Fourth Quarter and Full Year 2025 Financial Results

February 12, 2026

Presentation intended for the investment community

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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

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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 future financial and operating performance and statements regarding (i) expectations, goals, development and commercialization plans and timelines for the company's products, product candidates and pipeline programs, including beliefs regarding the emerging renal business, multiple launch opportunities, treatable patient populations, and additional opportunities in mid-and-late stage programs, including more than 10 disease areas with multi-billion dollar market potential, (ii) expectations for sustained growth with respect to the company's CF medicines, including with respect to the ongoing commercial launch of ALYFTREK, that the majority of eligible CF patients will switch from TRIKAFTA to ALYFTREK over time, treating younger patients, filing for approval for TRIKAFTA in patients 1 to 2 years of age in H1 2026, initiating global regulatory submissions in H1 2026, CF population growth and patients living longer, reaching additional geographies, the goal to advance additional small molecules to be able to bring all eligible patients to carrier levels of CFTR function, and extending the CF portfolio's market leadership with IP through 2040, (iii) plans to complete dosing in the MAD portion of the Phase 1/2 study of VX-522 to reach the ~5,000 CF patients who cannot benefit from a CFTRm and data in H2 2026, expectations to complete enrollment and dosing in the CF patient cohort for VX-828 in H1 2026, and plans to advance other next-generation CF compounds, (iv) expectations for CASGEVY, including with respect to the acceleration of patient infusions, CASGEVY's commercial potential, including as a potential multi-billion dollar franchise, reaching more eligible patients and treating younger patients, expanding patient access to CASGEVY in new countries, initiating submissions for regulatory approval for 5 to 11 year olds in H1 2026, beliefs regarding transformative patient outcomes and survival rates, and the potential to improve conditioning associated with CASGEVY, (v) expectations for JOURNAVX in 2026, including with respect to prescription and revenue growth in the U.S., the expansion of the number of covered lives and scaling the number of hospitals with pathways to JOURNAVX, converting prescriptions to revenue, doubling the commercial field team, targeting more than 3x prescription growth, and plans to file for regulatory approval in Canada H1 2026, (vi) expectations for the pain program, including plans to complete enrollment in both ongoing studies evaluating suzetrigine in DPN by the end of 2026 and to continue to progress the Phase 2 study of VX-993 in DPN, (vii) expectations regarding povetacicept in IgAN, including expectations to complete the BLA submission in H1 2026, if results are supportive, and secure accelerated approval in the U.S., and the company's beliefs regarding the clinical benefits of povetacicept in IgAN, including as a potential best-in-class asset, and for the potential launch of povetacicept in IgAN, (viii) expectations regarding the company's capabilities and potential leadership in renal medicine, including with respect to development and commercialization, and beliefs with respect to povetacicept as a potential a pipeline-in-a-product, povetacicept's clinical benefits and potential to treat additional B cell driven renal and other non-kidney diseases, and with respect to expectations to complete the Phase 2 portion of study in pMN and initiate Phase 3 in mid-2026, and to initiate a Phase 2 study in gMG in H1 2026, (ix) expectations for the T1D program, including with respect to zimislecel as a potentially curative treatment, and expectations to resume dosing in the Phase 1/2/3 study once internal manufacturing review is complete, (x) expectations for inaxaplin, including with respect to data from the Phase 3 interim analysis of AMPLITUDE at year end 2026 or in early 2027, filing for U.S. accelerated approval if results are supportive, and complete full enrollment in AMPLITUDE in H2 2026, and expectations to share data from AMPLIFIED by mid-2026, (xi) expectations for the clinical development of VX-407 in ADPKD, including to complete enrollment in the AGLOW study by the end of 2026, and plans for serial innovation to reach all ADPKD patients, and (xii) expectations for VX-670 in DM1 patients, including with respect to completing enrollment and dosing in the Phase 1/2 clinical trial of VX-670 in DM1 by mid-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 the company's expectations regarding future revenues or expenses may be incorrect, that the company may be unable to further successfully commercialize its marketed products, that regulatory submissions or approvals may not occur on the anticipated timeline, or at all, that data from clinical trials, especially if based on a limited number of patients, may not to be indicative of final results, that anticipated commercial launches may be delayed, if they occur at all, actual patient populations eligible for the company's products may be smaller than anticipated, that data from the company's development programs may not be available on expected timelines, or at all, that data may not support registration or further development of its potential medicines due to safety, efficacy or other reasons, that external factors may have different or more significant impacts on the company's business or operations than the company currently expects, 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. 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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 Q4 2025 press release dated February 12, 2026.

