

# CORPORATE PRESENTATION

January 2025

# Forward Looking Statements

Ventyx Biosciences, Inc. (“Ventyx” or the “Company”) cautions you that statements contained in this presentation regarding matters that are not historical facts are forward-looking statements. These statements are based on the Company’s current beliefs and expectations. Such forward-looking statements include, but are not limited to, statements regarding: the expected year-end 2024 cash balance based on preliminary, unaudited information for the year ended December 31, 2024; the potential of Ventyx’s product candidates, including the potential of meaningful value creation through clinical trial results, potential of VTX3232 to demonstrate best in class profile, treat various neuroinflammatory diseases, including Parkinson’s disease modification, or to achieve certain drug concentrations in the CSF, the potential of VTX2735 to demonstrate best in class profile or treat various systemic diseases, and the potential of VTX002 in UC and class-leading safety and efficacy profile; the design of clinical studies to be conducted by the Company; the total addressable market for a Parkinson’s disease modifying therapy; the timing of clinical updates for all three Phase 2 studies of VTX3232 and VTX2735, including the publication of any clinical data from these studies in 2025; the regulatory pathway for VTX2735 and any expedited pathways that may be available; management’s plans with respect to a potential pivotal Phase 3 trial for tamuzimod (VTX002) in UC, supported by a partner or other source of non-dilutive financing; the need for a single pivotal study for VTX002; and the expected timeframe for funding Ventyx’s operating plan with current cash, cash equivalents and marketable securities.

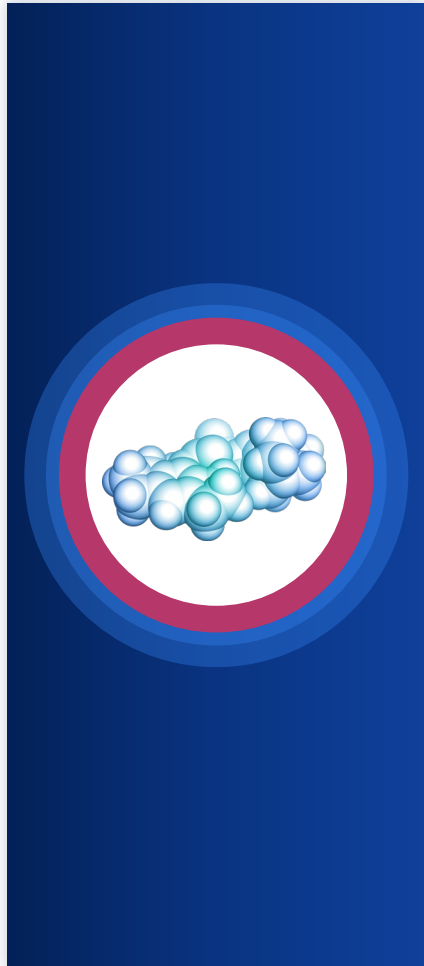
We are in the process of finalizing our financial statements for the year ended December 31, 2024, and the preliminary, unaudited information presented in this press release for the year ended December 31, 2024 is based on management’s initial review of the information presented and its current expectations and is subject to adjustment as a result of, among other things, the completion of Ventyx’s end-of-period reporting processes and related activities, including the audit by Ventyx’s independent registered public accounting firm of Ventyx’s financial statements. As such, any financial information contained in this press release may differ materially from the information reflected in Ventyx’s financial statements as of and for the year ended December 31, 2024. You should carefully review our audited, consolidated financial statements for the year ended December 31, 2024 when they become available.

The inclusion of forward-looking statements should not be regarded as a representation by Ventyx that any of its plans will be achieved. Actual results may differ from those set forth in this presentation due to the risks and uncertainties inherent in Ventyx’s business, including, without limitation: potential delays in the commencement, enrollment and completion of clinical trials; Ventyx’s dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; disruptions in the supply chain, including raw materials needed for manufacturing and animals used in research, delays in site activations and enrollment of clinical trials; the results of preclinical studies and early clinical trials not necessarily being predictive of future results; interim results not necessarily being predictive of final results; the potential of one or more outcomes to materially change as a trial continues and more patient data become available and following more comprehensive audit and verification procedures; regulatory developments in the United States and foreign countries; unexpected adverse side effects or inadequate efficacy of Ventyx’s product candidates that may limit their development, regulatory approval and/or commercialization, or may result in recalls or product liability claims; Ventyx’s ability to obtain and maintain intellectual property protection for its product candidates; the use of capital resources by Ventyx sooner than expected; disruption to Ventyx’s operations from the ongoing military conflicts in Ukraine and the Middle East, including clinical trial delays; and other risks described in Ventyx’s press releases and Ventyx’s filings with the Securities and Exchange Commission (SEC), including in Part II, Item 1A (Risk Factors) of Ventyx’s Quarterly Report on Form 10-Q for the quarter ended September 30, 2024, filed on or about November 7, 2024, and any subsequent filings with the SEC. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and Ventyx undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

This presentation includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties as well as our own estimates of potential market opportunities. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our products include several key assumptions based on our industry knowledge, industry publications, third-party research and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reliable, such assumptions have not been verified by any third party. The industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of important factors that could cause results to differ materially from those expressed in the estimates made by third parties and by us.

Trademarks in this presentation are the property of their respective owners and used for informational and education purposes only.

# Company Highlights



**NLRP3 inhibition** represents a paradigm shift in the treatment of autoimmune, inflammatory and neurodegenerative disorders via upstream regulation of key cytokines (e.g., IL-1, IL-18, IL-6)

**VTX2735** and **VTX3232** demonstrate potential best-in-class profiles: low nanomolar potency; proven target engagement; clinical proof-of-concept in CAPS; favorable safety profile

**Clinical catalysts represent three potential paths to meaningful value creation in 2025:**

- VTX2735 Phase 2 recurrent pericarditis trial – data expected **H2 2025**
- VTX3232 Phase 2 cardiometabolic trial in obese participants – data expected **H2 2025**
- VTX3232 Phase 2 early Parkinson’s disease study – data expected **H1 2025**

**Late-stage Inflammatory Bowel Disease portfolio provides potential additional source of value:**

- Tamuzimod is a Phase 3-ready, potential best-in-class S1P1R modulator for Ulcerative Colitis
- VTX958 (TYK2 inhibitor) demonstrated robust endoscopic response in a Phase 2 Crohn’s disease study

**Strong balance sheet:** \$252.9M\* in cash to fund operations into at least H2 2026

CAPS: Cryopyrin-associated autoinflammatory syndromes

\*Preliminary cash, cash equivalents and marketable securities balance as of December 31, 2024 (unaudited), subject to adjustments resulting from, among other things, the completion of our end-of-period reporting processes and related activities, including the audit by our independent registered public accounting firm of our financial statements.

# Experienced Leadership Team

## Executive Team



**Raju Mohan, PhD**  
CHIEF EXECUTIVE OFFICER,  
FOUNDER



**Mark Forman, MD, PhD**  
CHIEF MEDICAL OFFICER



**Matthew Moore**  
CHIEF OPERATING OFFICER



**John Nuss, PhD**  
CHIEF SCIENTIFIC OFFICER

## Board Of Directors

**Sheila Gujrathi, PhD**  
EXECUTIVE CHAIR, VENTYX

**Raju Mohan, PhD**  
CHIEF EXECUTIVE OFFICER, VENTYX

**Onaiza Cadoret-Manier**  
CHIEF EXECUTIVE OFFICER, STEALTH BIOTECH

---

**Allison Hulme, PhD**  
CHIEF EXECUTIVE OFFICER, AEOVIAN  
PHARMACEUTICALS

---

**Somu Subramaniam**  
MANAGING PARTNER, NEW SCIENCE VENTURES

---

**William White**  
CHIEF FINANCIAL OFFICER, AKERO THERAPEUTICS

# Internally Discovered Clinical-Stage Pipeline

Addressing Autoimmune, Inflammatory and Neurodegenerative Diseases with High Unmet Need

TARGET	PROGRAM	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	NEXT ANTICIPATED MILESTONES
	<b>VTX2735</b> <i>Peripheral</i>	Recurrent Pericarditis				Ph 2 data <b>H2 2025</b>
<b>NLRP3</b>	<b>VTX3232</b> <i>CNS-Penetrant</i>	Parkinson's Disease				Ph 2 data <b>H1 2025</b>
	<b>VTX3232</b> <i>CNS-Penetrant</i>	Cardiometabolic Diseases (CMD) / Obesity				Ph 2 data <b>H2 2025</b>
<b>S1P1</b>	<b>Tamuzimod*</b>	Ulcerative Colitis				Phase 3 Ready*
<b>TYK2</b>	<b>VTX958</b>	Crohn's Disease				Phase 2 analysis underway

Cash, cash equivalents and marketable securities of **\$252.9M (unaudited)\*\*** as of December 31, 2024 are expected to fund operations into at least the **second half of 2026**

\*Formerly VTX002. Available for partnering or non-dilutive financing.

\*\*Preliminary cash, cash equivalents and marketable securities balance as of December 31, 2024 (unaudited), subject to adjustments resulting from, among other things, the completion of our end-of-period reporting processes and related activities, including the audit by our independent registered public accounting firm of our financial statements.



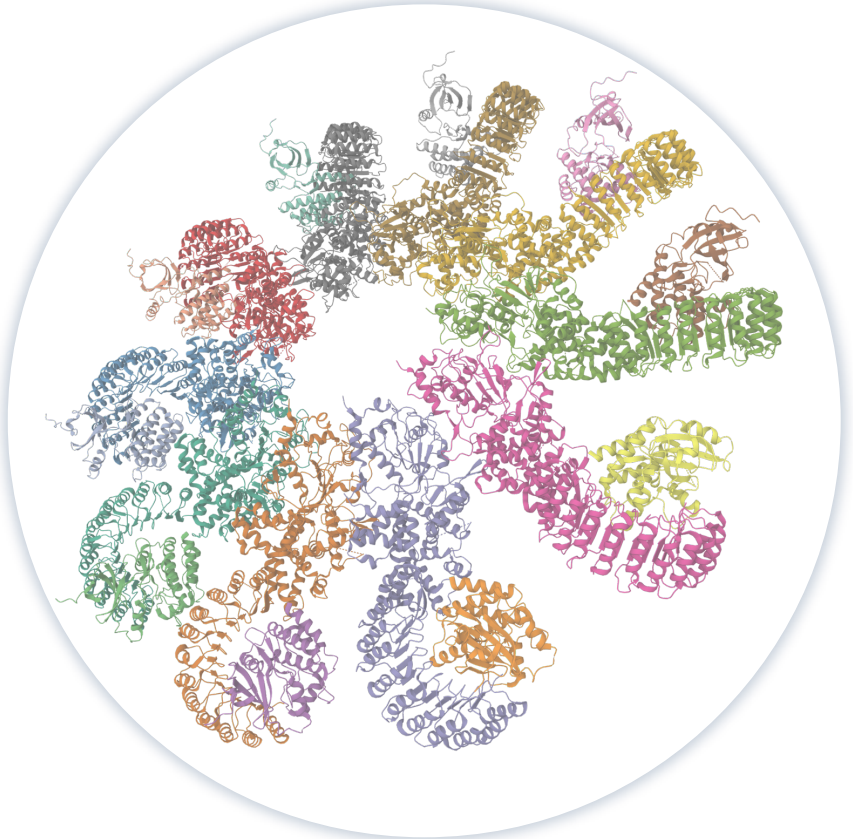


# NLRP3 Inhibition

**Broad potential in inflammatory diseases**

# NLRP3 Inflammasome: A Key Component of Innate Immunity

## Dysregulation Linked to a Broad Range of Inflammatory Diseases

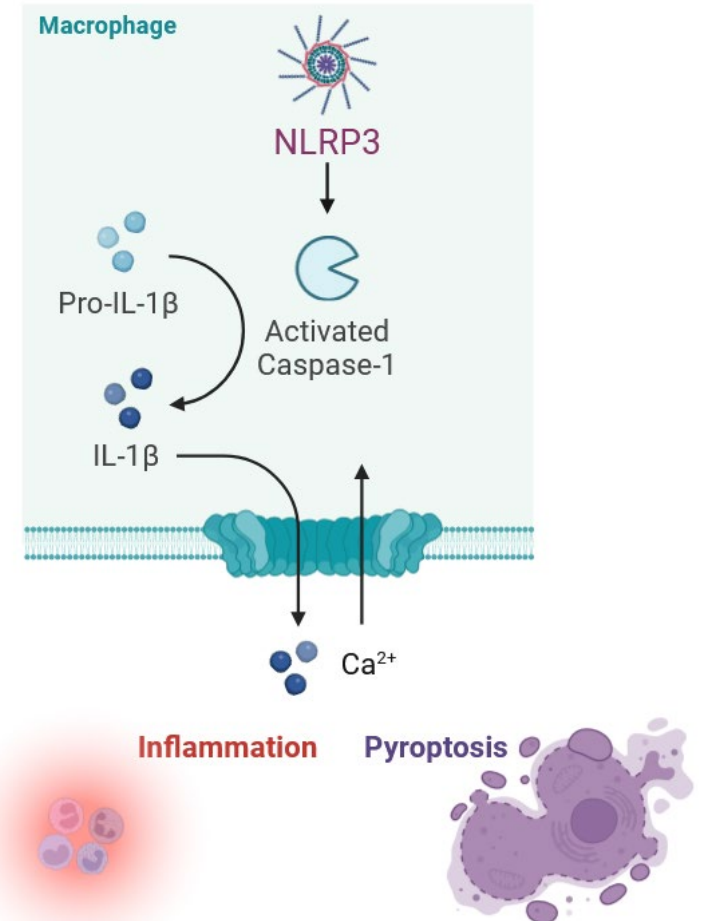


Active **NLRP3** inflammasome disk

Nod-Like Receptor family Pyrin domain containing 3

**INFLAMMASOMES**  
are activated by molecular  
hallmarks of infection  
or cellular injury

**NLRP3** mediates release  
of proinflammatory cytokines  
**IL-1 $\beta$**  and **IL-18** and drives a  
form of cell death called  
**PYROPTOSIS**



