First Quarter 2026 Financial Results

May 4, 2026

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 as defined in the Private Securities Litigation Reform Act of 1995, including, without limitation, the information provided regarding future financial and operating performance, including the statements under “Reiterate full year 2026 financial guidance,” and statements regarding (i) expectations, goals, development and commercialization plans and timelines for the company’s products, product candidates and pipeline programs, (ii) expectations to continue expand market leadership with respect to the company’s CF medicines, including with respect to treating younger patients, the progress of the ongoing commercial launch of ALYFTREK and continued uptake in younger patients, the clinical benefits of ALYFTREK, that the majority of eligible CF patients will switch from TRIKAFTA to ALYFTREK over time, initiating global regulatory submissions for ALYFTREK in patients 2 to 5 years of age in H1 2026, and advancing Phase 3 study of ALYFTREK in patients 1 to <2 years of age, (iii) expectations to complete enrollment and dosing and share results from the VX-828 study in H2 2026, and plans to advance other next-generation CF compounds, (iv) expectations regarding povetacicept in IgAN, including with respect to the company’s beliefs regarding the clinical benefits, safety, and potential as a best-in-class treatment for IgAN, securing accelerated approval in the U.S., for the potential launch of povetacicept in IgAN, including with respect to potential providers and capabilities of renal field force, expectations that approximately 70% of patients will have commercial coverage for povetacicept, and beliefs with respect to patient programs for access to povetacicept and treatment support, (v) expectations regarding the company's capabilities and potential leadership in renal medicine, including with respect to development and commercialization, beliefs with respect to povetacicept as a potential a pipeline-in-a-product, the clinical benefits and potential for povetacicept to treat additional B cell driven renal and other non-kidney diseases, with respect advancing the Phase 3 portion of study in pMN and enrolling and dosing patients in gMG study, (vi) expectations for CASGEVY, including with respect to the acceleration of patient infusions, CASGEVY’s commercial potential, including as a potential multi-billion dollar franchise and to contribute meaningfully to the $500 million revenue goal for non-CF products in 2026, reaching more eligible patients and treating younger patients, including with respect to the advancement of the pivotal study in patients 5 to <12 years of age, and expanding patient access to CASGEVY in new countries, (vii) expectations for JOURNAVX in 2026, including with respect to prescription and revenue growth in the U.S., transforming the standard of care for acute pain, the expansion of the number of covered lives, driving HCP adoption, progress towards more than 3x prescription growth in 2026 versus 2025, the anticipated benefits of being added to the NOPAIN List, and plans to file for regulatory approval in Canada H1 2026, (viii) 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, (ix) expectations for the T1D program, including with respect resumed dosing and sharing updated timelines for study completion in the coming months, (x) expectations for inaxaplin as a treatment for AMKD, including with respect to data from the Phase 3 interim analysis of AMPLITUDE in early 2027, filing for U.S. accelerated approval if results are supportive, to complete full study enrollment in H2 2026, and to complete the AMPLIFIED study and share data in H2 2026, (xi) expectations for the clinical development of VX-407 in ADPKD, including to complete enrollment in the AGLOW study in H2 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 and share data in H2 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 (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) an intangible asset impairment charge, 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. 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 2026 press release dated May 4, 2026.