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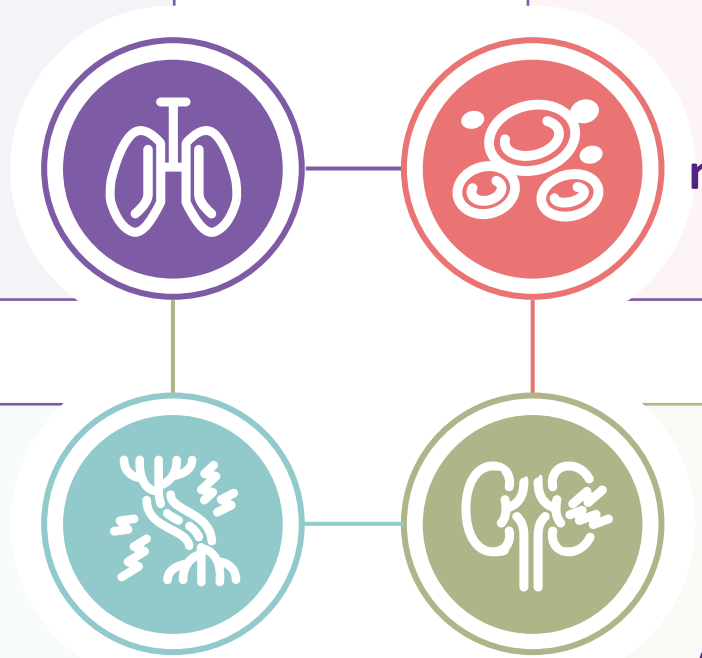
FY 2025 total revenue +9% Y/Y and creates strong base for 2026 commercial priorities

Cystic fibrosis portfolio

Continue to expand market leadership

CASGEVY

Leverage established global ATC network to drive patient infusions



JOURNAVX

Build on momentum of first year launch to grow Rx's and revenue

Povetacicept

Submit for U.S. Accelerated Approval; prepare to win with potential best-in-class asset

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ATC: Authorized treatment center

CF: Multiple factors extend leadership and drive sustained growth

Key CF Growth Factors

ALYFTREK launch	•Best CFTR protein function, as measured by sweat chloride, plus once-daily dosing •Approved for additional response mutations •Expect majority of patients to switch to ALYFTREK from TRIKAFTA over time
Younger patients	•Increases eligible population •TRIKAFTA: Target global regulatory submissions in patients ages 1-2 years, starting H1:26 •ALYFTREK: for patients ages 2-5 years, Phase 3 data demonstrated safety & efficacy, a 9.6 mmol/L reduction in sweat chloride from a TRIKAFTA baseline, and 65% of patients below carrier levels of sweat chloride; on track to initiate global regulatory submissions H1:26 •ALYFTREK: initiated study in patients ages 1 to <2 years
CF population growth	•CF patients are living longer •~3% CF population average annual growth rate 2020-2025[1]
Additional geographies	•Expanding beyond traditional core markets to new geographies •Brazil and Turkey
Additional therapies	•Serial innovation: NG 3.0 compounds, including VX-828 and VX-581 •VX-522 mRNA for last ~5,000 patients who do not make any CFTR protein; on track for data read-out in H2:26

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1. Vertex internal research

NG = next generation

Povetacicept: Potential best-in-class asset in IgAN

Specifically engineered to achieve improved…	RUBY-3 Phase 2 data demonstrated potential best-in-class profile	Differentiated monthly dosing and patient-centric features

✓ Binding affinity for BAFF + APRIL
✓ Potency
✓ Pharmacokinetics
✓ Tissue distribution, including the kidney
	✓ Reductions in
	  ✓ Proteinuria
	  ✓ Hematuria
	  ✓ Gd-IgA1
	✓ stable renal function (eGFR)
		✓ At-home administration
		✓ Subcutaneous autoinjector
		✓ Monthly dosing
		✓ Small volume (0.46mL)
		  ✓ 27 gauge needle
		  ✓ <1.5 second injection time

RUBY™-3

BLA submission for U.S. Accelerated Approval initiated Q4:25, on track to complete H1:26

