VERTEX

THE SCIENCE *of* POSSIBILITY

J.P. MORGAN HEALTHCARE CONFERENCE

RESHMA KEWALRAMANI, M.D.

CEO AND PRESIDENT

JANUARY 2025

SAFE HARBOR STATEMENT & NON-GAAP FINANCIAL MEASURES

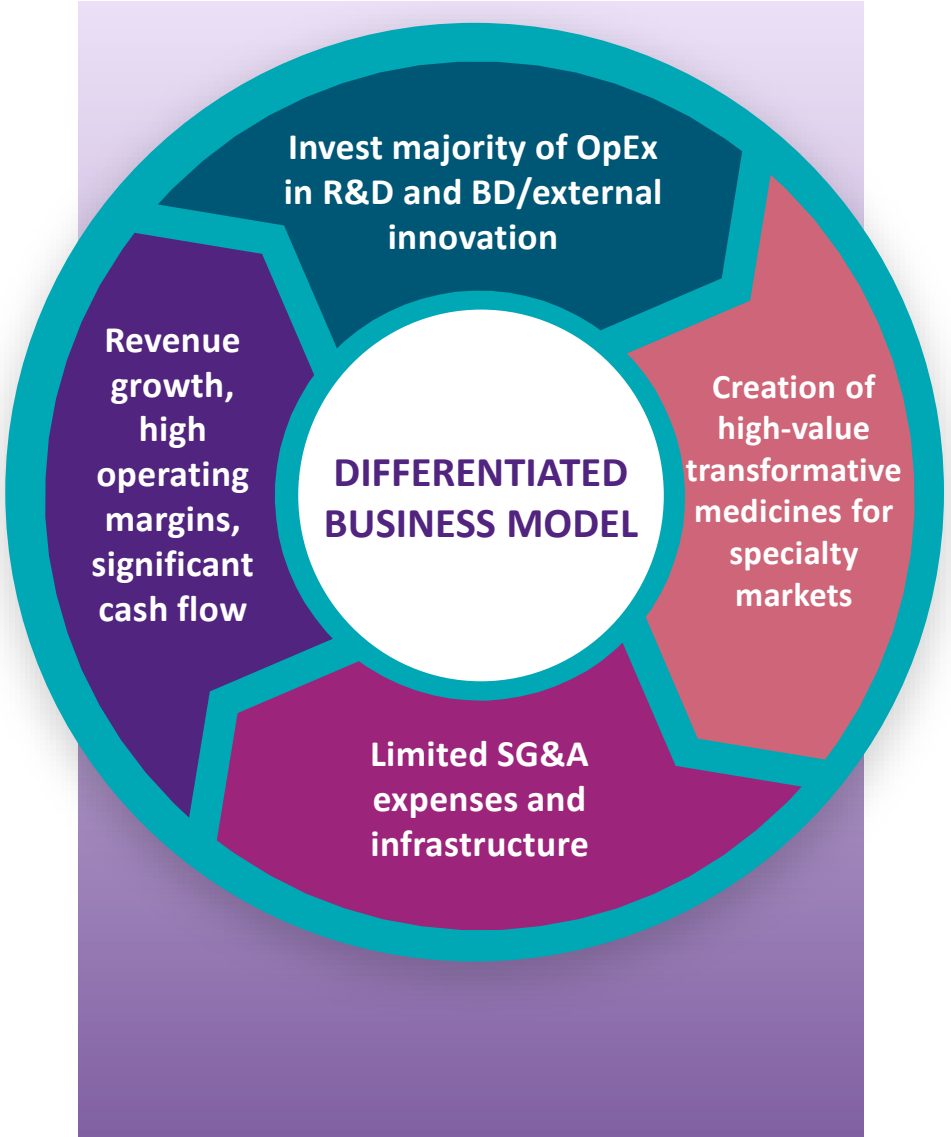
This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, including, without limitation, the information provided regarding future financial and operating performance and statements regarding (i) expectations, development plans and timelines for the company's products, product candidates and pipeline programs, including expectations that we are on track to complete five launches in five years, that we have pipeline diversification across diseases and geographies with pipeline opportunities across multiple multi-billion dollar markets, and the anticipated benefits of new products and regarding relevant patient populations, (ii) expectations for uptake of and expanded access to our products, (iii) expectations for sustained and profitable growth with respect to our CF medicines, including expectations that we will treat younger patients, patients will live longer, we will reach additional geographies, and expectations to attain carrier levels of CFTR function for all patients, (iv) our beliefs regarding the U.S. commercial launch of ALYFTREK, and expectations regarding global regulatory approvals and global launches for ALYFTREK, (v) plans to reach the last >5,000 CF patients with mRNA therapy, including expectations that we will complete the MAD portion of the Phase 1/2 study in VX-522 and share data in the first half of 2025, (vi) expectations for CASGEVY, including with respect to its commercial potential, reaching more patients across geographies, expanding manufacturing to support global demand, advancing studies in younger age groups, and the potential to improve conditioning associated with CASGEVY, (vii) expectations for our pain program, including beliefs that suzetrigine holds the promise to transform pain treatment in the U.S., particularly as a non-opioid treatment, anticipated FDA approval for suzetrigine and its commercial launch in the U.S., enrollment and dosing plans in peripheral neuropathic pain studies, and expectations for suzetrigine in LSR, including potential advancement to Phase 3, (viii) expectations for serial innovation in the treatment of pain, including the developments in clinical trials evaluating VX-993 in acute and peripheral neuropathic pain, (ix) expectations regarding povetacicept in IgAN and other serious renal diseases, including plans to complete enrollment in cohort for potential accelerated approval in the U.S., potential that povetacicept is a best-in-class approach to treat IgAN, advancing enrollment for Phase 3 trial, advancing RUBY-3 and RUBY-4 Phase 2 basket studies, and expectations for our collaboration with Zai Lab, (x) expectations for our T1D program, including with respect to zimislecel as a potentially curative treatment, completion of enrollment and dosing in the pivotal Phase 1/2/3 trial for zimislecel, and plans to share data from Parts A and B of the VX-264 trial in the first half of 2025, (xi) our beliefs that our business model will deliver long-term revenue growth, profitability, and consistently deliver transformative therapies and shareholder value, (xii) expectations for inaxaplin, including completion of enrollment in cohort for potential U.S. accelerated approval and advancing enrollment for full Phase 3 trial, (xiii) expectations with respect to VX-407, including with respect to completion of Phase 1 study and initiating a Phase 2 trial in ADPKD patients, and (xiv) expectations to advance the MAD portion of our study of VX-670 in DM1 patients. 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 may be incorrect, data from clinical trials, especially if based on a limited number of patients, may not to be indicative of final results, the company may not be able to scale up manufacturing of our product candidates, actual patient populations may be smaller than anticipated and that the patient populations able to participate in our trials or eligible for our products may be smaller than 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. Vertex disclaims any obligation to update the information contained in this presentation as new information becomes available.