Strong Q1 performance across the board, with total revenue +8% Y/Y

Cystic Fibrosis portfolio

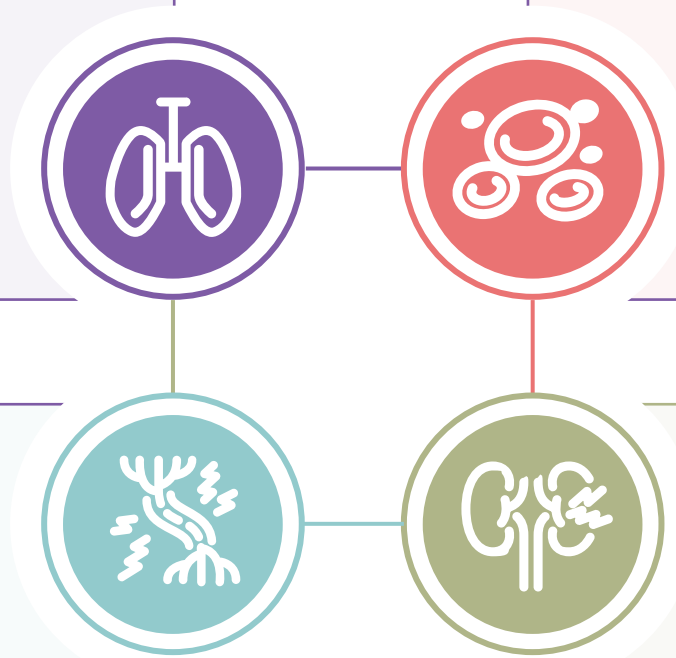
Continuing to expand market leadership

ALYFTREK > $1B revenue since launch

CASGEVY

Leveraging global ATC network to grow initiations and infusions

CASGEVY > 500 initiations since launch



JOURNAVX

Building on momentum to grow Rx's and revenue

JOURNAVX > 1M Rx's since launch

Povetacicept

- **Home run Phase 3 IA IgAN results**
- **IgAN BLA submitted for potential U.S. AA**
- **pMN Ph 2/3, gMG Ph 2 rapidly advancing**

Pove IgAN launch planning well underway

ATC: Authorized treatment center; IgAN: IgA nephropathy; IA: interim analysis; BLA: biologics license application; AA: accelerated approval; pMN: primary membranous nephropathy; gMG: generalized myasthenia gravis.

CF: Extending leadership and driving sustained growth

With recent label expansions, ALYFTREK & TRIKAFTA now reach ~95% of all people with CF

ALYFTREK launch

- Best CFTR protein function, as measured by sweat chloride, plus once-daily dosing
- Expect majority of patients to switch to ALYFTREK from TRIKAFTA over time
- Meaningful recent label expansion of eligibility – regardless of the location of the variant in the CFTR protein – reflects decades of investment and relentless pursuit of the science

Younger patients

- Increases eligible population
- TRIKAFTA in patients 1 to <2 years: began global regulatory submissions in H1:26
- ALYFTREK in patients 2 to 5 years: global regulatory submissions starting in H1:26
- ALYFTREK: ongoing study in patients ages 1 to <2 years

Serial innovation

- NG 3.0 compounds
  - VX-828: in a study in patients with CF; on track to share results H2:26
  - VX-581 and VX-272: both in Phase 1 healthy volunteer studies
- VX-522 mRNA: program discontinued due to tolerability issues

NG = next generation.

Recently announced Phase 3 IA data cements pove's potential as best-in-class in IgAN

Completed rolling BLA submission for potential U.S. Accelerated Approval

Specifically engineered to achieve improved…

- ✓ Binding affinity for BAFF + APRIL
- ✓ Potency
- ✓ Pharmacokinetics
- ✓ Tissue distribution, including the kidney

RAINIER IA data continue to support potential best-in-class profile

- ✓ Reductions in
  - ✓ Proteinuria
  - ✓ Hematuria
  - ✓ Gd-IgA1
- ✓ High rates of background supportive care

RAINIER™
povetacicept
Ph 3 IgAN

Differentiated monthly dosing & patient-centric features

- ✓ Monthly dosing
- ✓ Small volume (0.46mL)
  - ✓ 27-gauge needle
  - ✓ <1.5 second injection time
- ✓ At-home administration
- ✓ Subcutaneous autoinjector

IA: Interim Analysis; Gd-IgA1: galactose deficient immunoglobulin-A1

Positive RAINIER Phase 3 interim analysis results demonstrate best-in-class potential at just 36 weeks of treatment

RAINIER™ povetacicept Ph 3 IgAN

	Povetacicept	Povetacicept vs. placebo	*P* value vs. placebo
Primary endpoint			
% change in 24-hr UPCR	- 52.0%	- 49.8%	< 0.0001
Secondary endpoints			
% change in serum Gd-IgA1	- 77.4%	- 79.3%	< 0.0001
% patients achieving hematuria resolution	85.1%	61.7%	< 0.0001
Select exploratory endpoint			
% patients achieving 24-hr UPCR < 0.5 g/g	42.2%	36.0%	nominal < 0.0001

Pove was generally safe & well tolerated

Majority of AEs were mild to moderate; no SAEs related to pove

Low rate of SAEs of infection (0.5%) in both placebo and pove groups

No opportunistic infections and no discontinuations related to pove overall

Sample size of the IA: Efficacy: N=68 placebo, N=131 pove; patients with hematuria at baseline: N=36 placebo, N=67 pove; safety: N=185 placebo, N=372 pove

