




VERTEX

THE SCIENCE *of* POSSIBILITY

FOURTH QUARTER AND FULL YEAR 2024 FINANCIAL RESULTS

FEBRUARY 10, 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

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 “2025 Financial Guidance”, expectations for financial performance in Q1 2025, and statements regarding (i) expectations, development plans and timelines for the company’s products and pipeline programs, including expectations for preparation of additional launches, achievement of key enrollment milestones in 2025, advancement of multiple programs across multiple modalities, and relevant estimated patient populations, expectations for "five launches in five years", and expectations to continue CF revenue growth with incremental sales from launches in new disease areas in 2025, (ii) expectations for CF programs, including expectations to continue to reach more eligible CF patients and expand into younger age groups with existing CF medicines, and the goal to achieve carrier level of CFTR function for all patients, (iii) expectations for ALYFTREK, including potential additional approvals in 2025, launch expectations, expectations for TRIKAFTA patients switching to ALYFTREK, and expectations regarding a lower royalty rate, (iv) expectations that VX-522 will reach the >5,000 CF patients who cannot benefit from a CFTR modulator, VX-522 study progress and plans to share data in the first half of 2025, and expectations for the next generation 3.0 CFTRm regimen, (v) expectations for the T1D programs, including beliefs regarding a potentially curative treatment and treatable patient population, expectations for completion of enrollment and dosing in the zimislecel Phase 1/2/3 pivotal trial and potential filing for U.S. approval assuming positive data, and plans for the VX-264 study, including plans to share data from Phase 1/2 Part B full dose in 2025, (vi) 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. if positive, expectations for the RUBY-3 and RUBY-4 Phase 2 basket studies, and expectations for Vertex's collaboration with Zai Lab to develop and commercialize pove, (vii) 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, (viii) expectations for CASGEVY, including building momentum in 2025 off a foundational year in 2024 and reaching more eligible patients across geographies with regulatory approval and access, expectations for a potential multi-billion dollar opportunity, expectations with respect to ATC activations and patient cell collections, plans to expand manufacturing to support global demand, and expectations for study in 5-11 year olds with SCD or TDT, (ix) 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, including broad stocking agreements at top three national retail pharmacies and key regional chains to ensure patient access, and expectations regarding strong policy tailwinds, (x) expectations for the studies of the intravenous and oral formulations of VX-993 in acute pain and DPN, (xi) expectations to complete enrollment in IA cohort of inaxaplin study in 2025 and the potential to file for U.S. accelerated approval, (xii) expectations for VX-407 in ADPKD, including regarding completion of Phase 1 study and potential advancement to Phase 2, and (xiii) 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, and (vi) 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 includes 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 2024 press release dated February 10, 2025.

VERTEX DELIVERED STRONG Q4:24 RESULTS WITH DOUBLE DIGIT REVENUE GROWTH FOR 10TH CONSECUTIVE YEAR

Expand CF leadership

- ✓ **ALYFTREK: approved in the U.S. for patients with CF ages 6+, launch underway**
- Increased epidemiology estimates for people with CF to 109,000 due primarily to patients living longer, plus additional geographies
- Next gen 3.0 CFTRm regimen (VX-828, VX-118, tez triple) expected to initiate clinical trial in patients with CF this year
- VX-522: MAD portion of Ph 1/2 ongoing to reach the >5,000 patients who cannot benefit from CFTRm

Drive commercial diversification

- CASGEVY: Building momentum in 2025 off foundational year in 2024 (>50 ATCs, >50 cell collections)
- ✓ **JOURNAVX: approved in the U.S. for moderate to severe acute pain, launch underway**
- Prepare for additional launches given four programs in Phase 3 pivotal development

Advance broad and deep clinical-stage pipeline

- Achieve key enrollment milestones in 2025 in three pivotal studies: zimislecel (T1D), povetacicept (IgAN), and inaxaplin (AMKD) + continue to advance suzetrigine Ph 3 (diabetic peripheral neuropathy)
- Advance multiple programs across multiple modalities: VX-993 (moderate to severe acute pain and PNP), VX-670 (myotonic dystrophy type 1), povetacicept (renal/heme basket studies), VX-407 (ADPKD)

Deliver strong financial performance

- Q4:24 product revenue +16% versus Q4:23; FY 2024 product revenue +12% versus FY 2023
- Continue CF revenue growth, with incremental sales from launches in new disease areas in 2025
- Sustain industry-leading operating margins while continuing to invest in pipeline internally and externally; 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; ADPKD: autosomal dominant polycystic kidney disease.