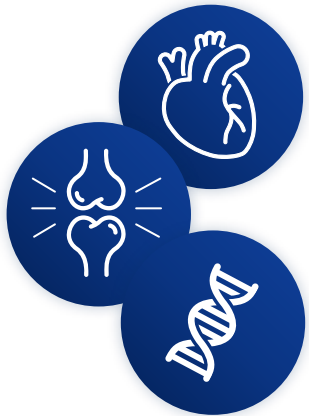
# NLRP3 is a High Value Therapeutic Target

## Broad Potential Across Systemic and CNS Inflammatory Disease

### VTX2735

#### Systemic Diseases

NLRP3 inhibition has therapeutic potential in a broad range of systemic diseases, particularly where IL-1 biologics have demonstrated therapeutic benefit



- Cardiovascular
- Dermatologic
- Rheumatic
- CAPS (FCAS)
- Other orphan indications

### VTX3232

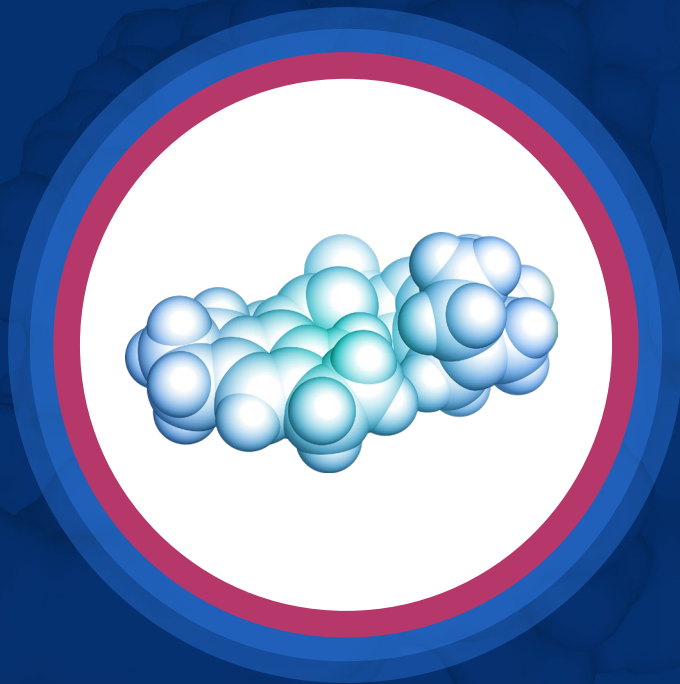
#### Neuroinflammatory Diseases

NLRP3 activation (inhibition) has been linked to a range of neuroinflammatory and neurodegenerative conditions with high unmet medical need



- Parkinson's Disease
- Multiple Sclerosis
- Alzheimer's Disease
- Cardiometabolic & obesity





**VTX2735**

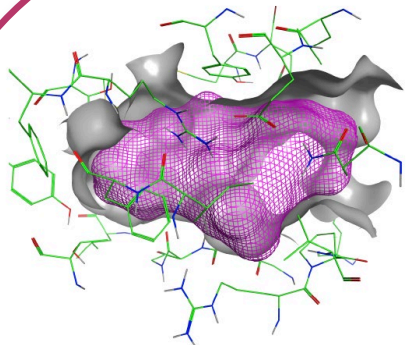
**Peripheral NLRP3 Inhibitor**

# VTX2735: Potent and Selective Peripheral NLRP3 Inhibitor

## Phase 2 Ready for Systemic Inflammatory Diseases

### POTENT & SELECTIVE

- hu WB IC<sub>50</sub> (IL-1 $\beta$ ) = 80 nM
- No inhibition of other inflammasomes



**PATENT GRANTED**  
(US Pat. No. 11,603,375)

### NONCLINICAL & PHASE 1 PACKAGE

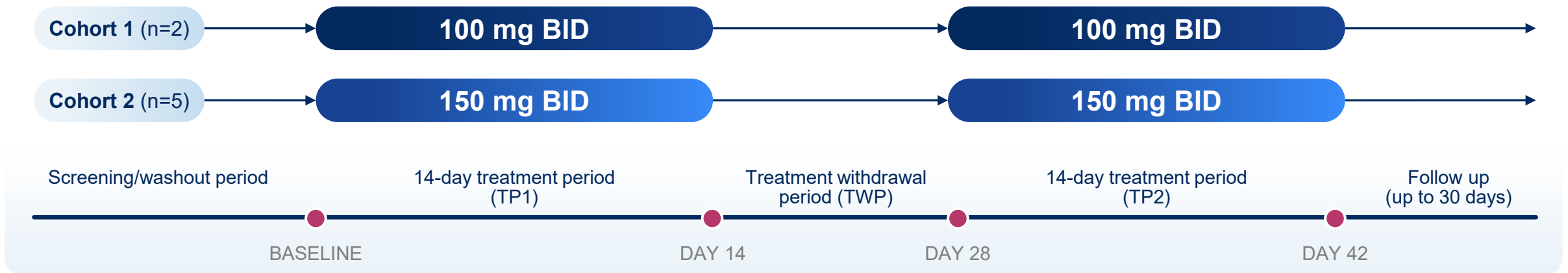
- Demonstrated pharmacodynamic effects and *in vivo* efficacy in rodent models
- High exposures and target coverage achieved in Phase 1
- Safety profile established in nonclinical and clinical studies
  - Well-tolerated in healthy adults
  - No safety signals in nonclinical *in vitro* and *in vivo* studies
  - Chronic tox studies completed
- Potent inhibitor of NLRP3 in PBMC from CAPS patients (FCAS mutations)

**Phase 2 proof-of-concept study in CAPS patients completed**

# VTX2735 Phase 2 Open-Label Trial in CAPS (FCAS)

## Trial Design

- **CAPS** is an ultra rare condition driven by **gain of function mutations in NLRP3 gene**; FCAS is the most common subtype
- Following washout of SoC, VTX2735 dosed for 14 days in two treatment periods (TP1 and TP2, 28 days total)
- Key endpoints: safety/tolerability and improvement in Key Symptom Score (**KSS**, mean of 5 symptom scores)
  - **Pharmacodynamic assessments:** hsCRP; acute phase reactants (SAA, IL-1 $\alpha$ , IL-1 $\beta$ , IL-6, and IL-18)
- **7 participants enrolled** (diverse NLRP3 mutations, prior SoC therapies, and symptoms)
  - 5 participants completed the trial; 2 participants withdrew consent after treatment period 1

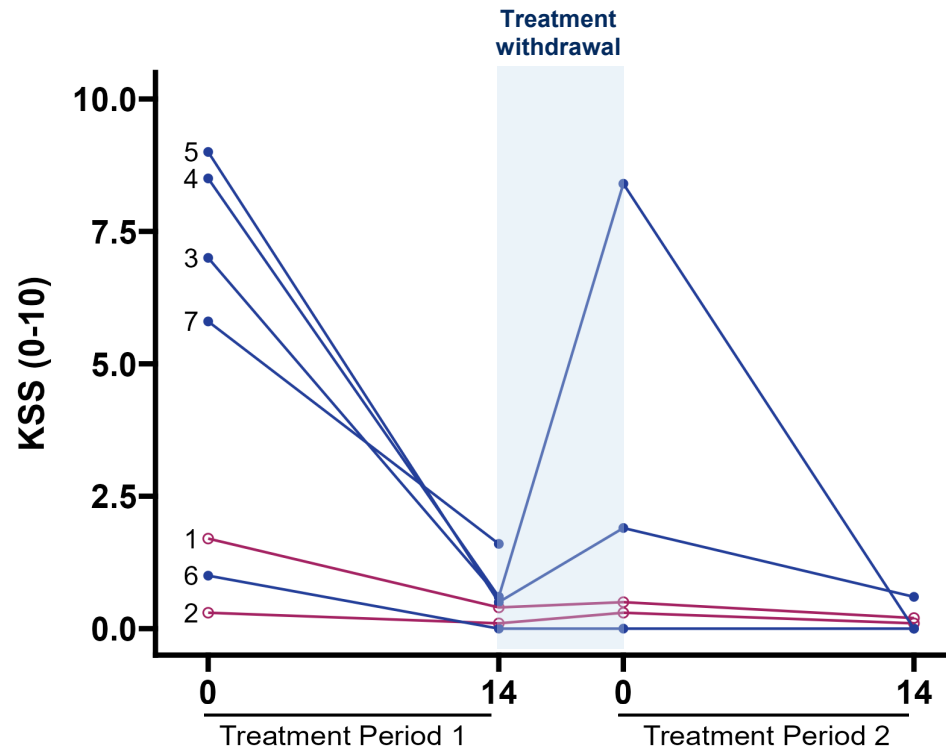


# Treatment with VTX2735 Drives Reductions in Disease Activity

## Disease Activity as Assessed by Key Symptom Score (KSS) and General Well-Being

### KEY SYMPTOM SCORE (0-10)\*

Daily mean of five symptom scores

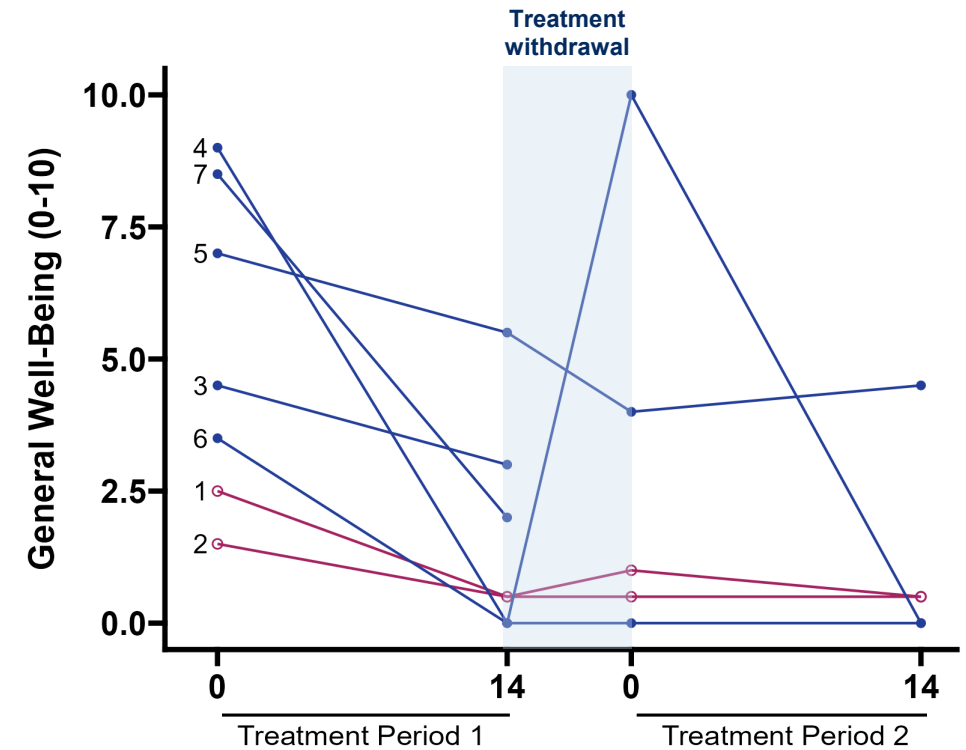


**Mean 85% reduction during Treatment Period 1**

○ 100 mg BID    ● 150 mg BID

### GENERAL WELL-BEING (0-10)\*

"Considering all the ways FCAS affects you, please rate how you are doing"

