

Third Quarter 2026 Financial Results

November 2, 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, including the statements under “Raising full year 2026 revenue guidance,” “Crinetics Pharmaceuticals acquisition impact,” and statements regarding (i) expectations, goals, development and commercialization plans and timelines for the company’s products, product candidates and pipeline programs, (ii) beliefs with respect to the treatable patient population for CF and the benefits of treatment early in life, expectations to continue to extend market leadership and sustain growth with respect to the company’s CF medicines, including from label expansions and treatment of younger patients, our our expectations regarding ALYFTREK, including with respect to clinical benefits, that the majority of patients will switch to ALYFTREK from TRIKAFTA over time, advancing global regulatory submissions for ALYFTREK in patients 2 to 5 years of age, the progress of the ongoing commercial launch of ALYFTREK, continued uptake in younger patients and expansion in to additional geographies, our expectations with respect to the clinical benefits of other next generation CF compounds, potential advancement of next-generation 3.0 CF regimen once all data are available, for continued progress in next-generation 4.0 programs, and the clinical benefits of VX-828, (iii) beliefs regarding the potential benefits of atumelnant for the treatment of CAH and ACTH-dependent Cushing’s Syndrome, including with respect to treatable patient population, significant unmet need, and potential clinical benefits, expectations for the Phase 3 study of atumelnant in adults with CAH, including to complete enrollment in the first quarter of 2027, share data at a medical conference in 2027, and for the Phase 2/3 pediatric study, including to engage with regulators and progress rapidly to Phase 3, and plans with respect to the Phase 2/3 study of atumelnant in ACTH-dependent Cushing’s Syndrome, (iv) expectations for the company’s T1D program, including with respect to study advancement for VX-017 as the lead islet therapy for T1D and thereby doubling the market opportunity as compared to zimislecel, and plans for enrolling and dosing patients in the Phase 1/2 study and targeting initiation of pivotal development in 2027, (v) expectations regarding progress across the company’s kidney portfolio, including with respect to estimated patient populations, the company’s beliefs regarding data from Phase 3 study of povetacicept in IgAN and that povetacicept is a potential best-in-class treatment for IgAN, our beliefs regarding launch readiness for povetacicept in IgAN, including with respect to the field team, commercial coverage and patient onboarding capabilities, our expectations to drive Phase 3 enrollment and continue dosing in the Phase 3 study of povetacicept in pMN, and to share data from the Phase 2 study of povetacicept in gMG in H1 2027, (vi) expectations for inaxaplin as a treatment for AMKD, including our beliefs around AMPLIFIED study data and plans to perform interim analysis and to share data in early 2027 from the AMPLITUDE pivotal trial, and our expectation that positive study data from the AMPLITUDE study will support accelerated approval in the U.S., (vii) expectations for CASGEVY, including with respect to reaching more eligible patients and securing additional pediatric approvals, acceleration of patient infusions, CASGEVY’s commercial potential, including potential as a multi-billion dollar franchise, progress toward contributing meaningfully to the $500 million revenue goal for non-CF products in 2026, and line of sight into 2026 and 2027 revenue, (viii) expectations for JOURNAVX, including with respect to launch momentum in the U.S. and continuing to drive prescriptions and revenue growth, our beliefs regarding strong clinical reception, physician enthusiasm, and a growing body of real world evidence, our expectations regarding the progress towards more than 3x prescription growth and more than 3x revenue growth in 2026 versus 2025, beliefs regarding the patient support program in 2026 and gross-to-net revenue in 2027, plans to secure regulatory approval in Canada, plans to complete enrollment in both ongoing studies evaluating suzetrigine in DPN by the end of 2026 and share data in 2027, and plans to complete enrollment in the Phase 2 study of VX-993 in DPN by the end of 2026 and share data mid-2027, (ix) beliefs regarding the expected clinical benefits, significant unmet need, and eligible patient population for PALSONIFY as a treatment for acromegaly, expectations regarding the integration of Crinetics’ business and launch progress for PALSONIFY in the U.S., including plans to grow the patient and prescriber bases and begin the European launch in H2 2027, (x) expectations to share data in 2027 from the AGLOW study of VX-407 in ADPKD, and (xi) expectations to share interim results in H2 2026 from the Phase 1/2 study of VX-670 in DM1. 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 continue increasing revenues from its commercialized medicines, that that regulatory submissions or approvals may not occur on the anticipated timeline, or at all, that data from clinical trials may not to be indicative of final results, that anticipated commercial launches may be delayed, if they occur at all, the company may not realize the anticipated benefits from acquisitions or collaborations with third parties, that 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) acquisition-related costs, (vi) acquired inventory fair value step-up expense, (vii) an intangible asset impairment charge, and (viii) 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 Q3 2026 press release dated November 2, 2026.