RECENT ACHIEVEMENTS AND ONGOING PROGRAMS TO SUSTAIN LONG TERM GROWTH

2

2 recent approvals

alyftrek™

For patients 6+ with CF

JOURNAVX™ (suzetrigine)

For adults with moderate to severe acute pain

3

3 key anticipated enrollment milestones in pivotal studies

- Zimislecel (T1D)
- Povetacicept (IgAN)
- Inaxaplin (AMKD)

4

4 ongoing pivotal trials

- Zimislecel (T1D)
- Povetacicept (IgAN)
- Inaxaplin (AMKD)
- Suzetrigine (DPN)

5

5 launches in 5 years (by 2028)

- ✓ CASGEVY (SCD)
- ✓ CASGEVY (TDT)
- ✓ ALYFTREK (CF)
- ✓ JOURNAVX (acute pain)
- Multiple options

T1D: type 1 diabetes; IgAN: immunoglobulin-A nephropathy; AMDK: APOL-1 mediated kidney disease; DPN: diabetic peripheral neuropathy; SCD: sickle cell disease; TDT: transfusion-dependent beta thalassemia

EXPANDING LEADERSHIP IN CF: ALYFTREK IS APPROVED IN THE U.S. RAISING THE BAR WITH SERIAL INNOVATION

kalydeco®	ORKAMBI®	symdeko®	trikafta®
Patients 1 month and older	Patients 1 year and older	Patients 6 years and older	NG 1.0 regimen, ages 2+

alyftrek™

- ✓ Now approved for ages 6+ in U.S.; potential to set new standard of CF care
- Serial innovation: 5th CF launch since 2012, NG 2.0 regimen
- Potential approvals 2025: UK, EU, Australia, New Zealand, Canada, Switzerland

Next-generation molecules

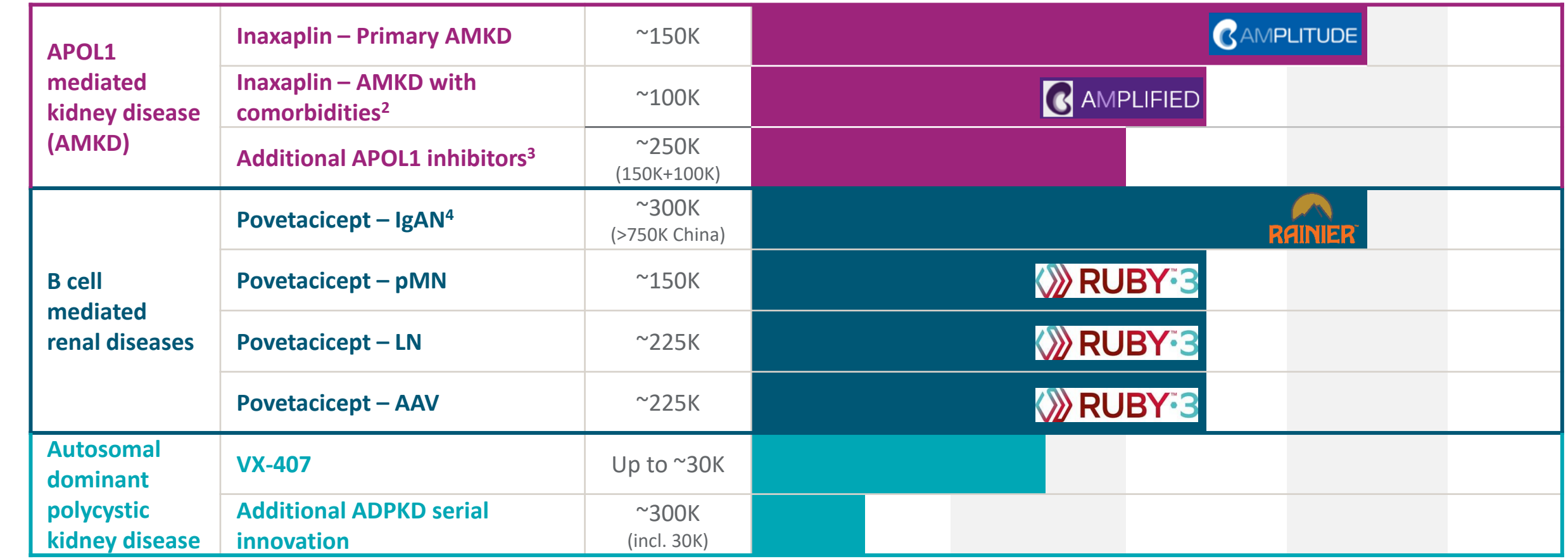
- Next generation 3.0 regimen:
  - Triple combo: VX-828 (CFTR corrector), VX-118 (CFTR potentiator), tezacaftor
  - Even greater potency and chloride transport in our HBE assays than ALYFTREK
  - We expect to be in the clinic in a study of CF patients this year