In this presentation, Vertex references financial guidance and results that have been provided in accordance with US GAAP and certain non-GAAP financial measures. 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. A reconciliation of the GAAP financial results to non-GAAP financial results is included in the appendix hereto.

DIFFERENTIATED VERTEX BUSINESS MODEL AND R&D STRATEGY CONTINUE TO DELIVER…

WE FOCUS ON

- Diseases where causal human biology is known
- Validated targets
- Biomarkers that translate from bench to bedside
- Best modality (i.e., modality agnostic)
- Efficient development & regulatory pathways



IN ORDER TO DELIVER

- Transformative medicines for patients
- Greater likelihood of clinical success
- Sustained innovation
- Shareholder value

…CF LEADERSHIP, NEW APPROVALS, AND PIPELINE ADVANCEMENT, WHICH DRIVE SUSTAINED AND PROFITABLE GROWTH

2012+ →

Expanding CF leadership

- ALYFTREK
- TRIKAFTA
- SYMDEKO
- ORKAMBI
- KALYDECO

2024-2028 →

Delivering commercial diversification*

- CASGEVY SCD
- CASGEVY TDT
- Suzetrigine acute pain

Pivotal trials:**

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

2028+ →

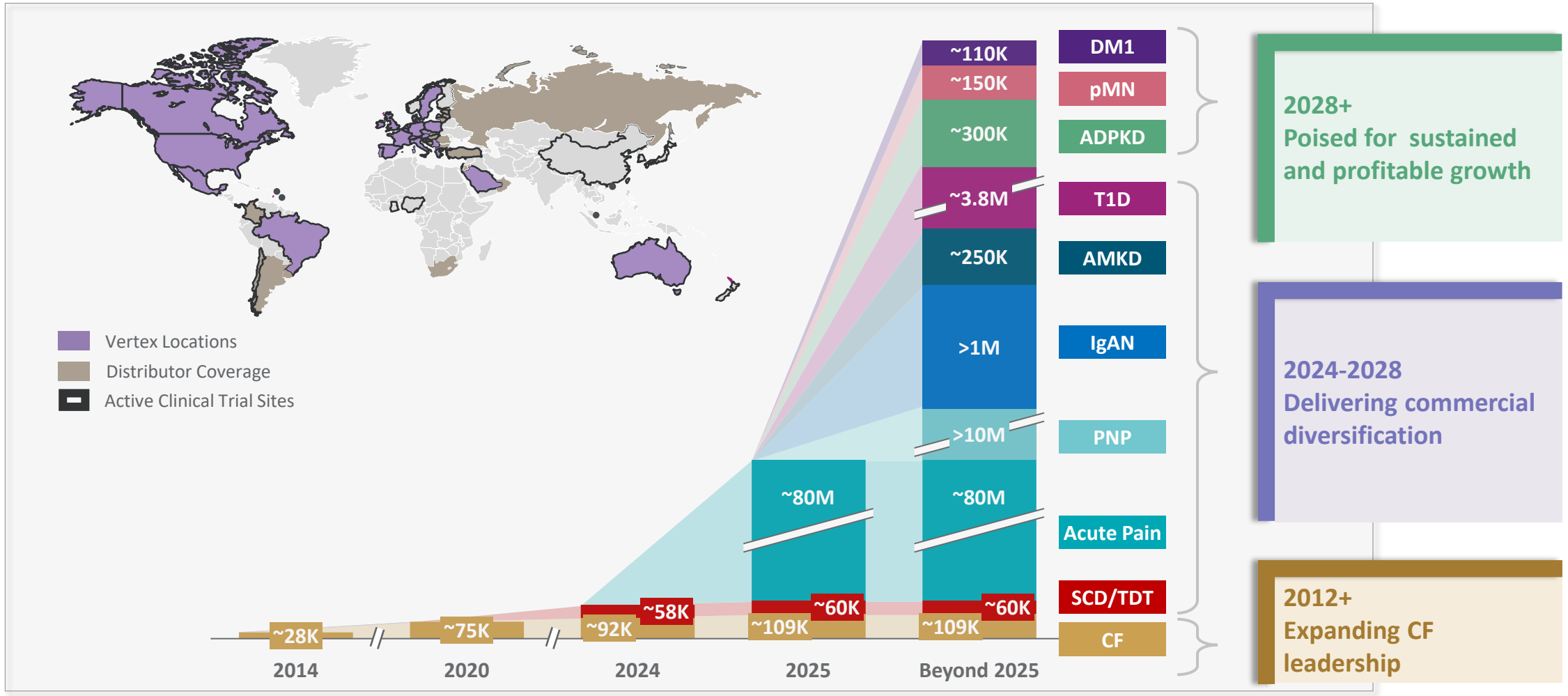
Poised for sustained and profitable growth

- VX-993, $Na_V1.7$ pain
- Suzetrigine PNP
- VX-522 CF
- VX-264, other T1D
- VX-670 DM1
- VX-407 ADPKD
- Povetacicept other indications (e.g., pMN)
- Improved conditioning for use with CASGEVY
- Additional sandbox disease areas and assets

*Approved or submitted for regulatory approval. **In Phase 3 clinical development.