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Excellent Q3:26 performance across the board

Commercial

- **Total revenue +12% Y/Y**
  - Strong growth across all products & regions
  - $10M contribution from Crinetics acquisition for month of September (closed 9/1)
- Meaningful progress gaining **reimbursed access** across CF, SCD/TDT, acute pain, acromegaly
- Launch-ready in **renal**, with pove IgAN PDUFA Nov 30, 2026

Clinical

- **Recently announced:**
  - Positive Inaxaplin AMPLIFIED Ph2
  - Positive VX-828 patient data in CF
  - ASN presentation & *NEJM* publication of pove IgAN Ph3 RAINIER IA
- **Completed enrollment:**
  - Inaxaplin AMPLITUDE Ph3 in AMKD
  - Povetacicept ETNA Ph2 in gMG
  - VX-407 AGLOW Ph2 in ADPKD
- **On track to complete enrollment by YE:**
  - 2 suzetrigine Ph3s in DPN
  - VX-993 Ph2 in DPN
- **Expect interim results by YE:**
  - VX-670 Ph2 PoC in DM1
- **Expect results early 2027:**
  - AMPLITUDE Ph2/3 IA in AMKD

Regulatory

- **Pove**: BLA for IgAN under priority review for accelerated approval in U.S. and KSA
- **CASGEVY**: Expanded labeling in SCD/TDT: 2 to <12 years in U.S., Bahrain, UAE; 5 to <12 years in the U.K.
- **VX-017** Ph1/2 study underway in T1D
  - Compatible with all blood types, doubling target patient population to ~120K from ~60K
  - Enrollment and dosing underway

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SCD: sickle cell disease; TDT: transfusion dependent beta thalassemia; IgAN: immunoglobulin-A nephropathy; ADPKD: autosomal dominant polycystic kidney disease; AMKD: APOL1 mediated kidney disease; DPN: painful diabetic peripheral neuropathy; DM1: myotonic dystrophy type 1; T1D: type 1 diabetes.

CF: Extending leadership and driving sustained growth

ALYFTREK

- 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
- New data at NACFC demonstrated that early intervention with ALYFTREK can help achieve independence from pancreatic enzyme replacement therapy (PERT)

Younger patients & rare mutations

- Treating early in life may prevent organ damage & holds promise to extend life expectancy
- Global regulatory submissions in progress for ALYFTREK in patients ages 2-5 years
- Recent label expansions increase eligible population: ~95% of people with CF now eligible for treatment with VRTX CFTR modulators

Serial innovation

- Next gen 3.0 family of compounds:
  - VX-828 triple combo: Phase 1 data in F/MF patients showed 6.6 & 9.4 mmol reductions in sweat chloride at & through Day 28, respectively, vs. TRIKAFTA baseline; safe & well tolerated, once daily dosing with favorable drug-drug interaction profile
  - VX-581 and VX-272: both in Phase 1 healthy volunteer studies
  - Given high bar set by ALYFTREK, wait for all next gen data to select regimen for advancement
- Next-generation 4.0 programs continue to make progress in pre-clinical development

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CFTR: cystic fibrosis transmembrane conductance regulator; SwCl: sweat chloride; NACFC: North American Cystic Fibrosis Conference.

Emerging VX-828 data in CF cohort resulted in improvement in sweat chloride versus a baseline on TRIKAFTA

Sweat chloride (SwCl) change from TRIKAFTA baseline by visit

Visit	Cohort E1 N=8
Baseline SwCl (Day 0) Mean (SD)	61.9 (8.7)
Absolute change *at* Day 28 Mean (95% CI)	-6.6 (-14.1, 1.0)
Absolute change *through* Day 28 Mean (95% CI)	-9.4 (-19.3, 0.5)

- ✓ Study assessed patients with F/MF genotype from TRIKAFTA baseline
- ✓ The VX-828 regimen is oral, once-daily
- ✓ Good safety and tolerability profile

†At Day 28 is the measurement taken on Day 28. Through Day 28 is the mean of the measurements on Days 15, 22, and 28.