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*Gd-IgA1: galactose deficient immunoglobulin-A1; eGFR: estimated glomerular filtration rate

Rapid progress across renal portfolio, with multiple near-term catalysts

		PATIENTS[1]	CURRENT PHASE	2026 MILESTONES
B cell driven renal diseases	Povetacicept – IgAN	~330K (>1.5M globally)	Phase 3 trial enrollment complete	• On track to complete submission H1:26 for U.S. AA, if results are supportive • Prepare for U.S. launch
	Povetacicept – pMN	~150K (>600K globally)	Phase 2/3 pivotal trial ongoing	• Complete Phase 2 portion and initiate Phase 3 mid-2026 ✓ Recently granted Orphan Drug status
Other non-kidney	Povetacicept – gMG	~175K (~300K globally)	Phase 2 trial initiating H1:26	• Initiate Phase 2 and drive enrollment
APOL1- mediated kidney disease (AMKD)	Inaxaplin – Primary AMKD	~150K	Phase 3 trial IA cohort enrollment complete	• Phase 3 IA results YE:26 or early 2027; file for U.S. AA thereafter, if results are supportive • Complete full trial enrollment H2:26
	Inaxaplin – AMKD with moderate proteinuria or diabetes	~100K	Phase 2 trial ongoing	• Share data mid-2026
Autosomal dominant polycystic kidney disease (ADPKD)	VX-407	Up to ~30K	Phase 2 trial	• Continue to enroll & dose patients
	Serial innovation to reach all ADPKD patients	~300K (incl. ~30K)	Research stage	• Progress research-stage assets

1. Estimated patient population in the U.S. and Europe, unless otherwise noted.

IgAN: IgA nephropathy; pMN: primary membranous nephropathy; gMG: generalized myasthenia gravis; IA: interim analysis; AA: accelerated approval

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R&D portfolio is broad, deep, and rapidly advancing

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	**VX-407** ADPKD	**Povetacicept** IgA nephropathy	JOURNAVX™ (suzetrigine)
$Na_V1.7$ inhibitor Pain		**VX-522** CFTR mRNA	**Povetacicept** pMN**	alyftrek™
Islet cells + alternative immunosuppression **Hypoimmune islet cells** Type 1 diabetes		**VX-670** DM1	**Suzetrigine** DPN (2 studies)	casgevy®
Small molecule Huntington's disease		**Povetacicept** wAIHA	**Inaxaplin** AMKD	trikafta®
		VX-993 DPN	**Zimislecel** Type 1 diabetes	symdeko®
		VX-828 Cystic fibrosis		ORKAMBI®
		Povetacicept gMG*		kalydeco®

*Phase 2 trial to initiate in H1:26. **In Phase 2 portion of Phase 2/3 trial.

SCD: sickle cell disease; TDT: transfusion-dependent beta thalassemia; alt. IS: alternative immunosuppression; CF: cystic fibrosis; AMKD: APOL1-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.

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CF: Q4 growth driven by multiple factors, including ALYFTREK launch and uptake in younger patients

U.S. highlights

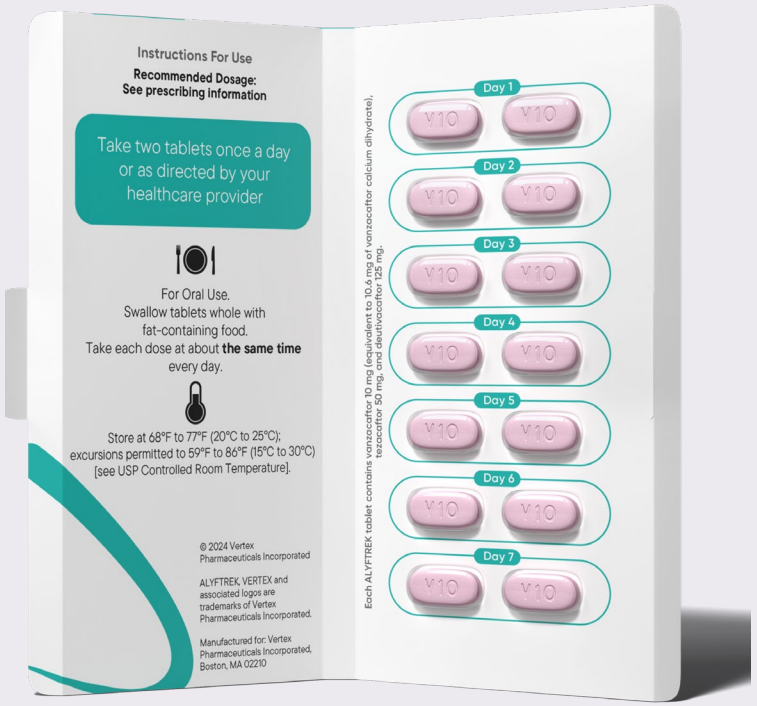
- ALYFTREK rollout continues to progress well
- Uptake in younger patients
- Higher net realized prices