Continued, rapid progress across renal portfolio, with multiple near-term catalysts

		PATIENTS[1]	CURRENT PHASE	2026 ACHIEVEMENTS AND MILESTONES
B cell driven renal diseases	Povetacicept – IgAN	~330K (>1.5M globally)	Phase 3 trial enrollment complete	✓ **Completed BLA submission** • Preparing for U.S. launch
	Povetacicept – pMN	~150K (>600K globally)	Phase 2/3 pivotal trial ongoing	✓ Completed Phase 2 enrollment ✓ **Initiated Phase 3 portion**
Other non-kidney	Povetacicept – gMG	~175K (~300K globally)	Phase 2 trial ongoing	✓ **Initiated Phase 2;** drive enrollment
APOL1- mediated kidney disease (AMKD)	Inaxaplin – Primary AMKD	~150K	Phase 3 trial IA cohort enrollment complete	• **Phase 3 IA data early 2027**; submit for U.S. AA thereafter, if results are supportive • Complete full trial enrollment H2:26
	Inaxaplin – AMKD with modest proteinuria or diabetes	~100K	Phase 2 trial ongoing	✓ Completed enrollment • **Share results H2:26**
Autosomal dominant polycystic kidney disease (ADPKD)	VX-407	Up to ~30K	Phase 2 trial	• Complete enrollment H2:26
	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

AMKD: Upcoming milestones for inaxaplin in APOL1-mediated kidney disease

First potential targeted therapy for patients with AMKD

AMPLITUDE

Primary AMKD

Patients with 2 APOL1 variants, heavy proteinuria and no other renal-related comorbidities

~150K patients

- **IA data expected early 2027** (after 48 weeks of treatment); if positive, file for potential accelerated approval in the U.S.
- **On track to complete full study enrollment by YE:26**
- **IA endpoints**: eGFR slope vs placebo and percentage change from baseline in proteinuria versus placebo

AMPLIFIED

AMKD + modest proteinuria

AMKD + mod/severe proteinuria + diabetes

~100K additional patients

- Phase 2 POC study of inaxaplin with **two patient cohorts not studied in AMPLITUDE**: AMKD with modest proteinuria and AMKD with moderate/severe proteinuria and diabetes
- On track to complete study and share **results H2:26**

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	Submitted for Accelerated Approval	Approved
Improved conditioning CASGEVY – SCD & TDT	Follow-on molecules for multiple programs	**VX-407** ADPKD	**Povetacicept** IgA nephropathy	**Povetacicept** IgA nephropathy	JOURNAVX®
$Na_V1.7$ inhibitor Pain		**VX-670** DM1	**Povetacicept** pMN		alyftrek®
Islet cells + alternative immunosuppression **Hypoimmune islet cells** Type 1 diabetes		**Povetacicept** wAIHA	**Suzetrigine** DPN		casgevy®
Small molecule Huntington's disease		**VX-993** DPN	**Inaxaplin** Primary AMKD		trikafta®
		VX-828 Cystic fibrosis	**Zimislecel** Type 1 diabetes		symdeko®
		Povetacicept gMG			ORKAMBI®
		Inaxaplin AMKD + modest proteinuria or diabetes			kalydeco®

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; DM1: myotonic dystrophy type 1; pMN: primary membranous nephropathy; gMG: generalized myasthenia gravis; wAIHA: warm autoimmune hemolytic anemia.