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Rare endocrine: Atumelnant, an oral, selective ACTH antagonist for Congenital Adrenal Hyperplasia and ACTH-dependent Cushing's Syndrome

Congenital Adrenal Hyperplasia (CAH)



- **Significant unmet need**
- **First therapy** with the potential to reduce **BOTH** excess adrenal androgens AND exogenous glucocorticoids
  - Orphan Drug Designation U.S., EU, Japan
- **Adult:** Phase 3 pivotal study underway
  - Goal to complete enrollment Q1:27
- **Pediatric:** Phase 2 study underway
  - Goal to progress rapidly to Phase 3, following regulatory interactions

ACTH-dependent Cushing's Syndrome (ADCS)

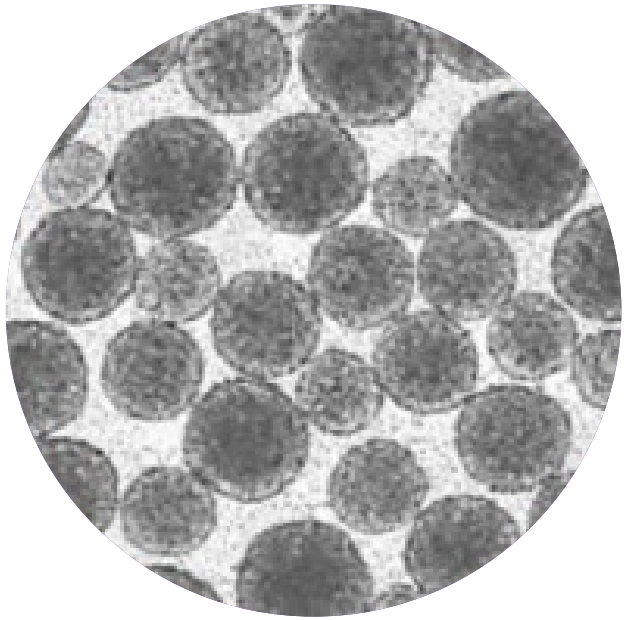


- **Significant unmet need**
- OUS: Phase 2/3 study initiated
- U.S.: Engaging with FDA on trial initiation
  - Granted Orphan Drug Designation

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T1D: Accelerating VX-017 as lead islet cell therapy for Type 1 diabetes

VX-017 is an allogenic, off-the-shelf, glucose-responsive, insulin-producing, fully differentiated islet cell therapy



- **Doubles initial market opportunity** for islet cell therapy to **~120K patients** from ~60K
- Similar target product profile to zimislecel
- **Enrolling and dosing patients in a Phase 1/2 study** for patients of all blood types
- Targeting initiation of pivotal development in 2027

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Nephrology: Rapid progress across the kidney portfolio

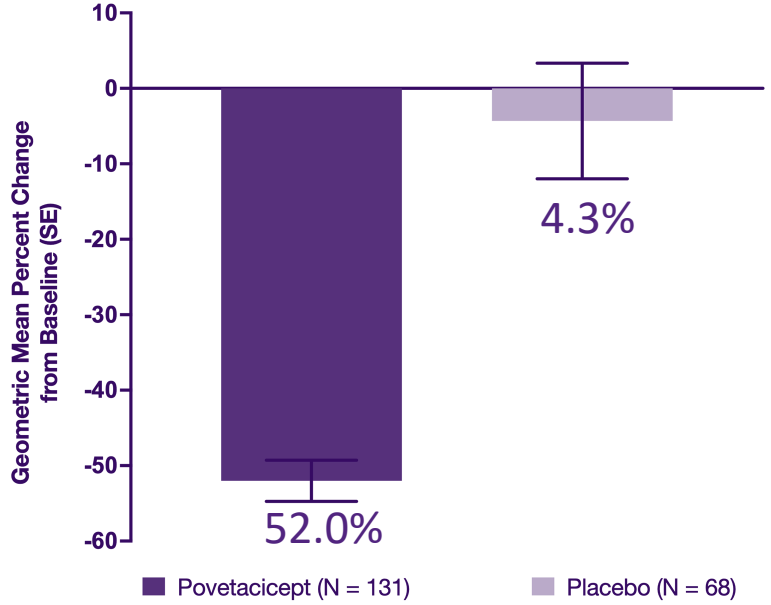
		PATIENTS[1]	RESEARCH	PHASE 1	PHASE 2	PHASE 3	APPROVED
B cell driven renal diseases	Povetacicept – IgAN[2]	~330K (1.5M globally)				RAINIER	*PDUFA: Nov 30*
	Povetacicept – pMN	~150K (>600K globally)				OLYMPUS	*Enrollment and dosing well underway*
Other B cell driven diseases	Povetacicept – gMG	~175K (>300K globally)			ETNA		*Proof-of-concept study fully enrolled, dosing continues*
APOL1- mediated kidney disease (AMKD)	Inaxaplin – AMKD	~150K				AMPLITUDE	*IA data in early 2027*
	Inaxaplin – AMKD with modest proteinuria or diabetes	~100K (with comorbidities)			AMPLIFIED		*Completed*
Autosomal dominant polycystic kidney disease	VX-407[3]	Up to ~30K			aglow Clinical Study		*Proof-of-concept study fully enrolled, dosing continues*
	Serial innovation to reach all ADPKD patients	~300K (incl. 30K)		*Pre-clinical progress continues*			

1. Estimated patient population in the U.S. and Europe, unless otherwise noted. 2. IgAN patients continue to be studied in RUBY-3. 3. Targets a patient population with a subset of variants in the *PKD1* gene.
IgAN: IgA nephropathy; pMN: primary membranous nephropathy; gMG: generalized myasthenia gravis; AMKD: APOL1-mediated kidney disease.