OUS highlights

- ALYFTREK launches off to a strong start in EU
- Secured reimbursement access H2:25:
  - England, Wales, Northern Ireland, Ireland, Germany, Denmark, Norway
- Recently gained reimbursement in Australia, New Zealand and Italy
  - ~1,500 CF patients in Italy now able to access a CFTR modulator for the first time

alyftrek™

(vanzacaftor/tezacaftor/deutivacaftor)



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

OUS: Outside U.S. *Lung function as measured by improvements in ppFEV1 vs. TRIKAFTA. **CFTR function as measured by improvements in sweat chloride vs. TRIKAFTA.

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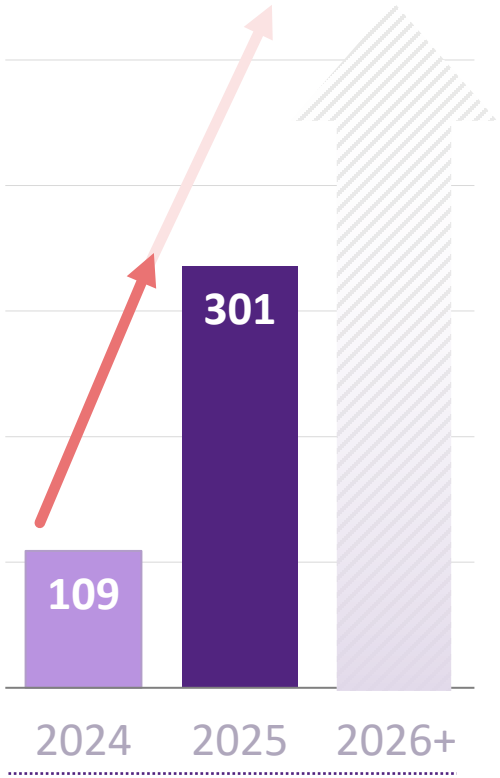
CASGEVY: Acceleration continues into 2026+ towards multi-$B potential

Delivered $116M CASGEVY revenue in FY 2025

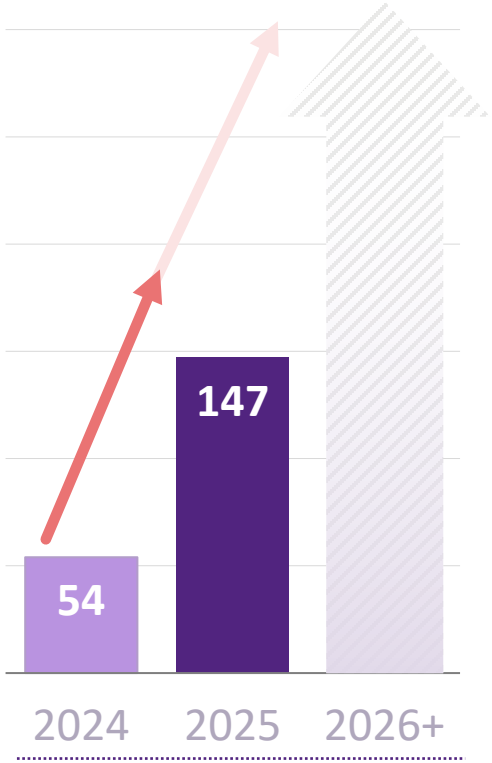
casgevy® (exagamglogene autotemcel) suspension for IV infusion