VX-522

- mRNA approach for <5,000 patients who cannot benefit from CFTRm
- MAD portion of the study is ongoing
- Data expected in H1:2025

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

RENAL: BROAD PIPELINE OF POTENTIALLY TRANSFORMATIVE MEDICINES IN MULTIPLE SERIOUS RENAL DISEASES



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

POVETACICEPT: GLOBAL PHASE 3 CLINICAL TRIAL IN IGAN UNDERWAY

POTENTIAL BEST-IN-CLASS APPROACH TO TREAT IGAN; ENROLLING AND DOSING PATIENTS IN NA, EUROPE, ASIA

Best-in-class potential

Strong preclinical profile:

- Dual BAFF/APRIL inhibitor 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:

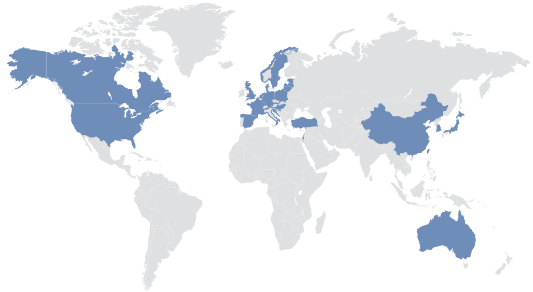
- Once every four weeks
- Subcutaneous
- Small volume

RAINIER global trial structure

RAINIER™

- **Pove 80mg vs placebo** on top of standard of care (n= ~480)
- Pre-planned **interim analysis (IA) when subset reaches 36 weeks** of therapy
  - Plan to complete IA cohort enrollment in 2025
  - Potential for accelerated approval

Enrollment/dosing underway



- **>100 clinical trial sites active** in >20 countries, across North America, Europe and Asia
- Strategic collaboration and licensing agreement with **Zai Lab** to develop and commercialize pove in China, Hong Kong, Macau, Taiwan and Singapore

*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.