CF: Q1 global revenue growth of 6%, balanced between U.S. +5% and OUS +8% Y/Y

$1B ALYFTREK cumulative revenue milestone achieved

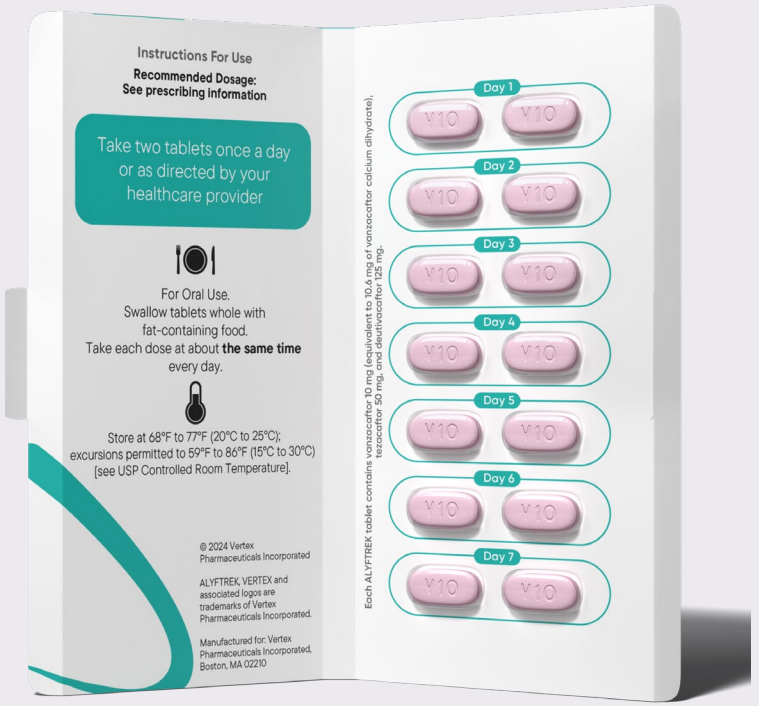
U.S. highlights

- ALYFTREK rollout continues to progress well
- Label expansions for ALY and TRI represent ~800 newly eligible CF patients
- Continued uptake in younger patients

OUS highlights

- ALYFTREK launches off to strong starts in EU
- Secured reimbursement access in 11 countries in Q1, building on access generated in the second half of 2025

alyftrek®



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 ppFEV$_1$ vs. TRIKAFTA. **CFTR function as measured by improvements in sweat chloride vs. TRIKAFTA.

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

Q1:26 CASGEVY revenue $43M

casgevy® (exagamglogene autotemcel) suspension for IV infusion

- **500** patient initiations since launch
- Submitted for ages 5 to <12 with Commissioner's National Priority Voucher in U.S.

- **Access agreement reached** to provide long term sustainable access for **German SCD & TDT** patients; working through final terms

- **Strong visibility for CASGEVY** to contribute meaningfully to $500M+ revenue goal for non-CF products in 2026

Pain: JOURNAVX transforming the standard of care for the treatment of acute pain

Q1:26 JOURNAVX revenue $29M

JOURNAVX®

	PATIENTS	PRESCRIBERS	PAYERS
Cumulative since launch	**>1M prescriptions** ~50-50 split between hospital and retail channels	**~50K prescribers** Excellent breadth and adoption across multiple specialties	**~240M covered lives** All 3 national commercial PBMs contracted
Q1:26	• >350K Rx's; on track to >3x Rx's in 2026 vs. 2025 • Direct-to-patient telehealth platform now available via Journavx.com	• ~300 sales representatives now in the field • Driving HCP adoption & depth in promotionally-sensitive market	• Signed first of the Big 4 Medicare Part D Plans; coverage began May 1 • Now eligible for separate payment under NOPAIN Act, retroactive to 1/23/26

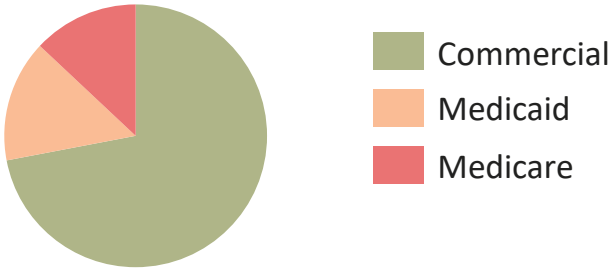
Nephrology: Building our fourth franchise, starting with povetacicept in IgAN

Providers

~4,000 nephrologists treat ~80% of U.S. IgAN patients

Specialty-sized renal field force to cover key nephrologists

Payers



~70% of IgAN patients have commercial coverage

High value of disease-modifying therapies recognized

Patients

Patient programs critical for chronic therapies, especially biologics

Program will enable speed to therapy & personalized support, leveraging best practices from CF