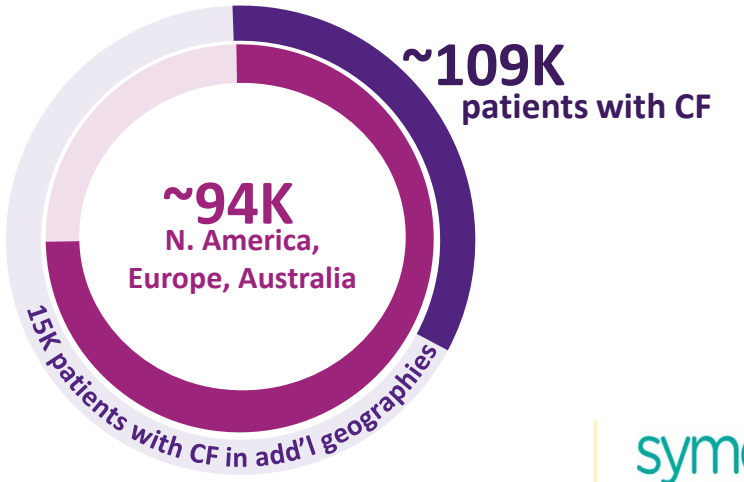
DIVERSIFICATION ACROSS DISEASES AND GEOGRAPHIES DRIVING SIGNIFICANT EXPANSION IN POTENTIAL TO SERVE PATIENTS

PIPELINE OPPORTUNITIES ACROSS MULTIPLE MULTI-$B MARKETS



*All epidemiological estimates include patients in North America and Europe, with three exceptions: 1) CF includes Australia and additional geographies as detailed on Slide 6; 2) SCD/TDT also includes the Middle East and 3) IgAN also includes diagnosed patients in China. All estimates reflect the ultimate target patient population; at initial launch, potential indications may be a subset of the total patient population opportunity.

CF: EXPANDING LEADERSHIP AND RAISING THE BAR WITH SERIAL INNOVATION



kalydeco (ivacaftor)

Patients 1 month and older

ORKAMBI (lumacaftor/ivacaftor)

Patients 1 year and older

symdeko (tezacaftor/ivacaftor & ivacaftor)

Patients 6 years and older

kaftrio / trikafta (elexacaftor/tezacaftor/ivacaftor and ivacaftor)

Current gold standard CFTRm treatment for patients 2 years and older

alyftrek (vanzacaftor/tezacaftor/deutivacaftor)

Highly effective triple CFTRm for patients 6 years and older; once-daily dosing

VX-522

- For the last >5,000 patients who cannot benefit from CFTRm
- SAD completed
- MAD ongoing; data expected H1:2025

ULTIMATE GOAL:

Carrier levels of CFTR function for all patients

- Additional regimens in Phase 1 and 2 trials
- Ongoing research

SUSTAINED DRIVERS OF CF GROWTH:

1. Treating younger patients
2. Patients living longer
3. Additional geographies

*In countries where vanzacaftor triple combination is not yet approved, TRIKAFTA is the current gold standard CFTRm treatment for patients 2y+ with TRIKAFTA-responsive mutations.

~75% of patients with CF in North America, Europe Australia and ~33% of patients in additional geographies are currently benefiting from CFTRm therapy.

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

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

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**

Payers - U.S.
Commercial – coverage not an obstacle
Medicaid – First-ever CMMI Demonstration Project launched: *Cell & Gene Therapy Access Model*

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

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). **Through 12/31/2024.
ATC: authorized treatment center; EAP: Early Access Program; CMMI: Center for Medicare and Medicaid Innovation.

Serial innovation includes improved conditioning in preclinical development, *in vivo* editing and small molecule programs in discovery research

PAIN: OPIOIDS ARE EFFECTIVE IN MODERATE TO SEVERE ACUTE PAIN, BUT HAVE SAFETY/TOLERABILITY CONCERNS AND ADDICTION POTENTIAL

40M

acute pain patients receive an opioid Rx annually[1]

78%

of healthcare providers surveyed were concerned about the risk of opioid addiction among their patients with acute pain[2]

10%

of acute pain patients treated initially with an opioid will go on to have prolonged opioid use[3]

85K

acute pain patients will develop opioid use disorder (OUD) annually[4]

$180B

estimated annual costs of OUD to the U.S. economy

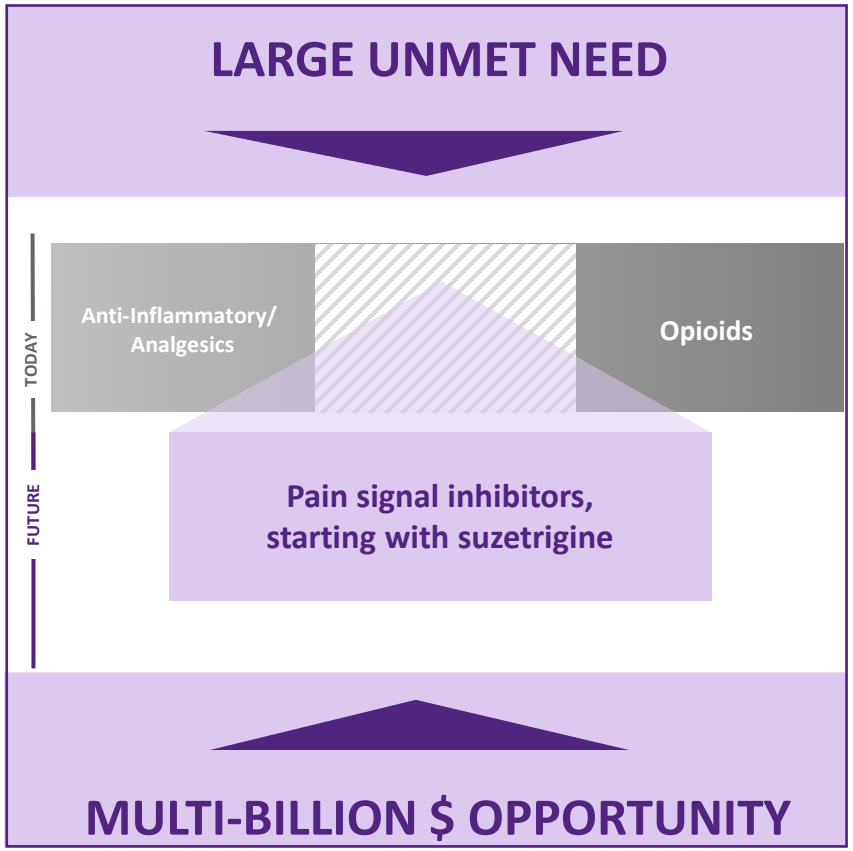
$10-20B

attributed to management of OUD stemming from opioids initially prescribed for acute pain[5]