Patients initiated



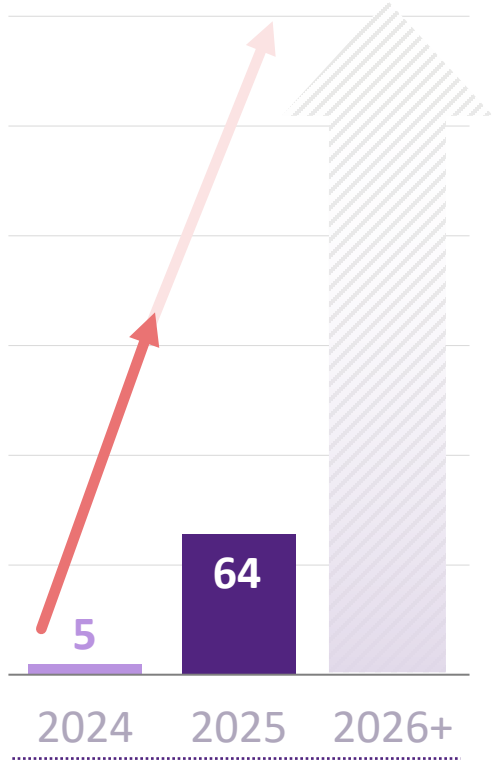
111 in Q4:25

1st Cell collections



37 in Q4:25

Cell infusions



30 in Q4:25

Accelerate patient infusions through existing global ATC network

Expand to younger patients

Broad coverage

U.S.: ~90% Medicaid & commercial

OUS: Access in 12 countries with more to come

Provide transformative patient outcomes*

+31 yrs survival SCD

+18 yrs survival TDT

>90% projected reduction in lifetime VOCs & RBCTs

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*VRTX data projections over a lifetime horizon from TDT and SCD models that apply CASGEVY clinical efficacy data from the U.S. prescribing information to a cohort of patients with TDT and SCD that are approximately 20 years old, based on mean age at baseline in CASGEVY pivotal trials. ATCs: Authorized Treatment Centers; VoCs: vaso-occlusive crises; RBCTs: red blood cell transfusions.

Pain: Transforming the standard of care for the treatment of acute pain

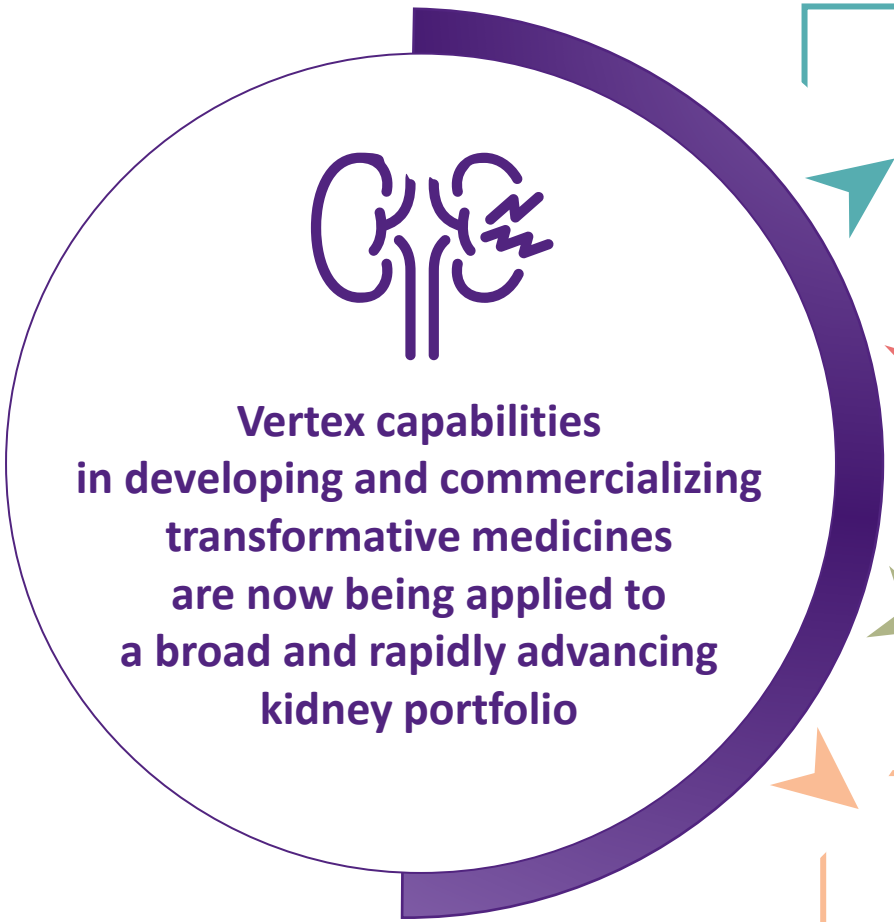
2025 execution positions JOURNAVX for significant growth in 2026 and beyond