VX-407 FOR ADPKD IS A FIRST-IN-CLASS PC1 CORRECTOR FOR A SUBSET OF VARIANTS IN *PKD1* GENE

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

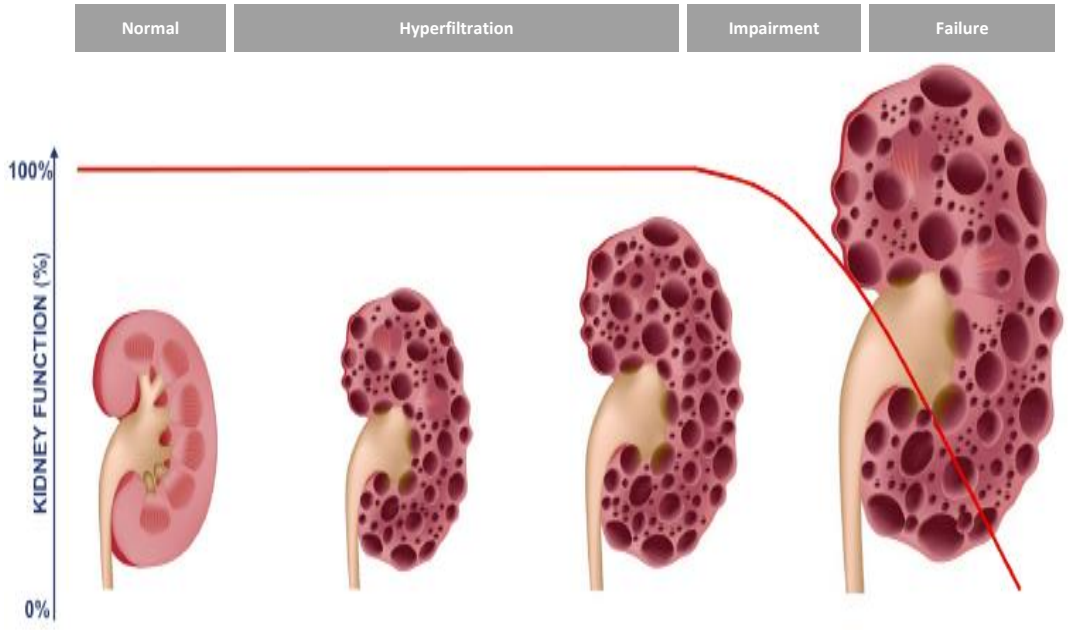
VX-407

- First-in-class, small molecule protein-folding corrector
- Designed to target 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

- Expect to complete Phase 1 HV study soon
  - If data are supportive, advance to Phase 2 study later this year

ADPKD: autosomal dominant polycystic kidney disease; HV: healthy volunteer

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



Goal: restore PC1 protein function in order to stop cyst growth, reduce total kidney volume and prevent progression to kidney failure

CLINICAL PORTFOLIO IS BROAD, DIVERSE AND RAPIDLY ADVANCING

ON TRACK TO MEET GOAL OF FIVE LAUNCHES OVER FIVE YEARS (2028)

Select, Next Wave Research-stage Programs	Phase 1 in Healthy Volunteers	Phase (1)/2 in Patients	Pivotal Development	Regulatory Submissions Completed or Underway	Approved
Improved conditioning CASGEVY – SCD & TDT	**Follow-on molecules:** • CF • Pain • AMKD	**VX-264 cells + device** Type 1 diabetes	**Inaxaplin** AMKD	**Exa-cel add'l geographies** SCD & TDT	JOURNAVX™ (suzetrigine)
$Na_V1.7$ inhibitor Pain	**VX-407** ADPKD	**Suzetrigine** LSR	**Suzetrigine** DPN	**Vanzacaftor triple add'l geographies** Cystic Fibrosis	alyftrek™
Hypoimmune islet cells Type 1 diabetes	**VX-993** Pain - Intravenous	**VX-993** Acute pain	**Povetacicept** IgA nephropathy		casgevy®
Small molecule Huntington's disease		**VX-993** PNP - DPN	**Zimislecel** Type 1 diabetes		trikafta®
		VX-522 CFTR mRNA			symdeko®
		VX-670 DM1			ORKAMBI®
		Povetacicept, RUBY-3 pMN, LN, AAV			kalydeco®
		Povetacicept, RUBY-4 ITP, AIHA, CAD			

SCD: sickle cell disease; TDT: transfusion-dependent beta thalassemia; CF: cystic fibrosis; AMKD: APOL-1 mediated kidney disease; ADPKD: autosomal dominant polycystic kidney disease; LSR: lumbosacral radiculopathy; PNP: peripheral neuropathic pain; DPN: painful 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. WITH POTENTIAL TO SET NEW STANDARD OF CF CARE

POTENTIAL APPROVALS IN UK, EU, AUSTRALIA, NEW ZEALAND, CANADA, SWITZERLAND IN 2025

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

INITIATE

~6,000 patients who discontinued prior CFTRm
~250 newly eligible patients with ultra-rare mutations

TRANSITION

current TRIKAFTA patients over time given
more convenient dosing and improved CFTR function

Launch Progress:

- Enthusiastic feedback from physicians and patients
- Prescriptions being written for both new patients and patients transitioning from TRIKAFTA
- Medicine is now available in pharmacies across the U.S.

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: FOUNDATIONAL 2024 BUILDS MOMENTUM FOR 2025 AND BEYOND FOR MULTI-$B OPPORTUNITY

Rapid pace of global approvals* underscores high unmet need and transformative potential of Casgevy

>50 ATCs activated and >50 cell collections initiated across U.S., Europe, Middle East**

Payer Highlights

OUS

Reimbursed access in multiple countries: U.K., Italy (EAP), Saudi Arabia, Bahrain

Achieved coverage agreement for SCD with NHS England

U.S.