*U.S. data 1. Lopez, et al., "An Evaluation of the Prevalence of Acute and Chronic Pain Medication Use in the United States: A Real-World Database Analysis," ASRA Annual Pain Meeting 2023; 2. Vertex Pharmaceuticals Incorporated "State of Pain in America," survey of 547 U.S. healthcare providers who treated acute pain in the last month and 1,001 U.S. adults treated for acute pain in the last year. Boston, MA. REF-26477 (v1.0); 2024. 3. Vertex Pharmaceuticals research; 4. Shoenfeld, et al., "An Evaluation of the Incidence of Opioid Use Disorder Among People with Acute and Chronic Pain Managed with Prescription Opioids and the Associated Economic and Societal Burden in the United States," PAINWeek 2024; 2019 report based upon 2018 data; 5. "The Society of Actuaries Report 2019: Economic Impact of Non-Medical Opioid Use in the United States." Of the $180B in annual costs of OUD, $60B is attributed to healthcare costs for the management of OUD, of which an estimated $10-20 billion is attributable to opioids initially prescribed for acute pain.

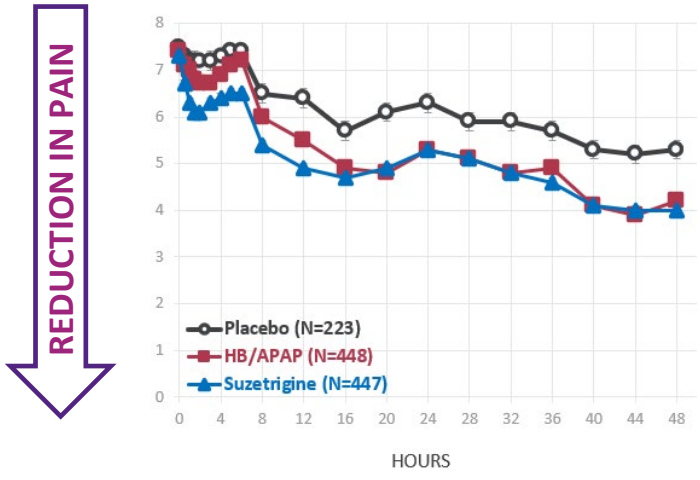
SUZETRIGINE HOLDS THE PROMISE TO FUNDAMENTALLY RESHAPE TREATMENT FOR 80M PATIENTS WITH MODERATE TO SEVERE ACUTE PAIN

PDUFA DATE: JANUARY 30, 2025

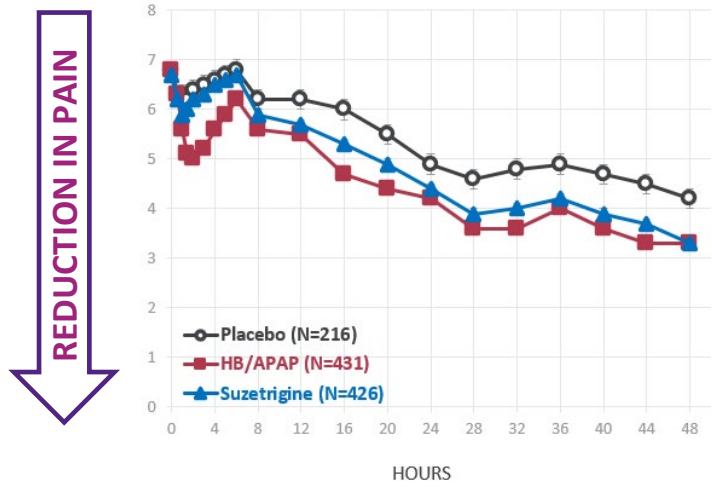


3.4 point (~50%)
reduction in NPRS scores from baseline in each trial

Phase 3 ABDOMINOPLASTY
Mean NPRS scores over the treatment period



Phase 3 BUNIONECTOMY
Mean NPRS scores over the treatment period



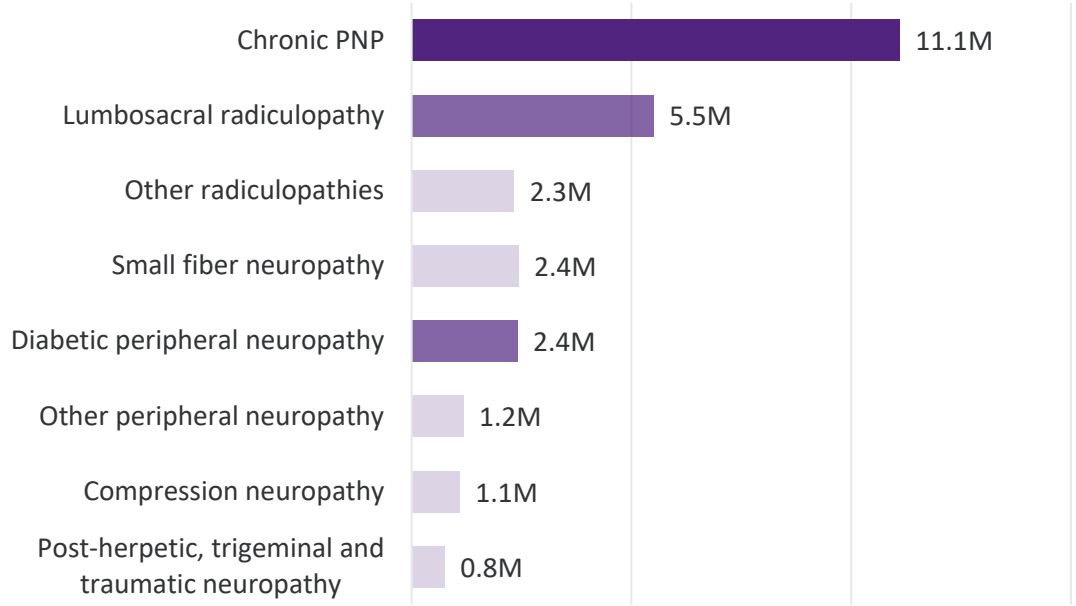
Vertex is LAUNCH READY

Source: https://investors.vrtx.com/news-releases/news-release-details/vertex-announces-results-phase-2-study-suzetrigine-treatment