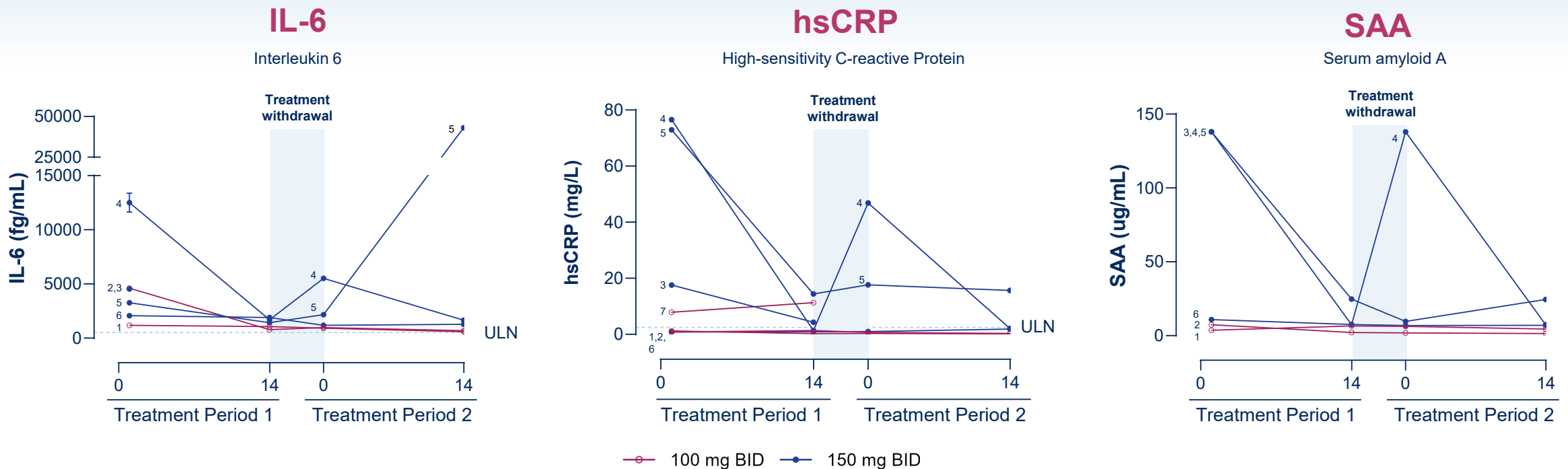


**Mean 68% reduction during Treatment Period 1**

# VTX2735 Biomarker Changes

## Reductions in IL-6, hsCRP and SAA Observed as Expected with NLRP3 Inhibition

- The pleiotropic cytokine IL-6 induces acute-phase reactant proteins, including C-reactive protein (CRP) and Serum amyloid A (SAA)
- Treatment with VTX2735 reduced plasma IL-6, hsCRP, and SAA in patients with elevations at baseline, consistent with reductions in disease activity
  - Lack of baseline elevations in some patients is likely attributable to long half-life of SoC treatment (canakinumab)



Source: Ventyx data on file. SoC: standard of care.

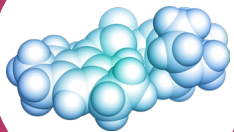
\*Note: Number next to each line represents individual participant number. One participant did not complete Treatment Period 1; the final measurement prior to study discontinuation is reported. No IL-6 or SAA data available for Participant No. 7.



# Conclusions from the Phase 2 Trial of VTX2735 in FCAS Patients

## Clinical Proof of Concept Achieved in CAPS Patients

VTX2735 showed clinically-meaningful effects on disease activity and relevant biomarkers



VTX2735 was well-tolerated; all adverse events categorized as mild or moderate and resolved without treatment interruption

Clinical outcomes and biomarker changes represent a major milestone for VTX2735 and for NLRP3 inhibition

- Dr. Hal Hoffman (UCSD): “Results similar to what we have seen with IL-1 targeted biologics; particularly impressive in a treatment-experienced population.”

# VTX2735 is a Phase 2 Ready Peripheral NLRP3 Inhibitor

## HIGHLY POTENT & SELECTIVE

- Structurally unique, selective inhibitor of NLRP3
- Potent inhibitor of NLRP3 with  $IC_{50} = 80$  nM in human whole blood assay
- Highly potent vs. CAPS mutation variants

## PROMISING SAFETY PROFILE

- Well-tolerated in healthy adults and CAPS patients
- No toxicological signals of concern
- No CYP, hERG or transporter interactions

## BIOLOGIC-LIKE ACTIVITY IN CAPS TRIAL

- Concentration dependent suppression of IL-1 $\beta$  *ex vivo*
- Reduction in hsCRP and other inflammation biomarkers (IL-6, SAA, neutrophils)
- Clinically-meaningful benefits observed in CAPS patients

## PHASE 2 READY

- IP position secure; patent issued (US Pat. No. 11,603,375)
- Multi-kilo API production completed
- Once-daily dosing form in development

# Attractive Opportunity for NLRP3 in Recurrent Pericarditis

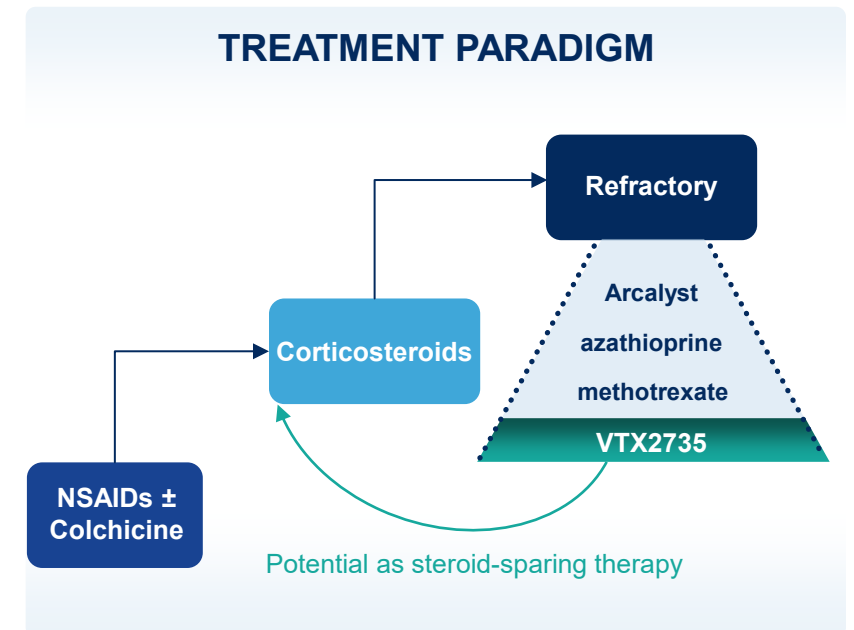
## De-risked Mechanism and Efficient Path to Market

**Recurrent pericarditis is a debilitating autoinflammatory condition**

~**40,000** patient U.S. prevalent population with recurrent pericarditis<sup>1</sup>

Autoinflammatory process characterized by IL-1 release (downstream of NLRP3)

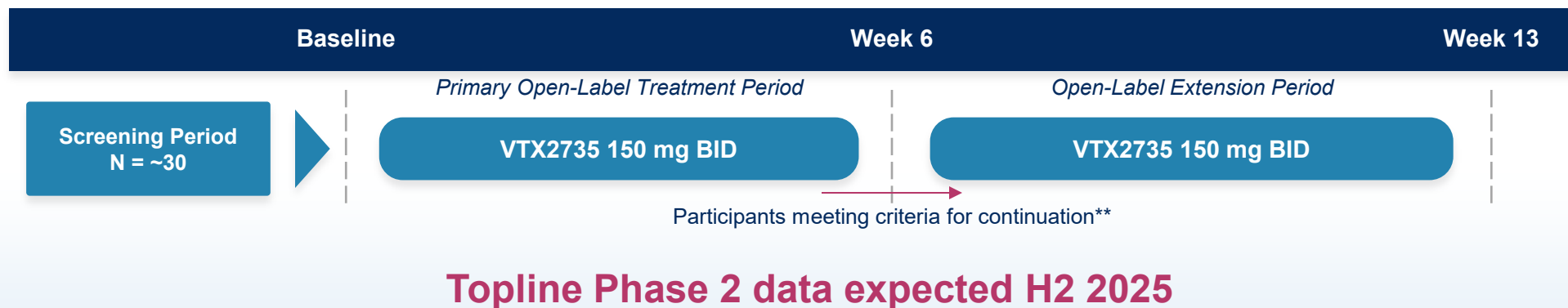
- 2021 approval of Arcalyst (rilonacept) validates IL-1 approach (de-risking for NLRP3)
  - Arcalyst generated \$233M in 2023 sales in 2nd full year of commercial availability; consensus sales >\$1B in 2030<sup>2</sup>
- Regulatory precedent for efficient path to market
  - Open-label Phase 2 trial followed by a single Phase 3 trial
- Topline Phase 2 data for VTX2735 expected in **H2 2025**



# Phase 2 Trial in Participants with Recurrent Pericarditis

## Designed to Efficiently Achieve Clinical Proof of Concept in RP

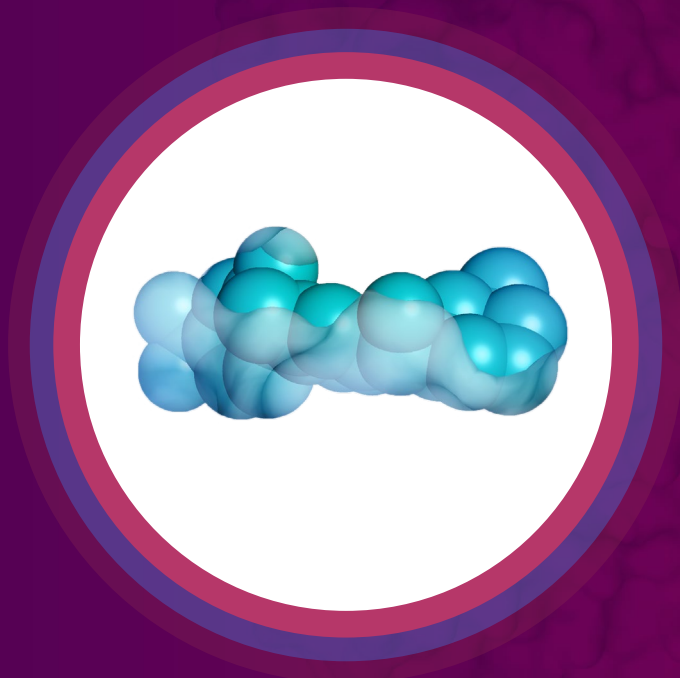
- Phase 2 trial evaluating the effects of VTX2735 in participants with active recurrent pericarditis
  - Acute symptoms of RP (pain, elevated hsCRP) despite standard therapy
- Measuring resolution of acute symptoms of RP as evidenced by:
  - Change from baseline in hsCRP (inflammatory marker)
  - Change from baseline in the NRS pain score
- Positive results may support rapid advancement to registrational Phase 3\*



RP: recurrent pericarditis. NRS: numerical rating scale (11-point scale). hsCRP: high sensitivity C-reactive protein. BID: twice daily.

\*Pending alignment with regulators.