JOURNAVX™ (suzetrigine)

	PAYERS	PRESCRIBERS	PATIENTS
2025	**>200M covered lives** **All 3 national PBMs* contracted** and **>950 hospitals** with access pathways	**>35K prescribers** **Excellent breadth** of prescribers and adoption across **multiple specialties**	**>550K prescriptions** **Strong early success** and positive reception from patients with surgical and non-surgical pain
2026	• Expand # of covered lives • Scale # hospitals with pathways • Convert Rx's to revenue	Double field team to drive HCP adoption and depth	Targeting >3x prescriptions vs. 2025

©2026 Vertex Pharmaceuticals Incorporated *Third national PBM contract effective 1/1/26. Hospital and ambulatory surgery center access pathways include formularies, order sets, and/or discharge protocols.

Renal: We plan to win in renal medicine, starting with pove in IgAN



Expertise in high-science sales informed by transformative therapies in CF, Heme, and moderate-to-severe Acute Pain; field force hiring well underway and first-contingent in the field

- Proven capabilities in **securing rapid & broad patient access**
- Completed engagement with 60+ payers representing ~190M covered lives in 2025

Comprehensive, dedicated patient support capabilities, informed by CF expertise

Establishing nephrology leadership with **pove pipeline-in-a-product potential,** including pMN**,** and additional programs in **AMKD** and **ADPKD**

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BIC: best-in-class; pMN: primary membranous nephropathy; AMKD: APOL1-mediated kidney disease; ADPKD: autosomal dominant kidney disease

Q4 and full year 2025 financial highlights

($ in millions except where noted or per share data and percentages)	Q4:24	FY24	Q1:25	Q2:25	Q3:25	Q4:25	FY25
TRIKAFTA/KAFTRIO	2.72B	10.24B	2.54B	2.55B	2.65B	**2.57B**	**10.31B**
ALYFTREK	-	-	54	157	247	**380**	**838**
Other product revenues*	191	782	171	236	176	**237**	**820**
Product revenues, net	2.91B	11.02B	2.76B	2.94B	3.08B	**3.19B**	**11.97B**
Other revenues	-	-	10	21	-	**-**	**31**
Total revenues	2.91B	11.02B	2.77B	2.96B	3.08B	**3.19B**	**12.00B**
Combined non-GAAP R&D, Acquired IPR&D and SG&A expenses	1.30B	8.82B	1.23B	1.24B	1.28B	**1.36B**	**5.12B**
Non-GAAP operating income	1.20B	696	1.18B	1.33B	1.38B	**1.37B**	**5.26B**
Non-GAAP operating margin %	41%	6%	43%	45%	45%	**43%**	**44%**
Non-GAAP net income	1.04B	111	1.05B	1.17B	1.24B	**1.29B**	**4.75B**
Non-GAAP net income per share – diluted	$3.98	$0.42	$4.06	$4.52	$4.80	**$5.03**	**$18.40**
Cash, cash equivalents & total marketable securities (period-end)	11.2B	11.2B	11.4B	12.0B	12.0B	**12.3B**	**12.3B**

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 press releases dated May 5, 2025, August 4, 2025, November 11, 2025, and February 12, 2026. 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. *Includes CASGEVY revenues of $8M Q4:24, $10M FY:24, $14M Q1:25, $30M Q2:25, $17M Q3:25, $54M Q4:25, $116M FY:25; JOURNAVX revenues of $1M Q1:25, $12M Q2:25, $20M Q3:25, $27M Q4:25, $60M FY:25.

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2026 financial guidance

	FY 2025 Actuals	FY 2026 Guidance	Commentary
Total Revenue	$12.00B	$12.95 - $13.1B	Full year revenue guidance includes expectations for continued growth in CF, as well as $500 million or more in revenue from non-CF products.
Combined GAAP R&D, Acquired IPR&D and SG&A Expenses*	$5.80B	$6.3 - $6.45B	Includes expectations for continued investment in multiple mid- and late-stage clinical development programs and commercial and manufacturing capabilities, as well as ~$100M of currently anticipated AIPR&D expenses.
Combined Non-GAAP R&D, Acquired IPR&D and SG&A Expenses*	$5.12B	$5.65 - $5.75B	
Non-GAAP Effective Tax Rate	17.3%	19.5% - 20.5%	

*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.