CONTINUE TO INNOVATE SERIALLY IN PAIN, INCLUDING PNP

CURRENT TREATMENT OPTIONS HAVE HIGH DISCONTINUATION RATES, POLYPHARMACY, INCONSISTENT DOSING

~11M chronic pain patients with PNP diagnosis*



Suzetrigine PNP program is well underway

DPN

- Strong Phase 2 results
- Phase 3 enrollment and dosing underway

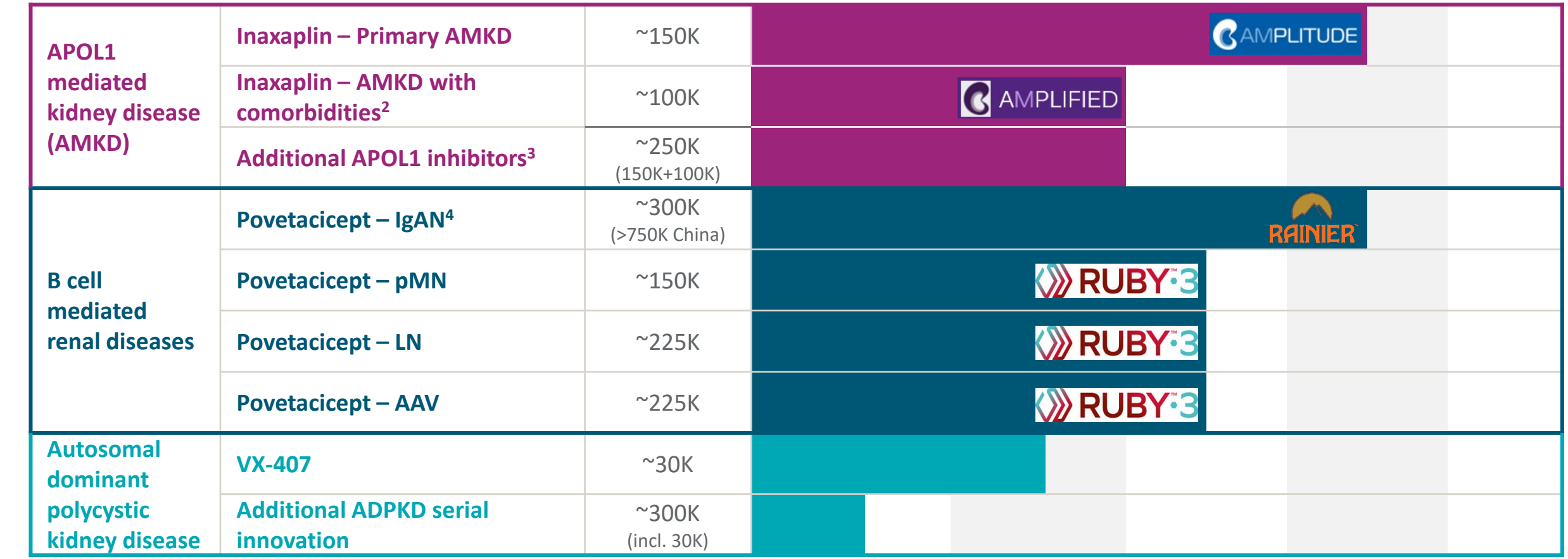
LSR

- Phase 2 study complete
- Suzetrigine demonstrated statistically significant and clinically meaningful within-group change in NPRS pain scores; however, curve did not separate from placebo
- Apply learnings, advance to Phase 3 pending FDA interactions

Serial innovation includes VX-993 oral (Phase 2 acute, Phase 2 DPN) and IV (Phase 1); additional $Na_V1.8$ and $Na_V1.7$ inhibitors in preclinical development

*Categories of PNP conditions are not mutually exclusive. PNP: peripheral neuropathic pain; M: million. Source: 2022 MarketScan Data.

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 trial to begin H1:25. 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 IGAN CLINICAL TRIAL UNDERWAY

POTENTIAL BEST-IN-CLASS APPROACH TO TREAT IGAN, AUGMENTED BY STRATEGIC COLLABORATION IN ASIA

Best-in-class potential

Strong preclinical profile:

- Dual BAFF/APRIL inhibitor with high affinity and potency

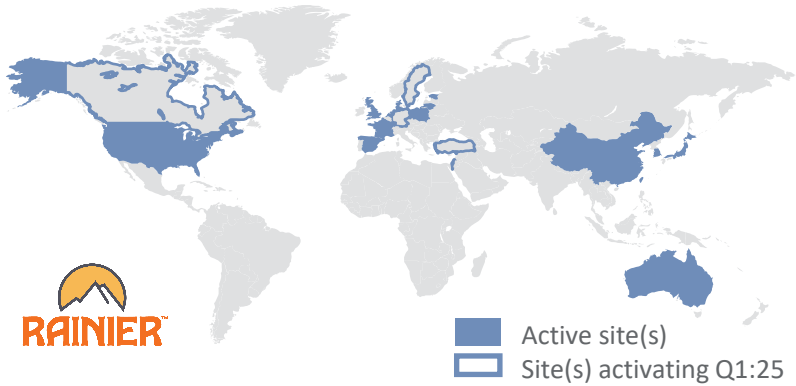
Compelling RUBY-3 data (ASN 2024):

- 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 underway



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

zai lab

- Strategic collaboration and licensing agreement to develop and commercialize pove in **China, Hong Kong, Macau, Taiwan** and **Singapore**
- Zai Lab brings regional expertise and footprint to accelerate clinical trials, make regulatory submissions and lead commercialization

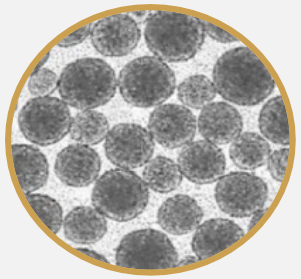
*Defined as UPCR (urine protein creatinine ratio) < 0.5 g/g, negative hematuria, and stable renal function.
BAFF: B-cell activating factor. APRIL: A Proliferation-Inducing Ligand; eGFR: estimated glomerular filtration rate.

