-GAAP Effective Tax Rate	17% - 18%	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

TRIKAFTA (CF)	Completed pivotal study for 12 to <24 months of age; **file for approval with global regulators in H1:2026**
ALYFTREK (CF)	**Continue to drive launch in U.S. and initiate OUS launch in 6+ yo** Complete Phase 3 study in children ages 2-5 years
VX-522 (CF)	Continue to enroll and dose in the MAD portion of the Phase 1/2 study
Next-generation 3.0 (CF)	**VX-828: CF patient cohort initiated**
CASGEVY (SCD/TDT)	• **Reach more eligible 12+ year-old patients** across geographies • Complete dosing in Phase 3 trials in 5–11-year-olds in Q4:2025
Suzetrigine (pain)	• **Acute: JOURNAVX – Continued U.S. launch** • **DPN:** Enroll and dose ongoing Phase 3 pivotal trial; **begin second DPN Phase 3** this month**; complete enrollment of** both studies by YE 2026
VX-993 (pain)	• **DPN: Continue to progress Phase 2 study**
Zimislecel/VX-880 (T1D)	• **Resume dosing,** once internal manufacturing review complete
Inaxaplin (AMKD)	• **AMPLITUDE: Completed enrollment in IA cohort**; following 48 weeks of treatment; potential to file for U.S. accelerated approval, if results supportive • **AMPLIFIED**: Complete enrollment of study by YE 2025
Povetacicept (IgAN, pMN)	• **IgAN: Submit first module of rolling BLA submission by YE 2025 and complete in H1 2026 for potential U.S. accelerated approval; full enrollment in RAINIER completed** • **pMN: Initiated Phase 2/3 pivotal trial;** received Fast Track Designation from FDA • **Other:** Prioritize gMG and wAIHA as next potential indications
VX-407 (ADPKD)	**Enroll and dose Phase 2 proof-of-concept study in ADPKD patients**
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

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November 3, 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)	Q3:24	FY:24	Q3:25
Combined R&D, Acquired IPR&D and SG&A			
GAAP	1.26B	9.72B	**1.48B**
Non-GAAP	1.08B	8.82B	**1.28B**
Operating income (loss)			
GAAP	1.12B	(233)	**1.19B**
Non-GAAP	1.31B	696	**1.38B**
Operating Margin %:			
GAAP	40%	(2)%	**39%**
Non-GAAP	47%	6%	**45%**
Net income (loss)			
GAAP	1.05B	(536)	**1.08B**
Non-GAAP	1.14B	111	**1.24B**
Net income (loss) per share – diluted			
GAAP	$4.01	$(2.08)	**$4.20**
Non-GAAP	$4.38	$0.42	**$4.80**
Shares used in diluted per share calculations			
GAAP	261.0	257.9	**257.6**
Non-GAAP	261.0	260.9	**257.6**

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 Q3:25 and Q4:24 press releases dated November 3, 2025, and February 10, 2025, respectively.

Appendix B

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 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 U.S./Europe >300K China
PIPELINE	DM1	VX-670	Oligonucleotide with cyclic peptide	~110,000
	CF	VX-522	mRNA	~5,000**
	ADPKD	VX-407 Other potential approaches	Small molecule corrector	Up to ~30K ~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.