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Anticipated Key Milestones

TRIKAFTA (CF)	Completed pivotal study for 12 to <24 months of age; **begin global regulatory submissions in H1 2026**
ALYFTREK (CF)	**Continue to drive adoption in U.S. and execute ongoing OUS launches in 6+ year olds** Following positive data from Phase 3 study in **children ages 2-5 years, initiate global regulatory submissions in H1 2026** Advance Phase 3 study in patients ages 1-2 years
VX-522 (CF)	Complete dosing in the MAD portion of the Phase 1/2 study; **share data in H2 2026**
Next-generation 3.0 (CF)	**VX-828:** Complete enrollment and dosing **in H1 2026**; advance VX-581 and other next-generation 3.0 candidates
CASGEVY (SCD/TDT)	• **Reach more eligible patients ages 12+ year-old and accelerate infusions** through global ATC network • **Initiate global regulatory submissions in patients ages 5-11 H1 2026;** received FDA Commissioner's National Priority Voucher
Suzetrigine (pain)	• **Acute: Leverage first year JOURNAVX success to drive Rx & revenue growth in U.S. launch;** file in Canada in H1 2026 • **DPN: Complete enrollment of both Phase 3 studies by YE 2026**
VX-993 (pain)	• DPN: Continue to progress Phase 2 study
Zimislecel/VX-880 (T1D)	• **Resume dosing** post completion of internal manufacturing review
Inaxaplin (AMKD)	• **AMPLITUDE: share data from Phase 3 interim analysis in late 2026 or early 2027;** complete full enrollment in H2 2026 • **AMPLIFIED** (AMKD patients with moderate proteinuria or diabetes): share data mid-2026 in this expanded population
Povetacicept (IgAN, pMN)	• **IgAN: First module of BLA submitted; complete submission of BLA in H1 2026 for potential U.S. accelerated approval; prepare for launch** • **pMN:** Continue to enroll and dose Phase 2/3 pivotal trial; **complete Phase 2 portion of study and initiate Phase 3 in mid-2026** • **gMG: Initiate gMG Phase 2 study H1 2026**
VX-407 (ADPKD)	**Complete enrollment in the AGLOW Phase 2 proof-of-concept study by the end of 2026**
VX-670 (DM1)	**Complete enrollment and dosing of DM1 patients in the Phase 1/2 study mid-2026**

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Appendix

GAAP to non-GAAP Financial Information

(in millions except per share amounts and percentages)	Q4:24	FY24	Q1:25	Q2:25	Q3:25	Q4:25	FY25
Combined R&D, Acquired IPR&D and SG&A							
GAAP	1.46B	9.72B	1.40B	1.41B	1.48B	**1.52B**	**5.80B**
Non-GAAP	1.30B	8.82B	1.23B	1.24B	1.28B	**1.36B**	**5.12B**
Operating income (loss)							
GAAP	1.03B	(233)	630	1.15B	1.19B	**1.21B**	**4.17B**
Non-GAAP	1.20B	696	1.18B	1.33B	1.38B	**1.37B**	**5.26B**
Operating Margin %:							
GAAP	35%	(2)%	23%	39%	39%	**38%**	**35%**
Non-GAAP	41%	6%	43%	45%	45%	**43%**	**44%**
Net income (loss)							
GAAP	913	(536)	646	1.03B	1.08B	**1.19B**	**3.95B**
Non-GAAP	1.04B	111	1.05B	1.17B	1.24B	**1.29B**	**4.75B**
Net income (loss) per share – diluted							
GAAP	$3.50	$(2.08)	$2.49	$3.99	$4.20	**$4.65**	**$15.32**
Non-GAAP	$3.98	$0.42	$4.06	$4.52	$4.80	**$5.03**	**$18.40**
Shares used in diluted per share calculations							
GAAP	260.5	257.9	259.5	258.9	257.6	**256.1**	**258.0**
Non-GAAP	260.5	260.9	259.5	258.9	257.6	**256.1**	**258.0**

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 press releases dated May 5, 2025, August 4, 2025, November 11, 2025, and February 12, 2026.

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