\*\*Defined as reduction in pain, hsCRP, and/or echographic effusion



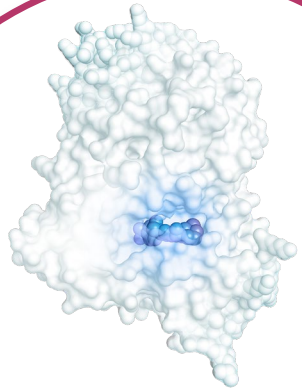
**VTX3232**

**CNS-Penetrant NLRP3 Inhibitor**



# VTX3232: Potent and Selective CNS-Penetrant NLRP3 Inhibitor

## RATIONALLY DESIGNED AND OPTIMIZED FOR CNS EXPOSURE



**RAPID EQUILIBRATION**  
across BBB to reach  
microglial target cells

### *In Vitro* Profile

- Hu WB IC<sub>50</sub> (IL-1 $\beta$ ) = 15 nM
- Mu WB IC<sub>50</sub> (IL-1 $\beta$ ) = 94 nM
- Inhibits palmitate-induced IL-1 $\beta$
- No inhibition of other inflammasomes

### *In Vivo* Profile

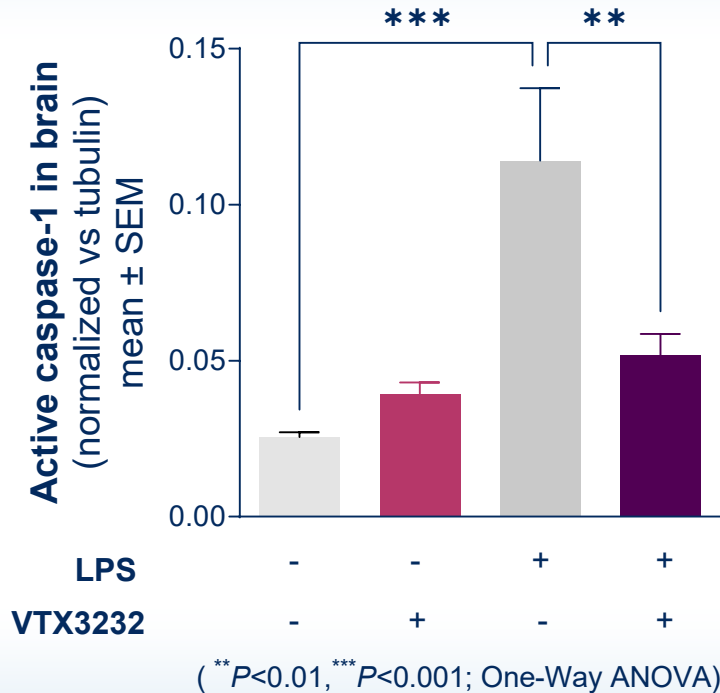
- Safe and well-tolerated in Phase 1 Study
- Equal CNS partitioning; human K<sub>p,uu</sub> = 0.5
- T<sub>1/2</sub> = ~17 h with high free-drug fraction
- Robust effects on inflammatory biomarkers

### Pharmaceutics

- Single polymorph
- BCS Class 1
- Solubility (pH 7.4 PB) = 0.4 mg/mL

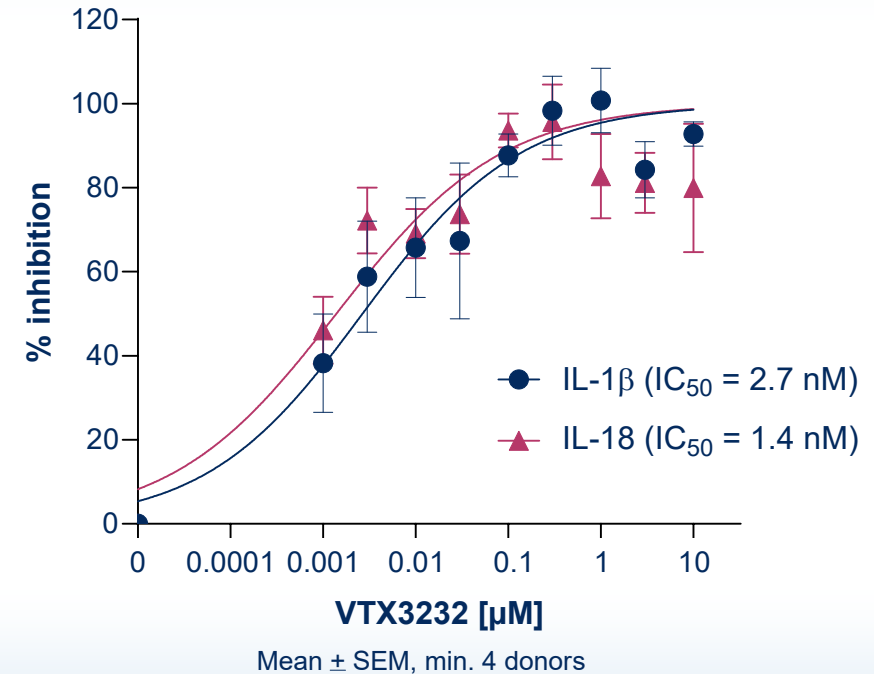
# VTX3232 Efficacy in Neuroinflammation Models

## MOUSE NEUROINFLAMMATION MODEL



**Inhibition of caspase-1 activation**  
(directly downstream of NLRP3)

## LPS-PRIMED HUMAN MICROGLIA

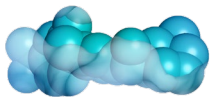


**Potent inhibition of induced IL-1 $\beta$  & IL-18**  
selective vs TNF $\alpha$

**VTX3232 activity translates to CNS-relevant assays and models**

# VTX3232 Phase 1 SAD and 14-Day MAD Trial in Healthy Volunteers

VTX3232 achieved optimal exposures in Phase 1 with favorable safety profile



Generally well-tolerated following single- and multiple-dose administration

- No dose-limiting toxicities
- All treatment emergent adverse events considered mild or moderate

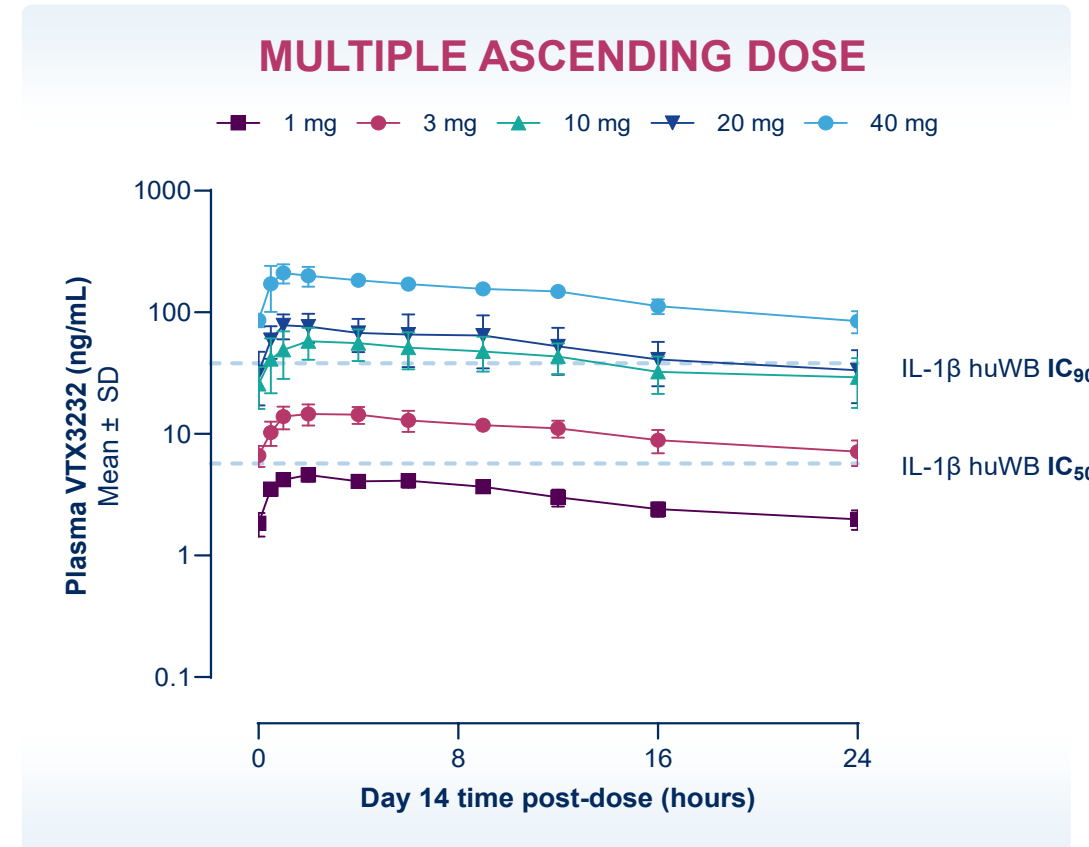
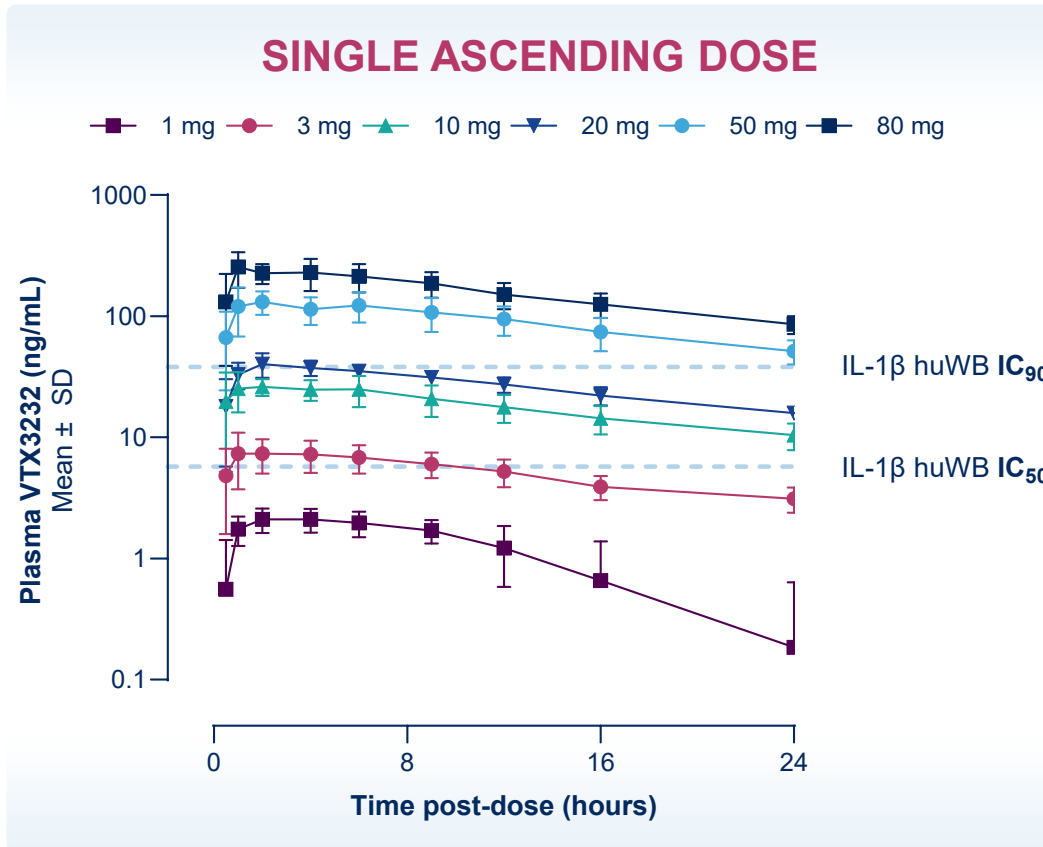
Pharmacokinetic profile consistent with once-daily dosing

- Comparable exposure in both plasma and CSF
- No effect of food on exposure

Potent target engagement at doses  $\geq 3$  mg

- Dose-dependent pharmacodynamic effects in *ex vivo* IL-1 $\beta$  assay and on downstream inflammatory biomarkers
- Predict trough drug concentrations in CSF above IC<sub>90</sub> at doses > 12 mg