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Povetacicept: Statistically significant and clinically meaningful reduction in proteinuria

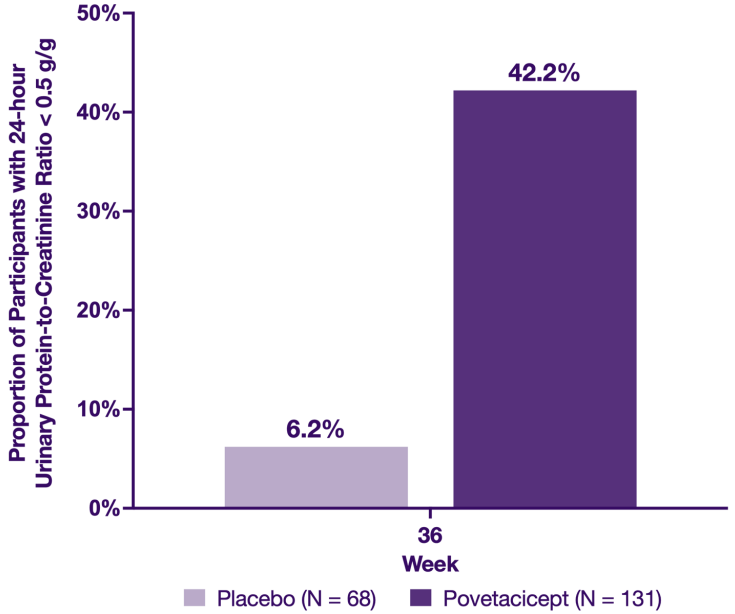
PRIMARY ENDPOINT: Percent Change from Baseline in 24-hour UPCR at Week 36



Substantial reductions in 24-hour UPCR with povetacicept

- **52.0% decrease** from baseline **with povetacicept at Week 36**
- **Povetacicept treatment effect at Week 36: 49.8%** (95% CI: 39.2%, 58.6%); ***P* <0.0001**

Proportion of Participants with 24-hour UPCR <0.5 g/g at Week 36



42.2% Achieved KDIGO-aligned goal of UPCR <0.5 g/g

- Proportion of patients who achieved **24-hour UPCR <0.3 g/g 18.0% with povetacicept** and 1.5% with placebo at Week 36

Pove was generally safe and well tolerated in the study; most AEs were mild-to-moderate, SAEs of infection were balanced at 0.5% in the both the pove and placebo groups; no opportunistic infections, and no discontinuations due to infections

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AMPLIFIED data add to evidence base for inaxaplin as potential first- and best-in-class treatment targeting the underlying cause of AMKD

PARAMETER	Cohort 1: Patients with AMKD with modest proteinuria N=22[a]	Cohort 2: Patients with AMKD and Type 2 diabetes N=17[a]
Primary Endpoint (UACR)		
Mean baseline UACR g/g (SD)	0.28 (0.09)	0.67 (0.87)
Geometric mean % change of UACR at Week 13 compared to baseline (95% CI)[b]	-42.7% (-58.3%, -21.1%)[c]	-17.3% (-36.3%, 7.2%)[c]
Other Endpoint (UPCR)		
Mean baseline UPCR g/g (SD)	0.46 (0.20)	1.12 (1.51)
Geometric mean % change of UPCR at Week 13 compared to baseline (95% CI)[b]	-44.7% (-60.9%, -21.9%)[c]	-25.4% (-45.1%, 1.4%)[c]

- Cohort 1 efficacy mirrors that of inaxaplin proof-of-concept Phase 2 study in AMKD patients with FSGS
- Majority of patients in both cohorts did not have FSGS
- Generally safe and well tolerated[d]