Commercial – continue to provide access

Medicaid – single case agreements and First-ever CMMI Demonstration Project launched: *Cell & Gene Therapy Access Model*

Expanding manufacturing to support global demand

*Approved in U.S., UK, EU, Kingdom of Saudi Arabia, Bahrain, Canada, Switzerland, United Arab Emirates (12/31/24). **FY 2024

ATC: authorized treatment center; EAP: Early Access Program; CMMI: Center for Medicare and Medicaid Innovation.

JOURNAVX: LANDMARK U.S. APPROVAL FOR 1ST NON-OPIOID IN >20 YRS. INDICATED FOR MODERATE TO SEVERE ACUTE PAIN

Launch progress

Establish conditions for patient access and long-term commercial success

- **Healthcare providers & physicians:** salesforce engaging broadly
- **Institutions:** focus on ~2,000 high-volume hospitals/~150 related health systems; working to accelerate P&T committee processes
- **Non-personal promotional initiatives:** promoting broad awareness online, embedded content in relevant websites, point of care marketing

Early momentum with payers and retailers

- **Working with payers and GPOs to provide access:** build on pre-approval work to accelerate formulary reviews, limit inappropriate utilization management controls
- **Retailers:** working to secure broad JOURNAVX stocking agreements at national retail pharmacies and key regional chains to ensure patient access

Strong policy tailwinds

- **Federal legislation: NOPAIN Act** launched on Jan 1, provides Medicare add-on payment for non-opioids in outpatient/ASC setting; **Alternatives to Pain Act** expected to be reintroduced in the new Congress with broad bipartisan support
- **State legislation to support use of non-opioids**: enacted by 7 states in 2024 and already proposed by 17 states in 2025; more states expected to join the movement

Q4 AND FULL YEAR 2024 FINANCIAL HIGHLIGHTS

($ in millions except where noted or per share data and percentages)	Q4 23	FY 23	Q1 24	Q2 24	Q3 24	Q4 24	FY 24
Total product revenues	$2.52B	$9.87B	$2.69B	$2.65B	$2.77B	**$2.91B**	**$11.02B**
TRIKAFTA/KAFTRIO	2.33B	8.94B	2.48B	2.45B	2.59B	**2.72B**	**10.24B**
Other product revenues*	184	925	207	196	187	**191**	**782**
Combined non-GAAP R&D and SG&A expenses	984	3.71B	942	978	1.06B	**1.21B**	**4.19B**
Acquired IPR&D expenses	18	527	77	4.45B	15	**88**	**4.63B**
Non-GAAP operating income	1.15B	4.37B	1.34B	(3.15)B	1.31B	**1.20B**	**696**
Non-GAAP operating margin %	46%	44%	50%	(119)%	47%	**41%**	**6%**
Non-GAAP net income	1.10B	3.97B	1.24B	(3.31)B	1.14B	**1.04B**	**111**
Non-GAAP net income per share – diluted	$4.20	$15.23	$4.76	$(12.83)	$4.38	**$3.98**	**$0.42**
Cash, cash equivalents & total marketable securities (period-end)	$13.7B	$13.7B	$14.6B	$10.2B	$11.2B	**$11.2B**	**$11.2B**

Notes: An explanation of non-GAAP financial measures and reconciliation of combined non-GAAP R&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 Q4 2024 press release dated 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.
*Includes CASGEVY revenue of $2M in Q3:24, $8M in Q4:24, and $10M FY 2024.

2025 FINANCIAL GUIDANCE

	FY 2024 Actuals	FY 2025 Guidance	FY 2025 Commentary
Total Revenue	$11.02B	$11.75 - $12.0B	Includes expectations for continued growth in CF, including the U.S. launch of ALYFTREK; continued uptake of CASGEVY in multiple regions; 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	$9.72B	$5.55 - $5.7B	Ranges include approximately $100 million in currently anticipated IPR&D expenses.
Combined Non-GAAP R&D, Acquired IPR&D and SG&A Expenses	$8.82B	$4.9 - $5.0B	
Non-GAAP Effective Tax Rate	91%	20.5%-21.5%	