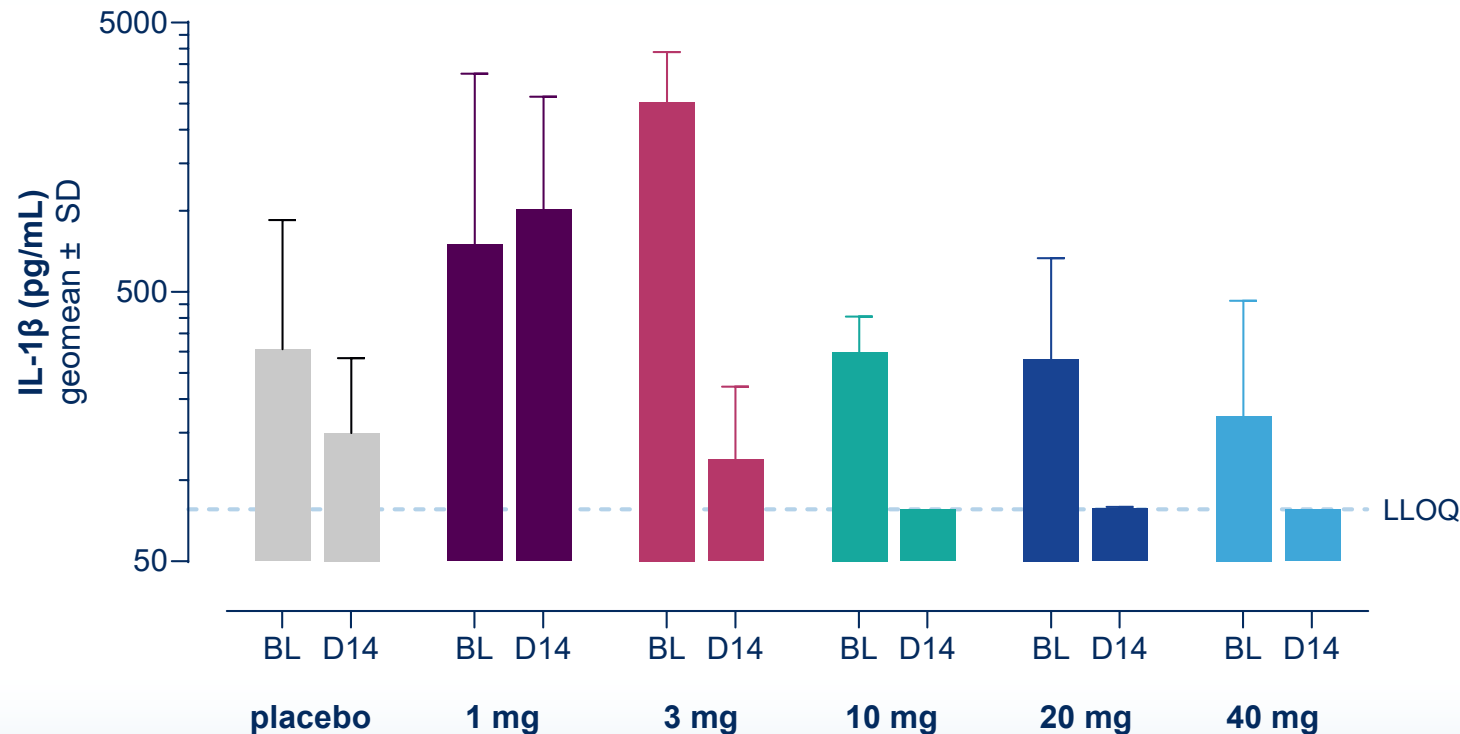
# VTX3232 Phase 1 SAD and 14 Day MAD Pharmacokinetics



Dose-related, linear exposure from 1 mg to 80 mg  
3 mg QD achieves 24 h IL-1 $\beta$  IC<sub>50</sub> coverage

# VTX3232 Whole Blood *Ex Vivo* IL-1 $\beta$ Stimulation Assay

## Potent Target Engagement Demonstrated At Doses $\geq 3$ mg QD



### DATA SUMMARY

- Blockade of NLRP3 mediated IL-1 $\beta$  secretion is maintained at Day 14 with repeat dosing
- Maximal inhibition achieved at doses of 10 mg QD and higher

1. Lower Limit of Quantitation (LLOQ)= 78 pg/mL. All subjects below LLOQ were assigned a value of 78 pg/mL.

2. Day 14 pre dose (D14). Pre dose baseline (BL).

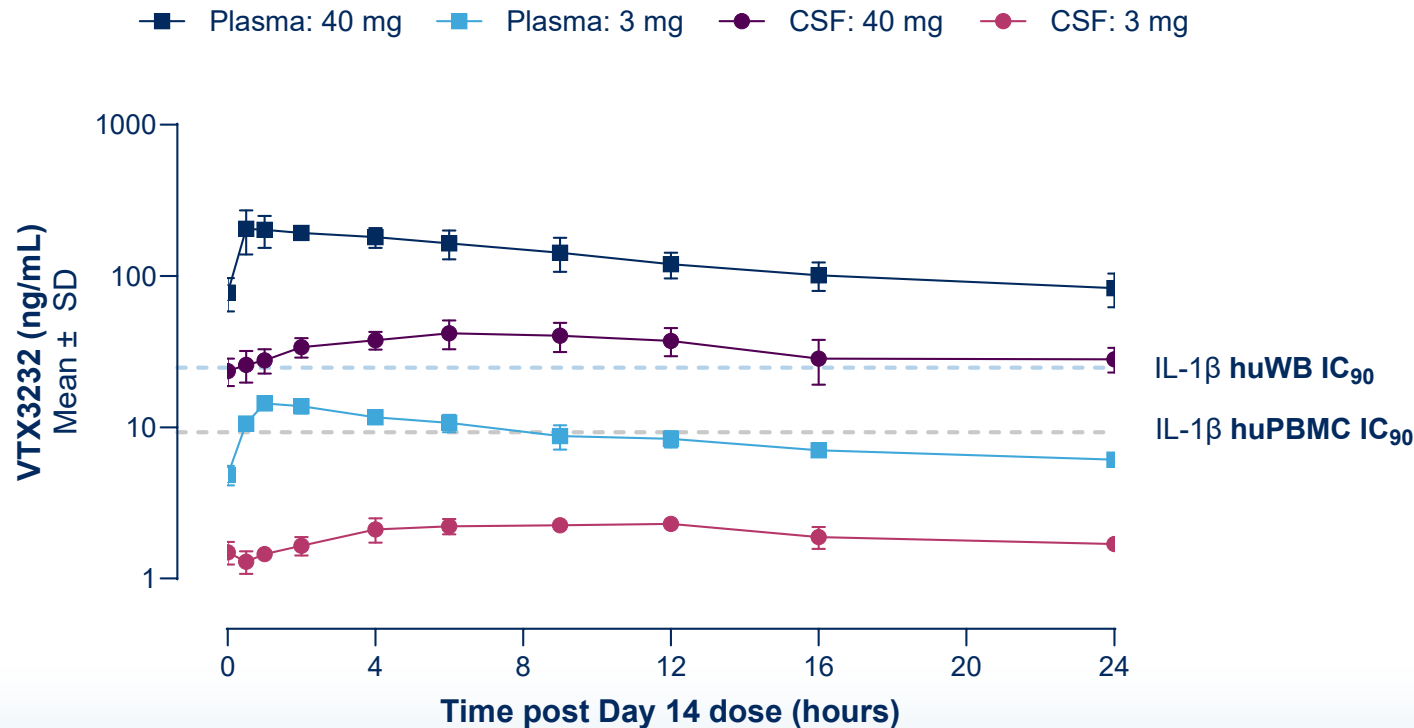
Source: Ventyx internal data. QD: once daily.



# VTX3232 Pharmacokinetics in Cerebrospinal Fluid (CSF)

## Comparable exposures in both plasma and CSF

### MATCHED PLASMA & CSF EXPOSURE IN MAD COHORTS

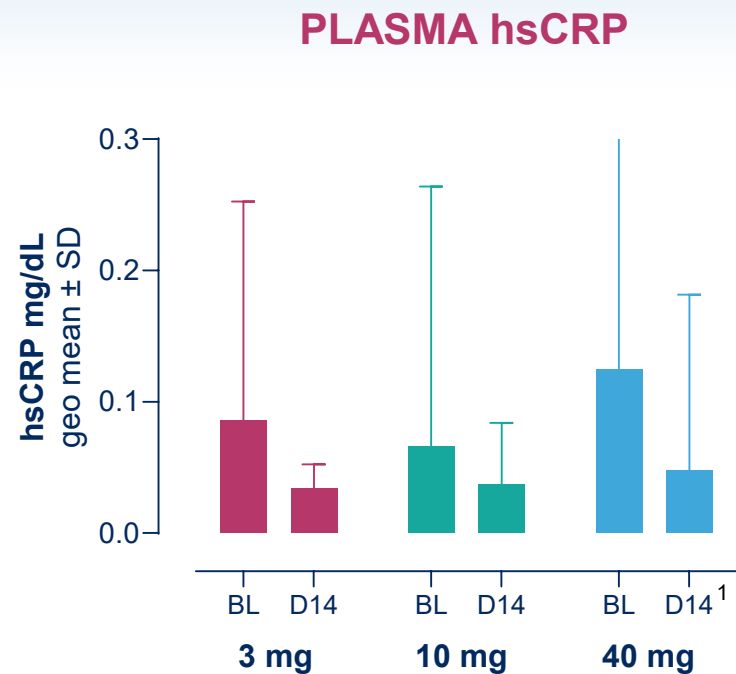


### DATA SUMMARY

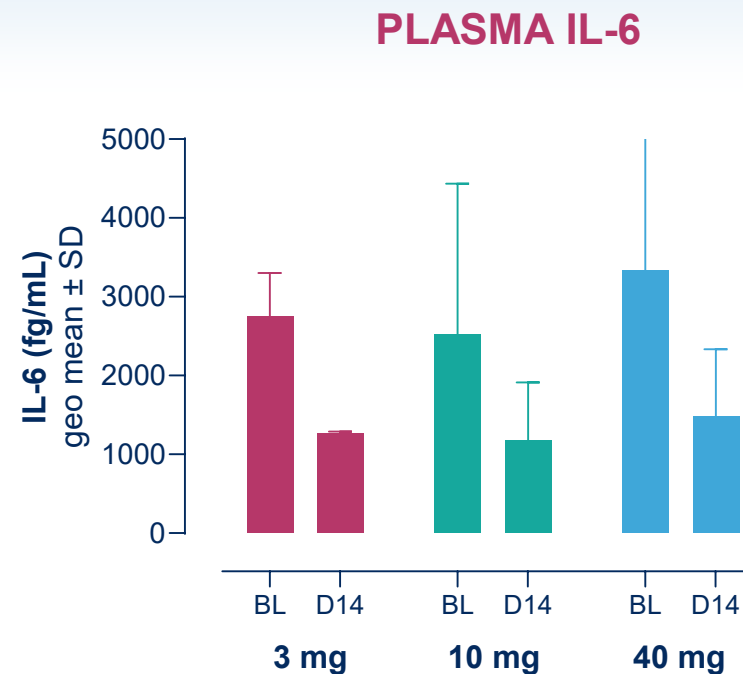
- 40 mg QD exceeds CSF IC<sub>90</sub> for 24 h, achieving robust target coverage for NLRP3 in microglia for neuroinflammatory conditions

# VTX3232 Effects on Inflammatory Biomarkers

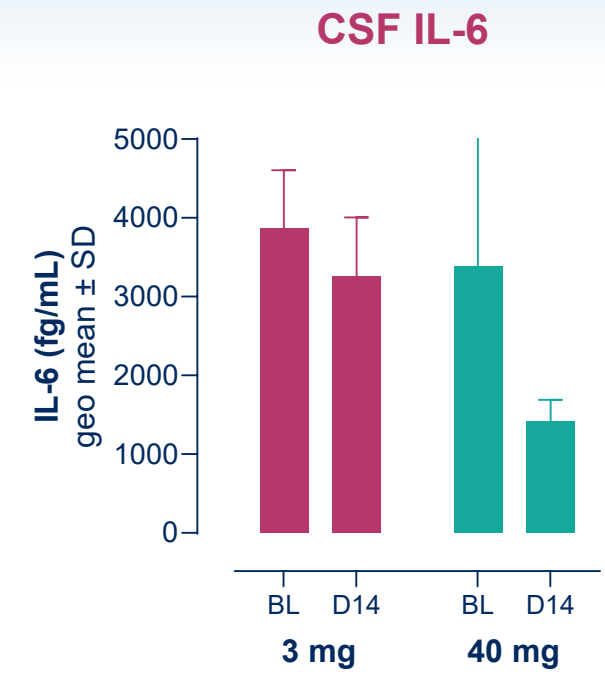
Reduction in hsCRP and IL-6 Comparable to that Achieved by Canakinumab (IL-1 $\beta$  mAb)