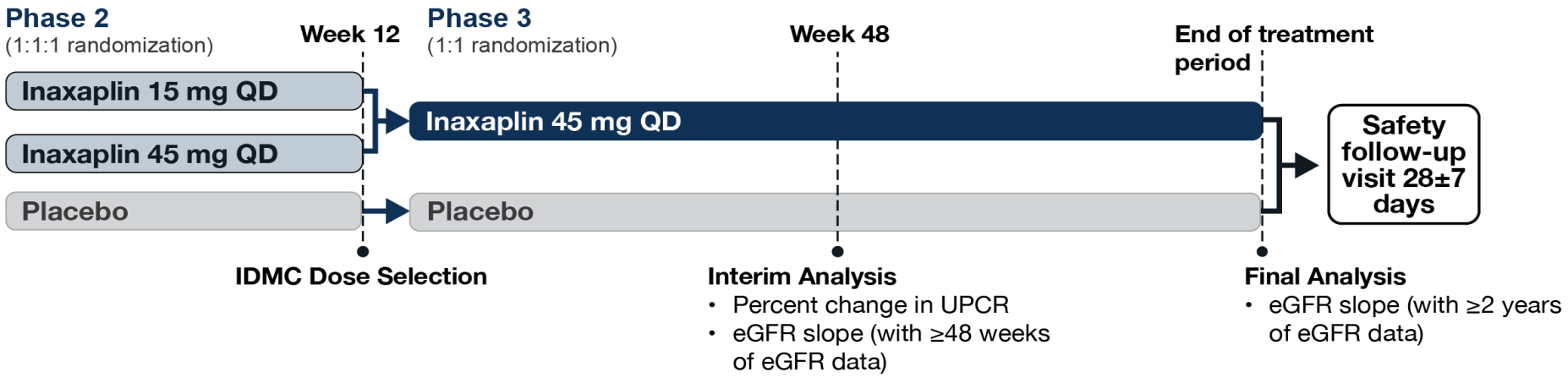
[a]According to the pre-specified statistical analysis plan, two people, one in each cohort, who were noncompliant with treatment were not included in the efficacy analyses; [b]Analyses include those on treatment who had an assessment at Week 13: 18 and 14 people in cohort 1 and 2, respectively; [c]95% CI were generated post-hoc. [d]No serious adverse events (SAEs) related to inaxaplin. All adverse events (AEs) were mild or moderate in severity. Most common AE (occurring in >5% of subjects) was headache (7.3%). Five patients had isolated, asymptomatic transaminase elevations, which resolved.

AMKD: APOL1-mediated kidney disease; CI: Confidence interval; SD: Standard deviation; UACR: Urine albumin to creatinine ratio; UPCR: Urine protein to creatinine ratio; FSGS: focal segmental glomerulosclerosis

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AMPLITUDE pivotal trial of inaxaplin in patients with AMKD with severe proteinuria fully enrolled; interim analysis on track for early 2027

Phase 2/3 Study Enrollment Complete With a Total of 522 Patients Enrolled



Note: At the end of treatment, patients have an option to enroll in a long-term open label extension study.

Assessments

Primary endpoints

- **Interim analysis (IA)**
  - Percent change in UPCR from baseline at Week 48
  - eGFR slope (with ≥48 weeks of eGFR data)
- **Final analysis**
  - eGFR slope (with ≥2 years of eGFR data)

Key Eligibility Criteria

Key inclusion criteria:

- Aged 10 to 65 years
- *APOL1* genotype of *G1/G1, G2/G2, G1/G2*
- Proteinuric kidney disease

Key exclusion criteria:

- History of diabetes mellitus
- Uncontrolled hypertension
- Solid organ or bone marrow transplant

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

Select next wave programs Research stage	Phase 1 in healthy volunteers	Phase (1)/2* (in patients, ongoing)	Pivotal development	Submitted for Accelerated Approval	Approved
Improved conditioning CASGEVY – SCD & TDT	**Follow-on molecules for multiple programs**	**VX-407** ADPKD	**Inaxaplin** AMKD	**Povetacicept** IgA nephropathy	Palsonify™
Small molecule Huntington's disease		**Atumelnant** **ACTH-dependent** Cushing's Syndrome	**Atumelnant** CAH		JOURNAVX®
$Na_V1.7$ inhibitor Pain		**VX-670** DM1	**Suzetrigine** DPN		casgevy®
Islet cells + targeted immunosuppression + hypoimmune islet cells Type 1 diabetes		**VX-993** DPN	**Povetacicept** IgA nephropathy		alyftrek®
		Povetacicept gMG	**Povetacicept** pMN		trikafta®
		VX-017 Type 1 diabetes	**Zimislecel** Type 1 diabetes		symdeko®
					ORKAMBI®
					kalydeco®

*In addition, the following Phase 1/2 trials have completed: Inaxaplin (AMPLIFIED: AMKD), VX-828 (CF), and pove (RUBY-4: immune thrombocytopenia, warm autoimmune hemolytic anemia, cold agglutin disease).
SCD: sickle cell disease; TDT: transfusion-dependent beta thalassemia; 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.