MULTIPLE CATALYSTS THROUGHOUT 2025

	ANTICIPATED KEY MILESTONES
ALYFTREK (CF)	**Drive U.S. launch; secure additional regulatory approvals and execute global launches**
VX-522 (CF)	Complete MAD portion of the Phase 1/2 study and **share data in 2025**
Next-generation 3.0 (CF)	**Triple combo: VX-828 (CFTR corrector), VX-118 (CFTR potentiator), and tezacaftor to enter the clinic in a study of CF patients this year**
CASGEVY (SCD/TDT)	• **Reach more eligible 12+ year old patients** across geographies with regulatory approval and access • Complete dosing for 5–11-year-olds with sickle cell disease or beta thalassemia
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 trial; advance pivotal program** • **PNP - LSR: Advance to Phase 3, pending regulatory discussions**
VX-993 (pain)	• **Acute: Advance Phase 2 study** (BUN; oral); complete Phase 1 IV • **PNP - DPN: Advance Phase 2 study** (DPN; oral)
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: complete enrollment in IA cohort in 2025**; following 36 weeks of treatment, potential to file for U.S. accelerated approval • **Other autoimmune renal/cytopenia indications:** Results from additional cohorts in RUBY-3/RUBY-4 Phase 2 basket studies in 2025
VX-407 (ADPKD)	**Complete Phase 1 study and initiate Phase 2 trial in ADPKD patients**
Zimislecel/VX-880 (T1D)	**Complete enrollment and dosing in Phase 1/2/3 pivotal trial** with potential to file for U.S. approval after patients reach 1 year of insulin-free follow-up, assuming positive data
VX-264 (T1D)	**Share data from Phase 1/2 Part B full dose in 2025**
VX-670 (DM1)	**Advance MAD portion of Phase 1/2 study in DM1 patients**, which will evaluate both safety and efficacy

 IA: interim analysis



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FEBRUARY 10, 2025

APPENDIX

GAAP TO NON-GAAP FINANCIAL INFORMATION

(in millions except per share amounts and percentages)	Q4 23	FY 23	Q1 24	Q2 24	Q3 24	Q4 24	FY 24
Combined R&D and SG&A							
GAAP	1.19B	**4.30B**	1.13B	1.34B	1.25B	1.38B	**5.09B**
Non-GAAP	984	**3.71B**	942	978	1.06B	1.21B	**4.19B**
Operating income							
GAAP	989	**3.83B**	1.14B	(3.51)B	1.12B	1.03B	**(233)**
Non-GAAP	1.15B	**4.37B**	1.34B	(3.15)B	1.31B	1.20B	**696**
Operating Margin %:							
GAAP	39%	**39%**	42%	(133)%	40%	35%	**(2)%**
Non-GAAP	46%	**44%**	50%	(119)%	47%	41%	**6%**
Net income							
GAAP	969	**3.62B**	1.10B	(3.59)B	1.05B	913	**(536)**
Non-GAAP	1.10B	**3.97B**	1.24B	(3.31)B	1.14B	1.04B	**111**
Net income per share – diluted							
GAAP	$3.71	**$13.89**	$4.21	$(13.92)	$4.01	$3.50	**$(2.08)**
Non-GAAP	$4.20	**$15.23**	$4.76	$(12.83)	$4.38	$3.98	**$0.42**
Shares used in diluted per share calculations							
GAAP	260.9	**260.5**	261.1	258.1	261.0	260.5	**257.9**
Non-GAAP	260.9	**260.5**	261.1	258.1	261.0	260.5	**260.9**

Note: An explanation of non-GAAP financial measures and reconciliation of combined non-GAAP R&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 Q4 2024 press release dated 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
NEAR-TERM APPROVAL	Acute Pain	Suzetrigine	Small molecule NaV1.8 inhibitor	~80M
IN PIVOTAL STUDIES	Peripheral neuropathic pain	Suzetrigine	Small molecule NaV1.8 inhibitor	>10M
	AMKD	Inaxaplin	Small molecule inhibitor	~250,000
	T1D	Zimislecel VX-264	Cell and gene therapy	~125,000 severe (60,000 v1*) ~3.8M
	IgA nephropathy	Povetacicept	Fusion protein	~300K U.S./Europe >750K China
PIPELINE	pMN	Povetacicept	Fusion protein	~150,000
	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 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.