Systemic inflammation biomarker  
hsCRP lowered by as much as 55%



IL-6 lowered by as much as 46% in plasma

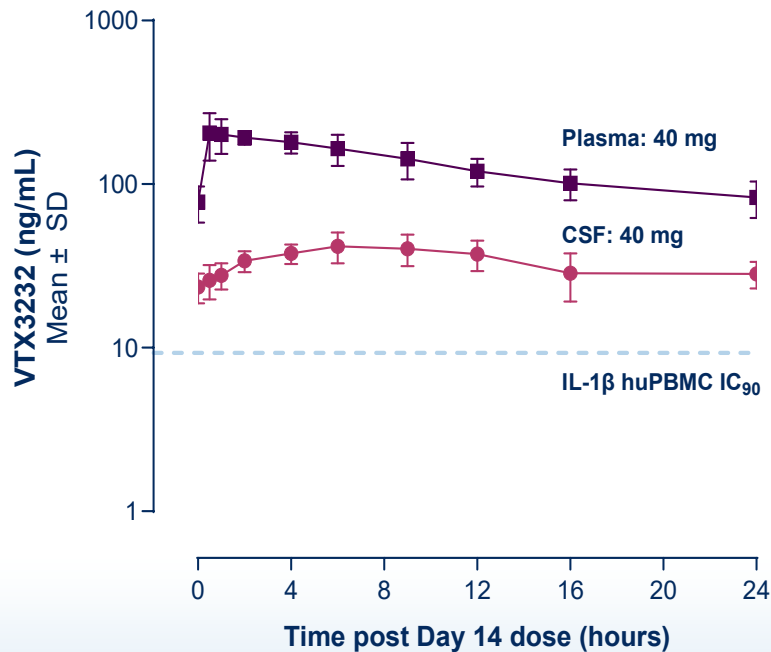


# Conclusions from the Phase 1 Trial of VTX3232 in NHV

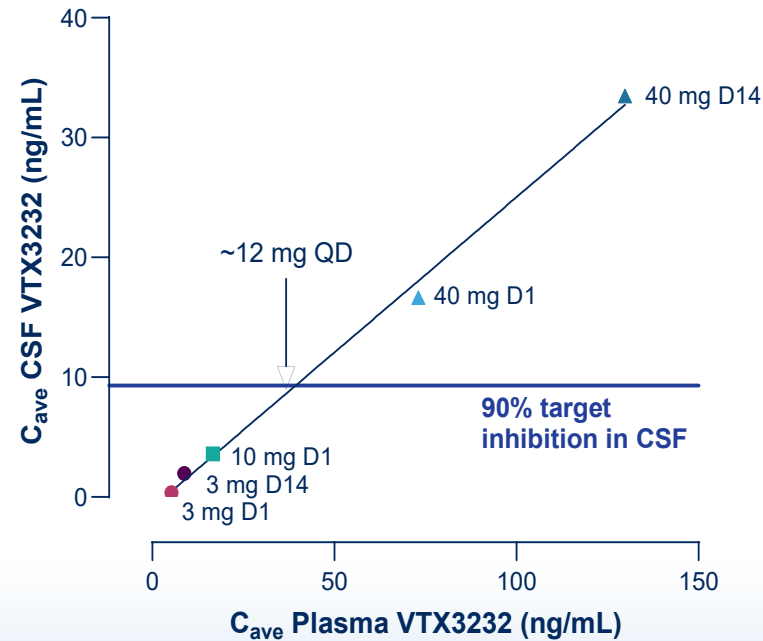
## Potentially Class-leading Safety and Efficacy Profile for Neuroinflammatory Diseases

### DATA SUMMARY

#### 40 MG QD DOSE: TARGET COVERAGE



#### DATA PREDICT LOW EFFICACIOUS DOSES



- Well-tolerated in healthy volunteers
- Robust target coverage achieved in the plasma and CNS
- Potent, dose-dependent PD effect in *ex vivo* IL-1 $\beta$  assay and on inflammatory biomarkers
- Data predict trough concentrations in CSF above IC<sub>90</sub> at doses > 12 mg

# VTX3232: Optimally Engineered to Target Neuroinflammatory Diseases

## POTENT & SELECTIVE

- Structurally unique
- $K_d < 1$  nM to NLRP3 NACHT domain
- $IC_{50} = 13$  nM hu WB, 2.7 nM in microglia
- Selective vs AIM2/NLRC4
- Doses  $>3$  mg suppress IL-1 $\beta$  release for  $>24$  h

## SAFETY PROFILE

- Well-tolerated in healthy adults
- No toxicological signals requiring further investigation
- No CYP, hERG, or transporter interactions

## PK & PD PROFILE

- $T_{1/2} = \sim 17$  h with high free fraction
- High CNS penetration; human  $K_{p,uu} = 0.5$
- Data predict trough concentrations in CSF above  $IC_{90}$  at doses  $> 12$  mg

## PHASE 2 READY

- IP position secure; patent application published 09/23
- Multi-kilo API production complete
- Solid-oral dosing form with high bioavailability

# VTX3232 Has Potential for Disease Modification in Parkinson's Disease

## Strong Mechanistic Rationale and High Unmet Need

### HIGH UNMET NEED

- **~1 million** U.S. patient prevalent population (2nd most common neurodegenerative disease)
- **No disease-modifying therapies** approved for Parkinson's disease

### LARGE ADDRESSABLE MARKET

- **>\$4B annual market** for symptomatic therapies in 2021<sup>1</sup>
- Estimated **~\$10-\$15B+ annual TAM** for first disease-modifying therapy<sup>2</sup>

### STRONG BIOLOGIC RATIONALE

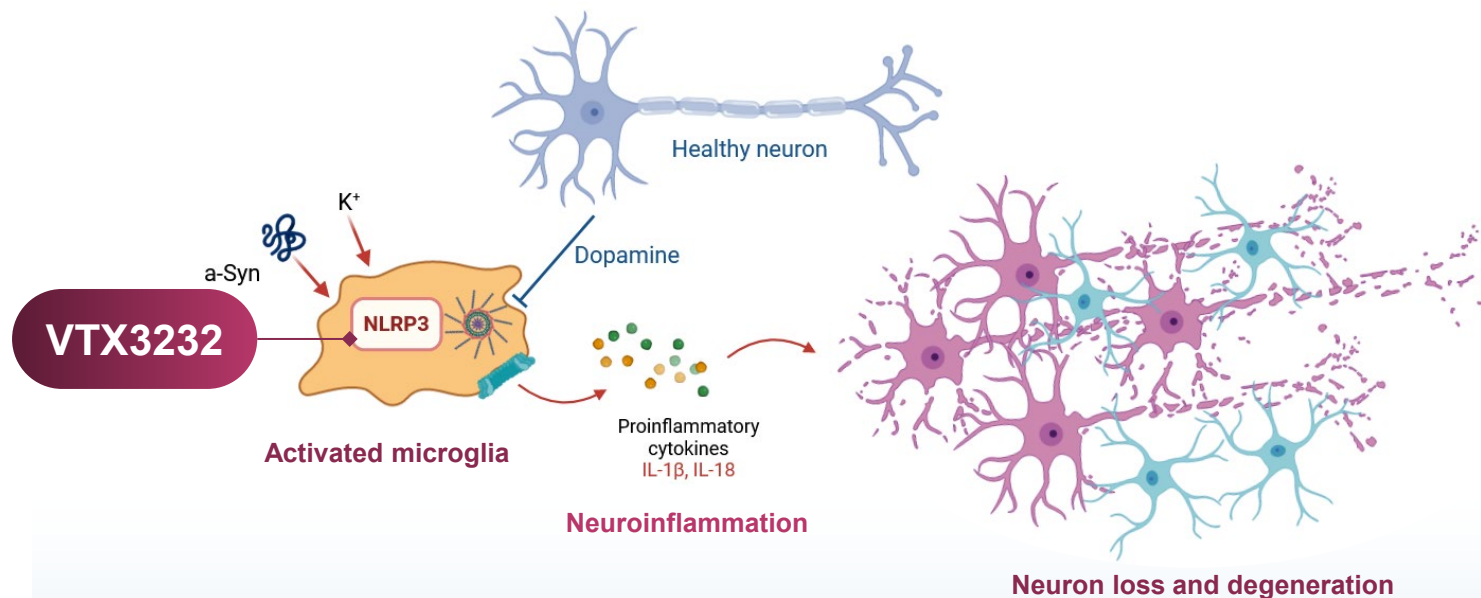
- **Neuroinflammation** is central to Parkinson's disease pathogenesis
- **Strong evidence** in preclinical models and PD patient samples for NLRP3 as a **key driver** of neuronal degeneration



# Rationale for Targeting NLRP3 in Parkinson's Disease (PD)

## Neuroinflammation May Play a Central Role in Disease Pathogenesis

There is a growing body of evidence for NLRP3 inhibition as a **potential disease-modifying approach** that may prevent dopaminergic neurodegeneration and clinical symptoms



NLRP3 inhibition **reduces motor symptoms, microglial activation, and dopaminergic neuron loss** in multiple animal models of PD

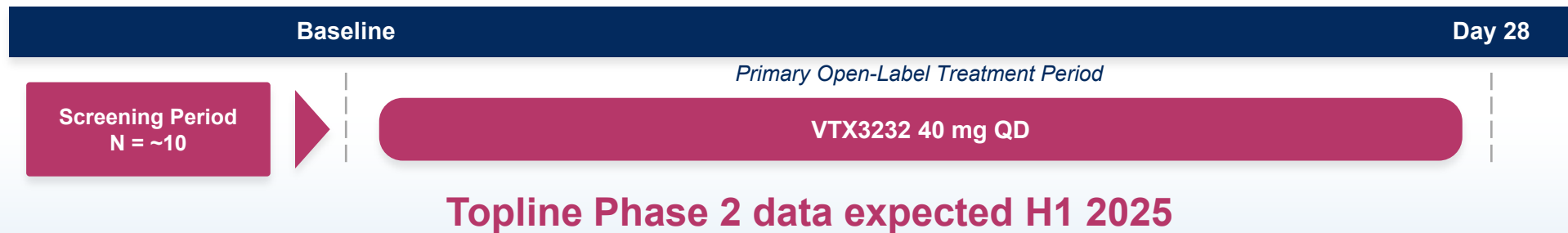
In patients, **NLRP3 expression is linked to progression and risk of disease**, and NLRP3-derived cytokines are elevated

**Neuroinflammation through excess NLRP3 activity may be the mechanistic link driving neuronal cell death in PD**

# Phase 2 Trial in Participants with Early Parkinson's Disease

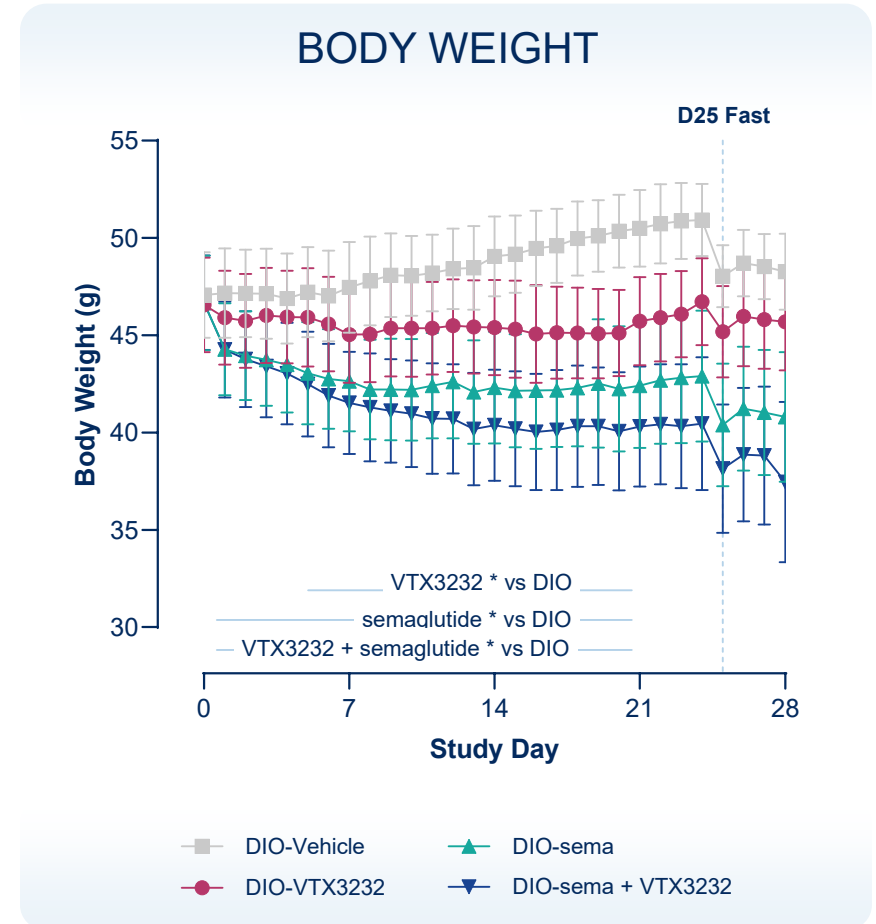
## Disease-Relevant Biomarkers and Exploratory Neuroimaging