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Strong commercial performance and outlook across all disease areas

Key performance indicators and growth drivers

alyftrek®

>18K

patients now benefiting from ALYFTREK worldwide

Growth from label expansions into rare mutations and younger patients, plus additional geographies



casgevy® (exagamglogene autotemcel) suspension for IV infusion

~200

infusions completed since launch

Growth from increased penetration and label expansion into younger patients



JOURNAVX®

>1.6M

patients treated since launch

Growth from increasing depth of use and continued positive real-world experience



Once-Daily Oral Palsonify™ (paltusotine) tablets

>40%

brand share among patients starting or switching therapy

Growth from new and repeat prescribers in patients initiating & switching therapies



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CF: Continued global revenue growth

$3.3B Q3 global CF revenue

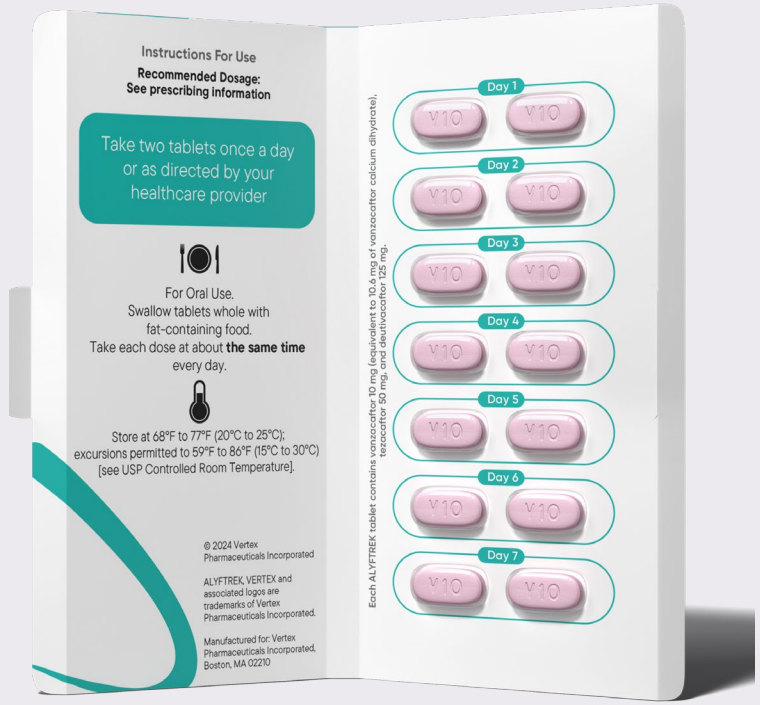
U.S. highlights

- **ALYFTREK sales Q1-Q3 surpassed $1B**
- Switching & new rare mutation patients

OUS highlights

- Strong ALY European launches
- 31 countries now with ALY reimbursement

18,000 patients worldwide now on ALYFTREK



ALYFTREK: A highly efficacious, once-daily CFTR modulator delivering equivalent improvement in lung function[1] and greater CFTR function[2] vs. TRIKAFTA

1. Lung function as measured by improvements in ppFEV$_1$ vs. TRIKAFTA.
2. CFTR function as measured by improvements in sweat chloride vs. TRIKAFTA.

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CASGEVY: Acceleration continues towards multi-$B potential

casgevy® (exagamglogene autotemcel) suspension for IV infusion

- Expanded pediatric labeling: ages 2 to <12 U.S., Bahrain, and UAE; ages 5 to <12 in the U.K.

- Four consecutive quarters of >100 initiations
- **Double number of infusions first 9 months 2026** vs. all 2025

- Contributing meaningfully to $500M+ revenue goal
- Excellent line of sight into FY2026 and 2027 revenue

UAE: United Arab Emirates.

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JOURNAVX: Strong Rx growth and gaining traction across customer base

JOURNAVX®

Strong clinical reception

>750,000 prescriptions in Q3

Over 1.6M patients treated

#1 Oral Branded Analgesic

Physician enthusiasm

~80,000 physicians prescribing JOURNAVX

Up from ~70,000 previously

Growing body of JOURNAVX real world evidence

Multiple studies show lower opioid utilization

Total Knee Arthroplasty, acute dental pain, etc.

On track to deliver >3x Rx growth and >3x revenue growth 2026 vs 2025
PSP to remain "on" through 2026, with GTN normalizing mid-2027

©2026 Vertex Pharmaceuticals Incorporated PSP: Patient Support Program.

Acromegaly is a rare, serious chronic disease with significant unmet need

Once-Daily Oral
Palsonify™
(paltusotine) tablets

Known causal biology

Benign pituitary tumor

A benign pituitary tumor produces excess growth hormone, driving acromegaly

Meaningful opportunity

~40K patients

across the U.S. and key OUS markets

In the U.S., patients are treated by approximately 3,000 endocrinologists.