TYPE 1 DIABETES: ADVANCING POTENTIALLY CURATIVE TREATMENTS AND SERIAL INNOVATION FOR ~3.8M PATIENTS IN NORTH AMERICA AND EUROPE

FULLY DIFFERENTIATED, STEM-CELL DERIVED, GLUCOSE-RESPONSIVE, INSULIN-PRODUCING ISLETS (ZIMISLECEL/VX-880) ARE FOUNDATIONAL AND UNIQUE TO VERTEX T1D PROGRAMS

Zimislecel (formerly VX-880)

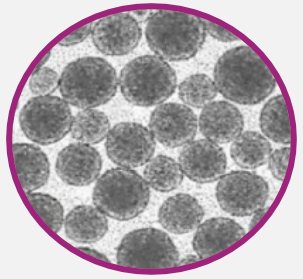
Stem-cell derived islets with standard immunosuppression (IS)



Phase 3 underway
Complete dosing YE 2025

VX-264

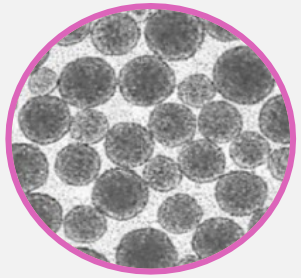
Stem-cell derived islets with encapsulation device



Phase 1/2 Part B full-dose data in 2025

Zimislecel + Alternative IS

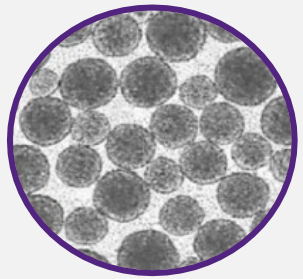
Stem-cell derived islets with alternative immunosuppression



Research stage

Hypoimmune

Stem-cell derived islets with hypoimmune gene editing



Research stage

ZIMISLECEL (VX-880) NOW IN PIVOTAL DEVELOPMENT

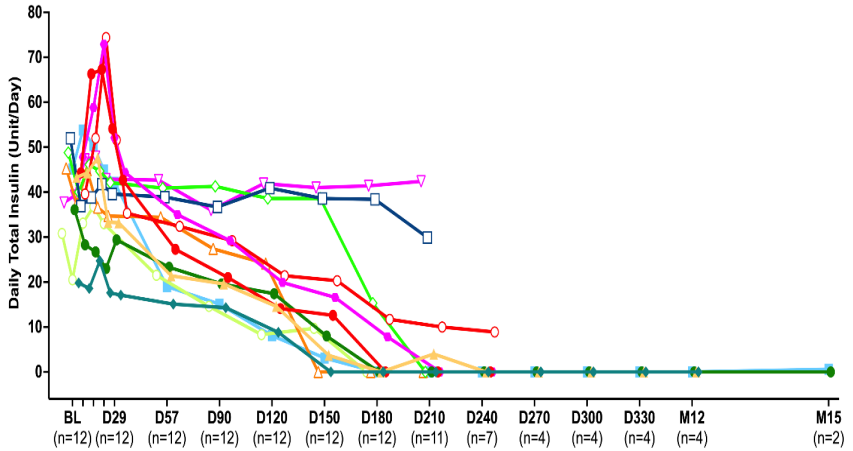
Patient Population: T1D patients with impaired hypoglycemic awareness and severe hypoglycemic events (SHEs)

Study design: Phase 1/2/3, single-arm, open-label, 3-part study

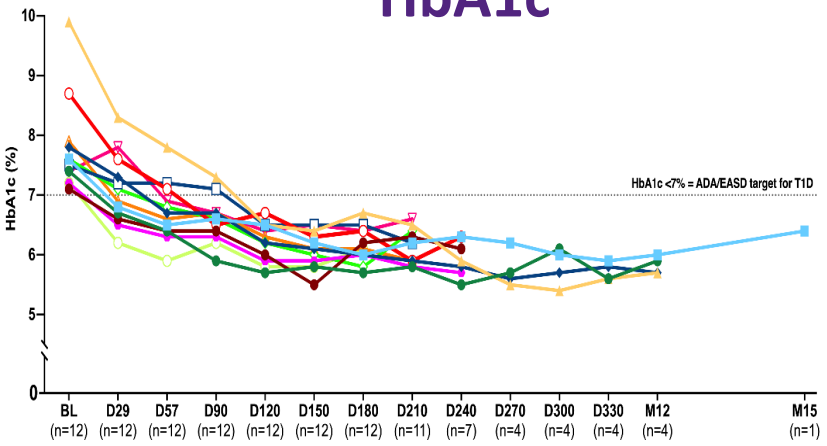
Sample Size: ~50 participants

Primary endpoint: Proportion of subjects who are insulin independent with freedom from SHEs

Total Daily Insulin



HbA1c



As of EASD 2024, 12 participants

completed the Day 180 visit:

12 All **12** patients achieved a **reduction in HbA1c to <7%**

11 had **elimination or reduction of exogenous insulin use**

9 were **no longer using exogenous insulin***

*Although prohibited by protocol, two patients had steroid use in the peri-infusion period. One participant had one dose of steroids on the day of zimislecel infusion and did reduce (43%), but not eliminate, exogenous insulin. One participant received four doses of steroids in the peri-infusion period and saw a 12% increase in their use of exogenous insulin.