- Conducting a Phase 2 safety and biomarker trial assessing NLRP3-, inflammatory, and disease-relevant biomarkers, with exploratory neuroimaging
  - Impact on relevant plasma and CSF biomarkers: hsCRP, IL-1 $\beta$ , IL-6, IL-18,  $\alpha$ -syn, NfL, sTREM2, GFAP
  - Impact on microglial inflammation via neuroimaging (TSPO-PET)
- Test of therapeutic hypothesis that CNS NLRP3 inhibition will result in reduced inflammation and potential early disruption of PD pathophysiology



# NLRP3 as a Target in Obesity and Obesity-Related Metabolic Disease

- Obesity is a chronic inflammatory condition associated with release of NLRP3-related cytokines such as IL-1 $\beta$  and IL-6
  - This inflammation may drive a range of metabolic disorders, including insulin resistance, diabetes, and atherosclerosis
  - Calorie restriction and exercise-mediated weight loss are associated with reduced expression of NLRP3 and decreased systemic inflammation<sup>1</sup>
  - In preclinical studies, NLRP3 activation is associated with obesity-related insulin resistance<sup>1</sup>
- VTX3232 demonstrates broad cardiometabolic benefits in diet-induced obesity (DIO) mouse model
  - Reduced food intake and decreased body weight
  - Decreased markers of systemic inflammation (IL-1 $\beta$ , IL-6, fibrinogen)
  - Improved markers of metabolic function (decreased cholesterol, triglycerides, insulin resistance, and HbA1c)

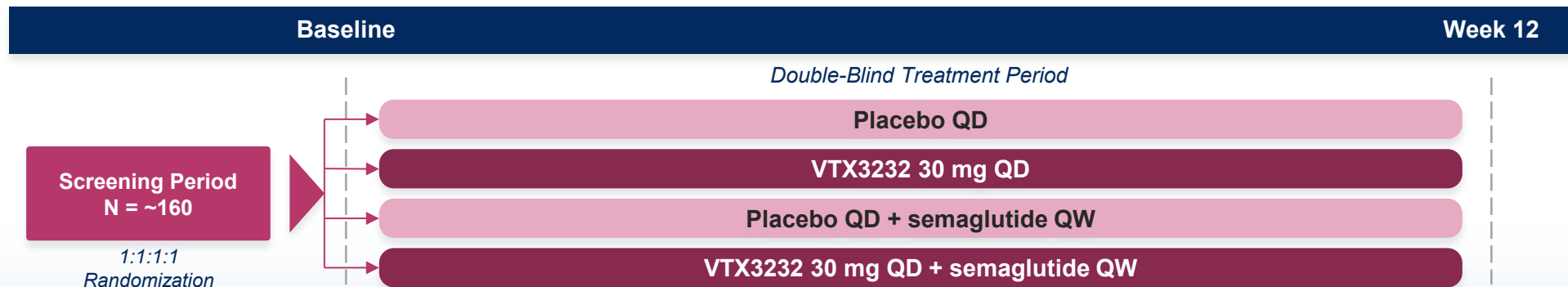


VTX3232 20 mg/kg BID orally; Semaglutide 10  $\mu$ g/kg QD subcutaneously; mean  $\pm$  SEM, \* p < 0.05 or more highly significant at all indicated timepoints, Mixed effects ANOVA, Sidak's post-hoc test.

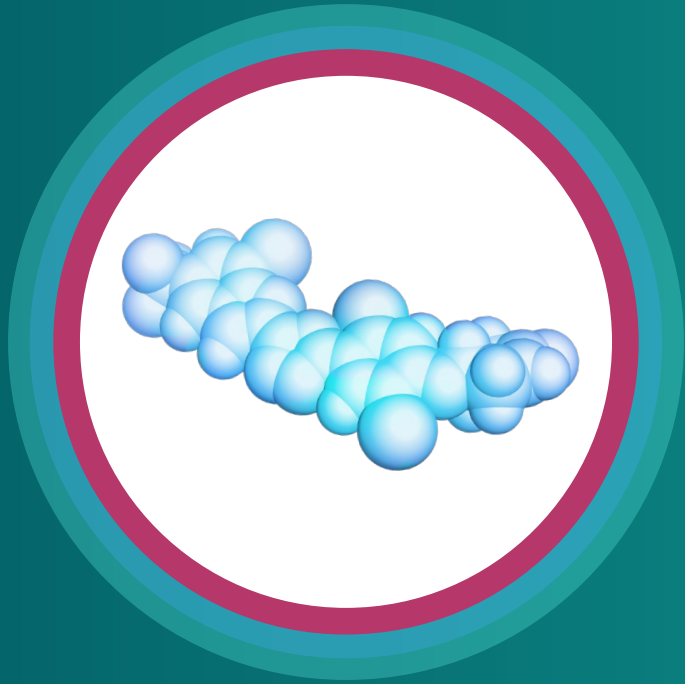
# Phase 2 Trial in Obese Participants with Cardiometabolic Risk Factors

## Measuring Key Inflammatory Biomarkers and Changes in Body Composition

- Conducting a Phase 2 trial in obese participants with cardiometabolic risk factors, exploring a broad panel of cardiometabolic and inflammatory endpoints:
  - **Inflammatory (cardiovascular) biomarkers**, including IL-6, hsCRP and other acute phase reactants
  - **Cardiometabolic markers**, including lipids and glycemic parameters
  - Impact on **body weight** and **body composition**, including liver steatosis
- Trial expected to support assessment of cardiometabolic development opportunities for NLRP3 portfolio



**Topline Phase 2 data expected H2 2025**



# Tamuzimod (VTX002)

S1P1 Receptor Modulator for Ulcerative Colitis

# Tamuzimod Phase 2 Study in Moderate-to-Severe UC

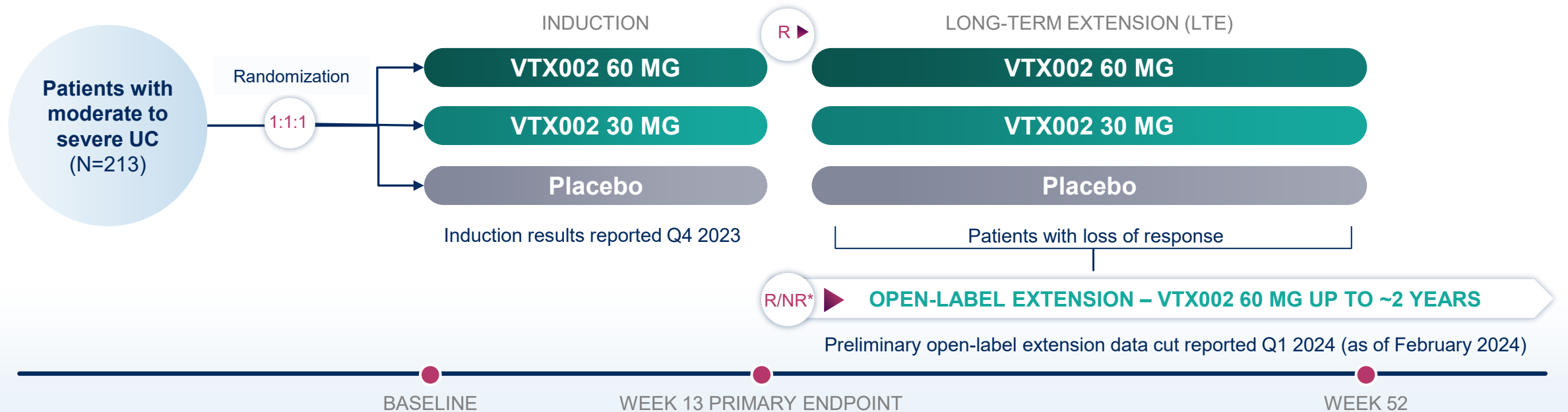
## Designed to Serve as the First of Two Pivotal Trials

### KEY ELIGIBILITY CRITERIA

- Patients with moderately to severely active UC as defined by the Modified (3-component) Mayo Score
- Insufficient response, loss of response, and/or intolerance to conventional or advanced therapies

### ENDPOINTS

- **Primary Endpoint:** Clinical remission at Week 13 as defined by the Modified Mayo Score
- **Key Secondary Endpoints:** Endoscopic improvement; symptomatic remission; histologic remission; endoscopic improvement-histologic remission



# Overview of Tamuzimod Induction Data

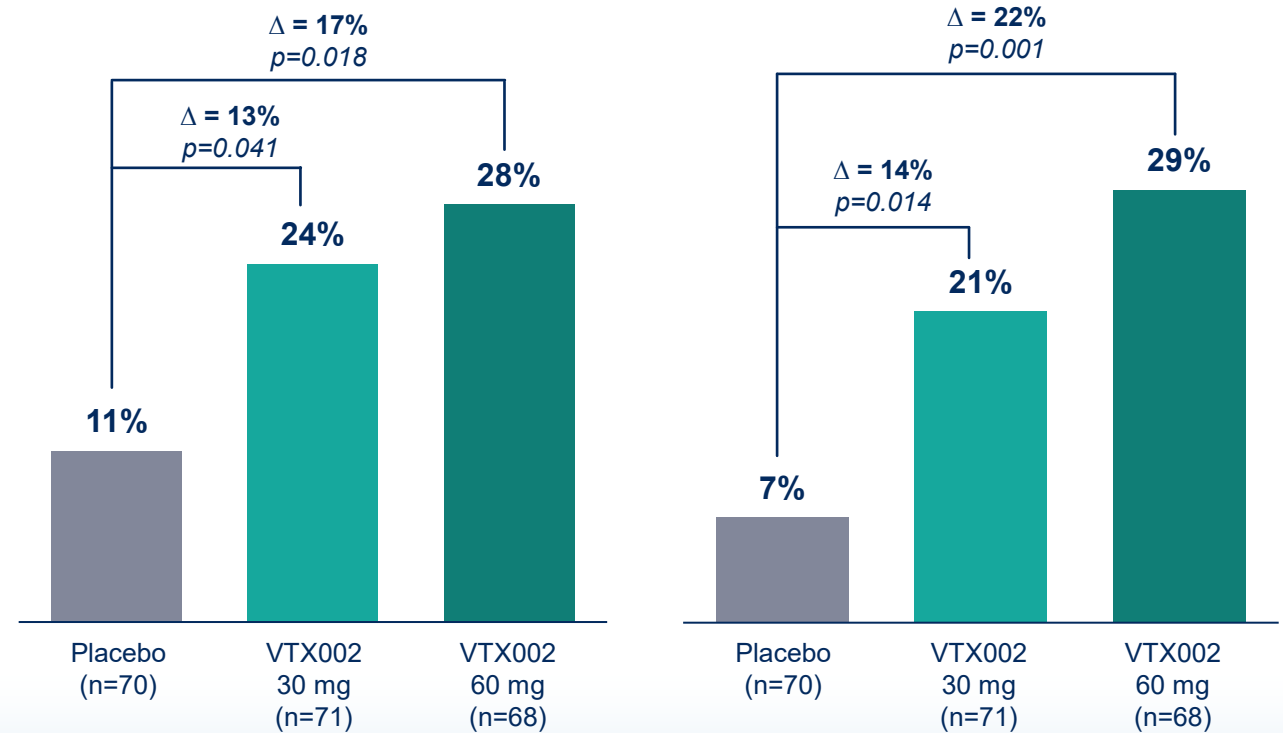
## Robust Week 13 Clinical Remission with Differentiated Complete Endoscopic Remission

### Key Takeaways from Tamuzimod Week 13 Data

- 1 Competitive week 13 clinical remission with differentiated endoscopic remission (MES=0)
- 2 Deep remission (endoscopic and clinical remission), **symptomatic remission** and **histologic endoscopic mucosal improvement** rates further support clinical profile
- 3 Subgroup analysis demonstrated **differentiated clinical remission and endoscopic remission** in patients with prior exposure to advanced therapies
- 4 **No cases** of atrioventricular block, bradycardia, serious or opportunistic infections, or macular edema