Ongoing disease burden

~50% patients

require lifelong treatment

Persistent disease causes most patients to require lifelong therapy

Unmet need

Oral therapy providing rapid and sustained biochemical + symptom control

First and only SST2-selective agonist designed for sustained control without injection-site burden

PALSONIFY: convenient once-daily oral option for patients who had an inadequate response to surgery or for whom surgery is not an option

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SST2-selective agonist: somatostatin receptor type 2.

PALSONIFY launch is off to a strong start

Once-Daily Oral Palsonify™ (paltusotine) tablets

Areas of focus

1. Build a broad base of repeat HCP writers for PALSONIFY
2. Drive growth in both the new and switch settings
3. Serve more patients around the globe

~80%

Broad payer access
of U.S. lives covered

~500

Repeat HCP prescribers

40%+

Leading brand share
among patients seeing their HCP

~$60M

Revenue through 9/30/26

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Renal: Building our fifth pillar, starting with povetacicept in IgAN

Povetacicept Trifecta

Differentiated profile
Ready to activate

- 89% of surveyed nephrologists anticipate prescribing pove[1], with proteinuria efficacy as leading motivator[2]
- 96% of surveyed patients prefer autoinjector* and 80% prefer Q4W dosing for greater convenience[3]

Launch Ready

Scaled field engine
Ready to engage

- Field team fully staffed and trained, largest in IgAN, >90% nephrology experience
- Engaged targeted HCPs in IgAN disease educational activities since early this year

Seamless Experience

Patient-first infrastructure
Ready to serve

- Personalized & seamless patient onboarding, leveraging Vertex's CF experience and capabilities
- Patient population is >70% commercial; VRTX has been engaging payers for >1 year

Due to needle concealment and easier administration

[1]Spherix Data, Q3 2026; [2]Povetacicept HCP ATU Pulse, Aug – Sep 2026 measuring intent among pipeline assets; [3]Health Economics and Outcomes Research (HEOR) ASN 2026 Patient Preference Poster by Joel Iff, et al.

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Q3 2026 financial highlights

($ in millions except where noted or per share data and percentages)	Q3:25	FY:25	Q3:26
TRIKAFTA/KAFTRIO	2.65B	10.31B	**2.44B**
ALYFTREK	247	838	**706**
Other CF product revenues	139	645	**131**
Total CF product revenues	3.04B	11.80B	**3.27B**
CASGEVY	17	116	**99**
JOURNAVX	20	60	**58**
PALSONIFY	—	—	**10**
Total product revenues	3.08B	11.97B	**3.44B**
Other revenues	—	31	**—**
Total revenues	3.08B	12.00B	**3.44B**
Combined non-GAAP R&D, Acquired IPR&D and SG&A expenses	1.28B	5.12B	**1.53B**
Non-GAAP operating income	1.38B	5.26B	**1.41B**
Non-GAAP operating margin %	45%	44%	**41%**
Non-GAAP net income	1.24B	4.75B	**1.21B**
Non-GAAP net income per share-diluted	$4.80	$18.40	**$4.76**
Cash, cash equivalents & marketable securities (period-end)	12.0B	12.3B	**9.8B**

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 November 2, 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.

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Raising full year 2026 revenue guidance

	Current FY 2026	Previous FY 2026	Commentary
Total revenue	$13.15B to $13.25B	$13.1B to $13.2B	Full year revenue guidance includes expectations for continued growth in CF, $500 million or more in revenue from CASGEVY & JOURNAVX, and contribution from PALSONIFY
Legacy non-CF product revenue (CASGEVY, JOURNAVX)	Unchanged	$0.5B or greater	
PALSONIFY revenue (Sept-Dec)	$40 to $50M		
Combined GAAP R&D, AIPR&D, and SG&A expenses *	$7.15 to $7.2B	$6.3 to $6.45B	Includes expectations for continued investment in multiple mid- and late-stage clinical development programs and commercialization capabilities, as well as ~$250M of Crinetics operating expenses and ~$100M of currently anticipated AIPR&D expenses.
Combined non-GAAP R&D, AIPR&D, and SG&A expenses*	~$6.0B	$5.65 to $5.75B	
Non-GAAP effective tax rate	Unchanged	19.5% to 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, and approximately $500 million of compensation and transaction costs related to the Crinetics Pharmaceuticals acquisition.