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	alyftrek™
$Na_V1.7$ inhibitor Pain	**VX-407** ADPKD	**Suzetrigine** LSR	**Suzetrigine** DPN	**Suzetrigine** Acute Pain	casgevy®
Hypoimmune islet cells Type 1 diabetes	**VX-993** Pain - Intravenous	**VX-993** Acute pain	**Povetacicept** IgA nephropathy	**Vanzacaftor triple add'l geographies** Cystic Fibrosis	trikafta®
Small molecule Huntington's disease		**VX-993** PNP - DPN	**Zimislecel** Type 1 diabetes		symdeko®
		VX-522 CFTR mRNA			ORKAMBI®
		VX-670 DM1			kalydeco®
		Povetacicept, RUBY-3 pMN, LN, AAV			
		Povetacicept, RUBY-4 ITP, AIHA, CAD			

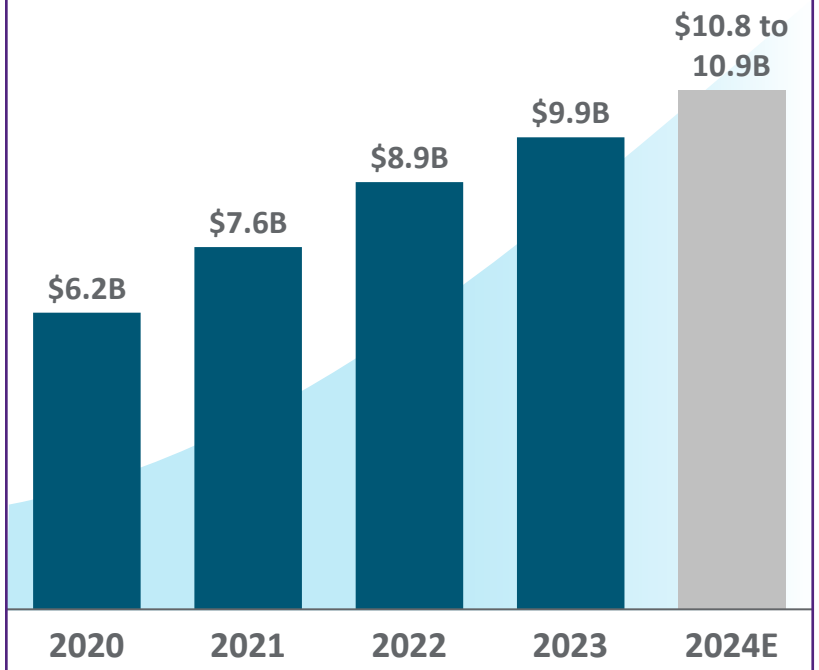
SCD: sickle cell disease; TDT: transfusion-dependent beta thalassemia; CF: cystic fibrosis; AMKD: APOL-1 mediated kidney disease; ADPKD: autosomal dominant polycystic kidney disease; LSR: lumbosacral radiculopathy; PNP: peripheral neuropathic pain; DPN: painful diabetic peripheral neuropathy; CFTR mRNA: 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.

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**
CASGEVY (SCD/TDT)	• **Reach more eligible 12+ yo patients** across geographies with regulatory approval and access • Complete dosing for 5-11 yo in SCD and TDT
Suzetrigine (pain)	• **Acute: Jan. 30, 2025 PDUFA; secure approval and drive launch** • **DPN: Enroll and dose Phase 3 trial** • **LSR: Advance to Phase 3, pending regulatory discussions**
VX-993 (pain)	• **Acute: Advance Phase 2 study for acute** (BUN; oral); complete Phase 1 IV • **DPN: Advance Phase 2 study** (DPN; oral)
Inaxaplin (AMKD)	**Complete enrollment in cohort for potential U.S. accelerated approval,** once cohort reaches 48 weeks treatment
VX-407 (ADPKD)	**Complete Phase 1 study and initiate Phase 2 trial in ADPKD patients**
Povetacicept (IgAN, etc.)	• **IgAN: complete enrollment in cohort for potential U.S. accelerated approval,** once cohort reaches 36 weeks treatment • **Advance RUBY-3 and RUBY-4** Phase 2 basket studies in autoimmune renal diseases and cytopenias
Zimislecel/VX-880 (T1D)	**Complete enrollment and dosing in Phase 1/2/3 pivotal trial**
VX-264 (T1D)	**Share data from Phase 1/2 Part B full dose in 2025**
VX-670 (DM1)	**Advance MAD portion of study in DM1 patients**, which will evaluate both safety and efficacy

DIFFERENTIATED BUSINESS MODEL DELIVERS LONG-TERM REVENUE GROWTH, FUELING CONTINUED INVESTMENT IN INNOVATION AND ATTRACTIVE PROFITABILITY

Strong, sustained **revenue growth**



Total Product Revenue

Commitment to disciplined **investment in innovation**

26%

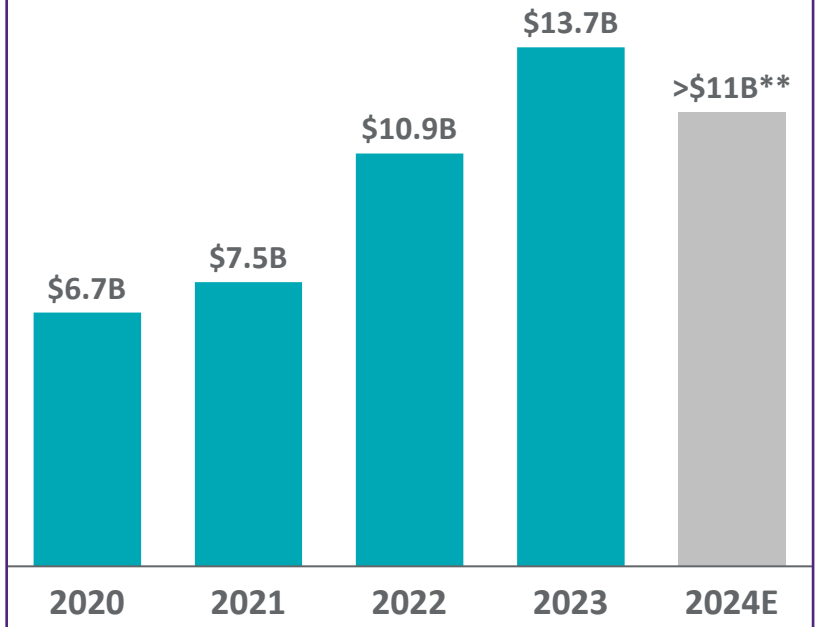
of revenue invested in R&D 2024 YTD*:
Late-stage clinical trials, new disease areas, manufacturing, etc.