Q1 2026 Financial Highlights

($ in millions except where noted or per share data and percentages)	Q1:25	FY:25	Q1:26
TRIKAFTA/KAFTRIO	2.54B	10.31B	**2.35B**
ALYFTREK	54	838	**424**
Other CF product revenues	155	645	**136**
CF product revenues, net	2.74B	11.80B	**2.92B**
CASGEVY	14	116	**43**
JOURNAVX	1	60	**29**
Total product revenues	2.76B	11.97B	**2.99B**
Other revenues	10	31	**—**
Total revenues	2.77B	12.00B	**2.99B**
Combined non-GAAP R&D, Acquired IPR&D and SG&A expenses	1.23B	5.12B	**1.29B**
Non-GAAP operating income	1.18B	5.26B	**1.31B**
Non-GAAP operating margin %	43%	44%	**44%**
Non-GAAP net income	1.05B	4.75B	**1.15B**
Non-GAAP net income per share-diluted	$4.06	$18.40	**$4.47**
Cash, cash equivalents & marketable securities (period-end)	11.4B	12.3B	**13.0B**

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 press releases dated February 12, 2026 and May 4, 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.

Reiterate full year 2026 financial guidance

	Current FY 2026 Guidance	Commentary
Total Revenue	$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*	$6.3 - $6.45B	Includes expectations for continued investment in multiple mid- and late-stage clinical development programs and commercialization capabilities, as well as ~$100M of currently anticipated AIPR&D expenses.
Combined Non-GAAP R&D, Acquired IPR&D and SG&A Expenses*	$5.65 - $5.75B	
Non-GAAP Effective Tax Rate	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.

Anticipated Key Milestones

Marketed CFTRm	• Expand number of people treated: ultra-rare mutations, younger patients, additional geographies; continue ALYFTREK U.S. & ex-U.S. launches
TRIKAFTA (CF)	• Completed pivotal study for 1 to <2 years; **began global regulatory submissions in H1 2026**
ALYFTREK (CF)	• **Expand CF leadership and reach more patients around the globe by driving U.S. adoption and ongoing OUS launches in 6+ year olds** • Completed pivotal study for 2 to 5 years; **begin global regulatory submissions in H1 2026** • Advance Phase 3 study in patients ages 1 to <2 years
Next-generation 3.0 (CF)	• **VX-828:** Complete enrollment and dosing in CF patients and share results in **H2 2026** • Continue to **advance VX-581 and VX-272** in FIH studies
CASGEVY (SCD/TDT)	• **Reach more eligible patients ages 12+ year-old** through global ATC network • **Completed U.S. regulatory submission in patients ages 5 to <12 years;** awarded 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)	• Post completion of internal manufacturing review, **resumed dosing with multiple patients dosed** • In coming months, share updated pivotal study completion and filing timelines
Inaxaplin (AMKD)	• **AMPLITUDE** (primary AMKD)**: complete Phase 3 interim analysis and share data in early 2027;** complete full enrollment in H2 2026 • **AMPLIFIED** (AMKD patients with modest proteinuria or diabetes): complete study and share data in H2 2026
Povetacicept (IgAN, pMN)	• **IgAN: BLA submitted for potential U.S. Accelerated Approval; prepare for launch** • **pMN: Enrollment in Phase 2 pivotal trial complete and Phase 3 initiated; drive Phase 3 advancement** • **gMG: Enroll and dose patients in gMG Phase 2 study**
VX-407 (ADPKD)	• **Complete enrollment in the AGLOW Phase 2 proof-of-concept study in H2 2026**
VX-670 (DM1)	• **Complete enrollment and dosing and share results of DM1 patients in the Phase 1/2 study in H2 2026**

First Quarter 2026 Financial Results

May 4, 2026

Presentation intended for the investment community

Appendix
GAAP to non-GAAP Financial Information

(in millions except per share amounts and percentages)	Q1:25	FY:25	Q1:26
Combined R&D, AIPR&D and SG&A			
GAAP	1.40B	5.80B	**1.46B**
Non-GAAP	1.23B	5.12B	**1.29B**
Operating income			
GAAP	630	4.17B	**1.14B**
Non-GAAP	1.18B	5.26B	**1.31B**
Operating Margin %			
GAAP	23%	35%	**38%**
Non-GAAP	43%	44%	**44%**
Net income			
GAAP	646	3.95B	**1.03B**
Non-GAAP	1.05B	4.75B	**1.15B**
Net income per share-diluted			
GAAP	$2.49	$15.32	**$4.02**
Non-GAAP	$4.06	$18.40	**$4.47**
Shares used in per share calculations			
GAAP	259.5	258.0	**256.3**
Non-GAAP	259.5	258.0	**256.3**

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 February 12, 2026 and May 4, 2026.