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Crinetics Pharmaceuticals acquisition impact

Q3:26 results and revised FY26 guidance

Q3:26 Results		
	Crinetics impact (Sep.)	**Total company (Vertex + Crinetics)**
Revenue	**$10M**	**$3,441M**
Non-GAAP OpEx*	**~$60M** OpEx & integration costs	**$1,533M**
Non-operating items		
Interest expense & non-GAAP other expense, net	**(~$50M)**	**($50M)**
Interest income	**($15M)** forgone interest	**$118M**

FY 2026 Guidance		
Prior guidance (Aug. 3)	**Projected Crinetics impact (Sep–Dec)**	**Current total company guidance**
$13.1–$13.2B	**~$40-50M**	**$13.15–$13.25B**
$5.65–$5.75B Expect to be at high end of range	**~$250M** OpEx & integration costs	**~$6.0B**
	(~$105M)	**N/A**
	($60M) forgone interest	**N/A**

**Combined non-GAAP R&D, Acquired IPR&D and SG&A expenses; Crinetics Pharmaceuticals acquisition impact reflects the Sept. 1 - Dec. 31 post-close period. An explanation and reconciliation of combined GAAP R&D, Acquired IPR&D and SG&A expenses to non-GAAP R&D, Acquired IPR&D and SG&A expenses for Q3:26 is included in the company's press release dated November 2, 2026. Q3:26 interest expense and non-GAAP other expense, net in the table above includes ~$36M of GAAP interest expense and ~$14M of non-GAAP other expense. A reconciliation of GAAP other income (expense), net to non-GAAP other expense, net is included in the company's press release dated November 2, 2026.*

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Anticipated key milestones

Marketed CFTR modulators	• Expand number of people treated: ultra-rare mutations, younger patients, additional geographies
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; **began global regulatory submissions**
Next-generation 3.0 (CF)	• **VX-828:** Study completed, delivered positive results; continue to **advance VX-581 and VX-272** in FIH studies; determine next steps based on all data
CASGEVY (SCD/TDT)	• **Reach more eligible patients ages 2+ year-olds** through global ATC network, where approved • Secure additional pediatric approvals around the globe
JOURNAVX (pain)	• **Acute: Continue to drive JOURNAVX Rx & revenue growth;** plan forward to sunset PSP to normalize gross-to-net • Secure approval in Canada • **DPN:** Complete enrollment of both Phase 3 studies by YE 2026; **share data mid-2027**
VX-993 (pain)	• DPN: Complete enrollment of Phase 2 study by YE 2026; **share data mid-2027**
PALSONIFY (acromegaly)	• Drive U.S. launch to grow patients and prescriber base • Plan forward for **EU launch in H2 2027**
VX-017 and Zimislecel (T1D)	• **Enroll and dose Phase 1/2 evaluating VX-017** (Type O, “universal donor”) in people with T1D; zimislecel trial continues
Inaxaplin (AMKD)	• **AMPLITUDE Phase 3 study** (“primary” AMKD population) completed full enrollment; **perform interim analysis and share data in early 2027** • If positive, AMPLITUDE will support potential accelerated approval in the U.S.; discuss AMPLIFIED Ph 2b results with FDA in the context of AMPLITUDE
Povetacicept (IgAN, pMN, gMG)	• **IgAN: PDUFA target action date of November 30 in U.S.**; launch ready • **pMN:** Drive Phase 3 enrollment and dosing well underway • **gMG:** Completed enrollment in Phase 2 study; **share data in H1 2027**
VX-407 (ADPKD)	• Completed enrollment in the AGLOW Phase 2 proof-of-concept study; **share data in 2027**
VX-670 (DM1)	• Completed enrollment and dosing in Phase 1/2 study; **share interim results in H2 2026**
Atumelnant (CAH and Cushing’s Syndrome)	• **CAH (adult): Complete enrollment in Q1 2027** • **CAH (pediatric): Continue to enroll and dose Phase 2 study**; engage with regulators to advance to pivotal trial • **ACTH-dependent Cushing’s Syndrome: Enroll and dose Phase 2/3 trial OUS** and engage with regulators to initiate pivotal study in U.S.

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Third Quarter 2026 Financial Results

November 2, 2026

Presentation intended for the investment community

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Appendix
GAAP to non-GAAP financial information

($ in millions except where noted or per share amounts and percentages)	Q3:25	FY:25	Q3:26
Combined R&D, AIPR&D and SG&A			
GAAP	1.48B	5.80B	**2.21B**
Non-GAAP	1.28B	5.12B	**1.53B**
Operating income			
GAAP	1.19B	4.17B	**0.71B**
Non-GAAP	1.38B	5.26B	**1.41B**
Operating Margin %			
GAAP	39%	35%	**21%**
Non-GAAP	45%	44%	**41%**
Net income			
GAAP	1.08B	3.95B	**0.65B**
Non-GAAP	1.24B	4.75B	**1.21B**
Net income per share-diluted			
GAAP	$4.20	$15.32	**$2.56**
Non-GAAP	$4.80	$18.40	**$4.76**
Shares used in per share calculations			
GAAP	257.6	258.0	**255.2**
Non-GAAP	257.6	258.0	**255.2**

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 November 2, 2026.

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