$4.5B

AIPR&D YTD 2024*:

ALPINE ImmuneSciences™
TreeFrog therapeutics
GENOMICS
ORNA®
Lonza
ORUM THERAPEUTICS

Attractive profitability drives durable cash flow



Cash & Investments

Note: 2024E total product revenue reflects total product revenue guidance provided on 11/4/24. This slide is intended to be illustrative and is not intended to be a reiteration of guidance.
*Non-GAAP R&D expenses as a percentage of total product revenue and total AIPR&D expenses, in each case, for the nine-month period ending 9/30/2024. See appendix for a reconciliation of the non-GAAP R&D figure.
**2024E Cash & Investments of $11.2B as of 9/30/24.

OUR GOAL IS TO CONSISTENTLY DELIVER TRANSFORMATIVE THERAPIES AND SHAREHOLDER VALUE

Expand CF leadership

- ❑ Launch ALYFTREK (vanzacaftor triple) globally
- ❑ Advance additional small molecules to bring all eligible patients to carrier levels of CFTR function
- ❑ Advance VX-522 to reach the >5,000 patients who cannot benefit from a CFTRm

Execute to deliver commercial diversification

- ❑ Bring CASGEVY to more patients around the world
- ❑ Secure approval and launch suzetrigine in moderate to severe acute pain in the U.S.
- ❑ Build for future commercialization in T1D, renal therapies and neuropathic pain

Advance broad and deep R&D pipeline

- ❑ Rapidly progress the four Phase 3 programs through pivotal development
  - Pove IgAN, zimislecel, inaxaplin, suzetrigine DPN
- ❑ Advance early- and mid-stage programs in clinical development
- ❑ Progress next wave of innovation into the clinic

Deliver financial performance

- ❑ Sustain CF product revenue growth
- ❑ Diversify revenue base with CASGEVY, suzetrigine in acute pain + launches in additional disease areas
- ❑ Sustain strong operating margins, continue to invest in pipeline, execute specialty model
- ❑ Prioritize cash deployment for external innovation, share repurchase

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THE SCIENCE *of* POSSIBILITY

APPENDIX

MULTIPLE CATALYSTS THROUGHOUT 2025 AND BEYOND

	RECENT HIGHLIGHTS	ANTICIPATED KEY MILESTONES
Vanzacaftor triple	**Approved in U.S. 12/20/24; global reviews underway** EU, U.K., Canada, Australia, Switzerland and New Zealand	**Drive U.S. launch; secure additional regulatory approvals and execute global launches**
VX-522	**CFTR mRNA Phase 1/2 study** SAD completed; MAD underway	Complete MAD portion of the Phase 1/2 study and **share data in 2025**
CASGEVY	• Continued **strong early launch** progress across all regions • **Received regulatory approvals** in Canada, Switzerland, UAE for SCD/TDT	• **Reach more eligible 12+ yo patients** across geographies with regulatory approval and access • Complete dosing for 5-11 yo in SCD and TDT
Suzetrigine	• **Acute: NDA accepted with Priority Review** • **DPN: Initiated Phase 3 trial** • **LSR: Completed Phase 2 study**	• **Acute: Jan. 30, 2025 PDUFA; secure approval and drive launch** • **DPN: Enroll and dose Phase 3 trial** • **LSR: Advance to Phase 3, pending regulatory discussions**
VX-993	• **Acute: Initiated Phase 2 study** (BUN; oral); **enrolling/dosing Phase 1 IV** • **DPN: Initiated Phase 2 study** (DPN; oral)	• **Acute: Advance Phase 2 study for acute** (BUN; oral); complete Phase 1 IV • **DPN: Advance Phase 2 study** (DPN; oral)
Inaxaplin (AMKD)	**Enrolling and dosing patients in Phase 3**	**Complete enrollment in cohort for potential U.S. accelerated approval,** once this cohort reaches 48 weeks of treatment
VX-407 (ADPKD)	**Phase 1 clinical trial in healthy volunteers underway**	**Complete Phase 1 study and initiate Phase 2 trial in ADPKD patients**
Povetacicept (IgAN)	**Initiated Phase 3 trial; shared additional IgAN data and promising, emerging RUBY-3 data on pMN at ASN**	• **In IgAN, complete enrollment in cohort for potential U.S. accelerated approval,** once this cohort reaches 36 weeks of treatment • **Advance RUBY-3 and RUBY-4** Phase 2 basket studies in autoimmune renal diseases and cytopenias
VX-880 (T1D)	**Phase 1/2 trial converted to Phase 1/2/3 with ~50 total patients**	**Complete enrollment and dosing in Phase 1/2/3 pivotal trial**
VX-264	**Phase 1/2 trial Parts A and B enrollment and dosing complete**	**Share data from Phase 1/2 Part B full dose in 2025**
VX-670 (DM1)	**Completed SAD portion of Phase 1/2 clinical trial for DM1 patients; Initiated MAD portion**	**Advance MAD portion of study in DM1 patients**, which will evaluate both safety and efficacy

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.

RECONCILIATION OF GAAP TO NON-GAAP FINANCIAL INFORMATION

All numbers in the reconciliation tables below are in millions except where noted.

	Nine Months Ended September 30, 2024
Product Revenue, Net	$8.11B
GAAP Research and Development ("R&D") Expenses	$2.63B
Stock-based compensation expense	(327)
Intangible asset amortization expense	(1)
Acquisition-related costs	(172)
Non-GAAP R&D Expenses	$2.13B
GAAP R&D Expenses as % of Product Revenues	*32%*
Non-GAAP R&D Expenses as % of Product Revenues	*26%*