#### CLINICAL REMISSION (PRIMARY)

#### ENDOSCOPIC REMISSION (MES=0)



Baseline MMS 5 to 9 (N=209): Week 13

Clinical remission by modified Mayo Score (MMS) is defined as stool frequency subscore = 0 or 1, rectal bleeding subscore = 0, and endoscopic subscore  $\leq 1$  (excluding friability). Endoscopic remission is defined as a Mayo endoscopic subscore of 0. P-value for testing the treatment difference is based on Cochran-Mantel-Haenszel test adjusted for prior use of advanced therapies, baseline corticosteroid use and baseline disease activity. Full analysis set with non-responder imputation. Source: Ventyx data on file

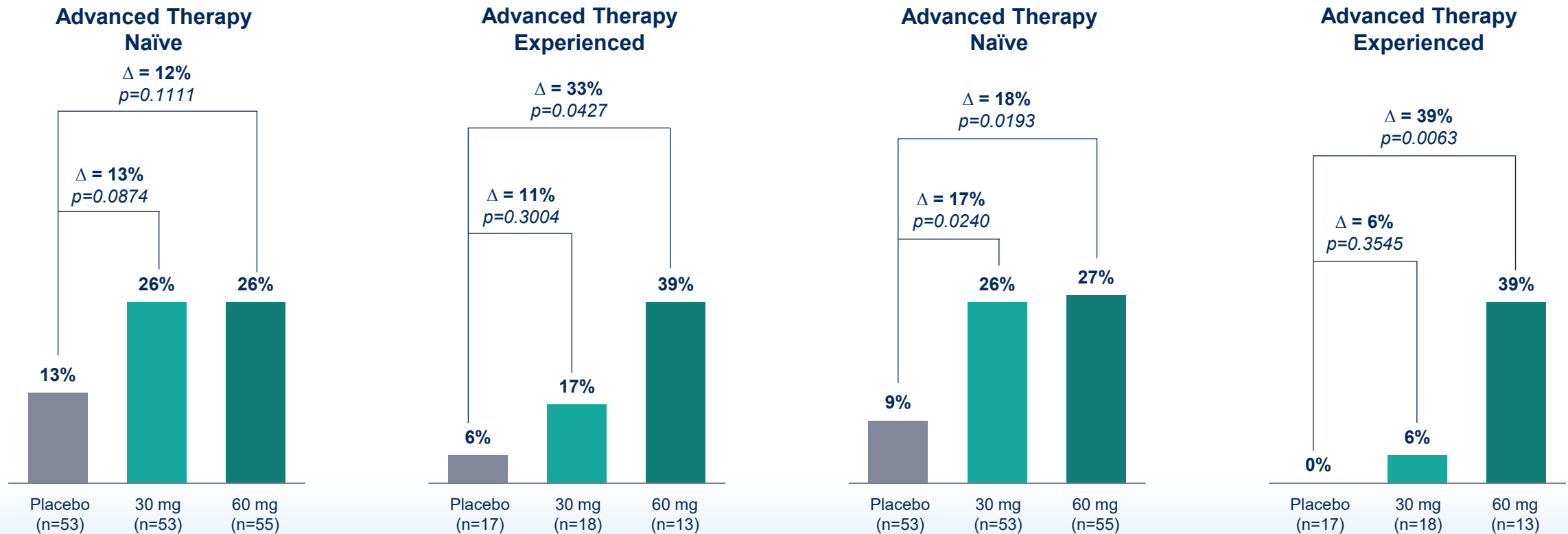


# Induction Subgroup Analysis: Advanced Therapy Prior Use

Clinical and Endoscopic Remission in both advanced therapy naïve and advanced therapy experienced subgroups

## CLINICAL REMISSION

## ENDOSCOPIC REMISSION



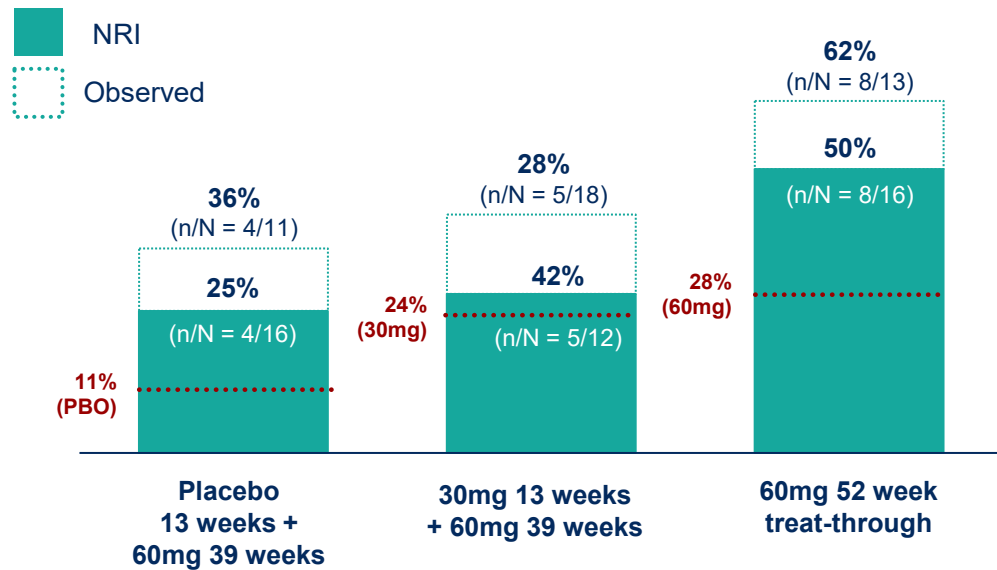
Clinical remission by modified Mayo Score (MMS) is defined as stool frequency subscore = 0 or 1, rectal bleeding subscore = 0, and endoscopic subscore  $\leq 1$  (excluding friability). Endoscopic remission is defined as a Mayo endoscopic subscore of 0. P-value for testing the treatment difference is based on Cochran-Mantel-Haenszel test adjusted for prior use of advanced therapies, baseline corticosteroid use and baseline disease activity. Full analysis set with non-responder imputation. Source: Ventyx data on file

# Preliminary Open-Label Extension Data

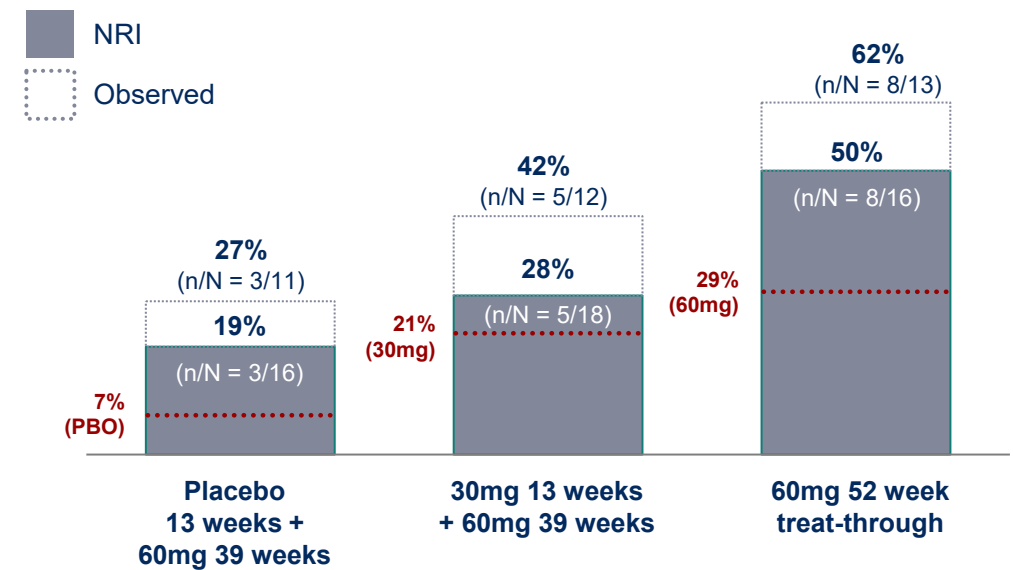
## Further improvement in clinical and endoscopic remission rates at OLE week 39

..... % absolute endpoint rate (clinical or endoscopic remission) in induction dose arm at 13 weeks

### % CLINICAL REMISSION AT OLE WEEK 39<sup>1</sup> BY INDUCTION DOSE ARM



### % ENDOSCOPIC REMISSION<sup>2</sup> AT OLE WEEK 39<sup>1</sup> BY INDUCTION DOSE ARM



**At least half (NRI) of patients in 60mg treat-through group reach clinical remission or endoscopic remission at week 52**

Note: NRI = non-responder imputation; participant discontinuations are assumed to be non-remitters

1 Irrespective of the clinical response at the end of the 13-week induction phase; VTX002 60mg / 60mg represents 52 weeks treat-through efficacy; other groups received 60mg for 39 weeks post-induction; 2 MES = 0; Source: Ventyx data on file.

# Endoscopic Remission is a Consensus Long-Term Treatment Goal

Current therapeutic outcomes remain disappointing: Tamuzimod has demonstrated the potential to set a new bar

## CURRENT ENDOSCOPIC REMISSION OUTCOMES

- 1 The vast majority of patients on advanced therapy fail to reach endoscopic remission, particularly within the induction period<sup>1</sup>:

**82-95%** Absolute % patients in Phase 3 for advanced UC agents that fail to achieve MES=0 at induction

- 2 Achievement of endoscopic remission (MES=0) vs. mild endoscopic activity (MES=1) is associated with improved long-term patient outcomes<sup>2</sup>:

### 12-month risk of clinical relapse

(meta-analysis of 17 studies):



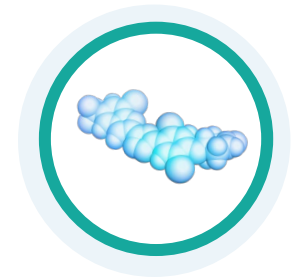
- 3 Achievement of endoscopic remission (MES=0) is recognized in STRIDE II<sup>3</sup> guidelines as an aspirational target of long-term treatment:

<b>MES=0</b>	Lower risk of disease recurrence	Decreased steroid use
	Lower rate of surgical intervention & hospitalization	Superior patient-reported outcomes

## TAMUZIMOD PROFILE

### Induction data

- Competitive clinical remission and differentiated endoscopic remission
- Differentiated clinical and endoscopic outcomes in prior advanced therapy subgroup



### OLE data

- Clinical remission and endoscopic remission rates at **OLE week 39** further differentiate VTX002
- Differentiated endoscopic remission rates achieved in 52-week 60mg VTX002 treat-through group
- Competitive rates of **sustained clinical and endoscopic remission**:
  - At least 38% (NRI) of patients in 60mg 52wk treat-through arm were in clinical remission at both week 13 and week 52
  - Patients in clinical remission were also in endoscopic remission

# Tamuzimod (VTX002) Program Status

**OLE/LTE data continue to support the differentiated profile** of tamuzimod in ulcerative colitis

**LTE phase completed mid 2024**; data presented at UEGW in October 2024

**Tamuzimod is Phase 3 ready** (clinical, CMC, regulatory)

- End of Phase 2 meeting with FDA completed; EMA Scientific Advice meeting completed
- Phase 2 trial expected to serve as the first of two pivotal trials\*

**Ventyx working to identify partner** or other source of non-dilutive financing to support future trials of VTX002 in ulcerative colitis

# Internally Discovered Clinical-Stage Pipeline

Addressing Autoimmune, Inflammatory and Neurodegenerative Diseases with High Unmet Need

TARGET	PROGRAM	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	NEXT ANTICIPATED MILESTONES
	<b>VTX2735</b> <i>Peripheral</i>	Recurrent Pericarditis				Ph 2 data <b>H2 2025</b>
<b>NLRP3</b>	<b>VTX3232</b> <i>CNS-Penetrant</i>	Parkinson's Disease				Ph 2 data <b>H1 2025</b>
	<b>VTX3232</b> <i>CNS-Penetrant</i>	Cardiometabolic Diseases (CMD) / Obesity				Ph 2 data <b>H2 2025</b>
<b>S1P1</b>	<b>Tamuzimod*</b>	Ulcerative Colitis				Phase 3 Ready*
<b>TYK2</b>	<b>VTX958</b>	Crohn's Disease				Phase 2 analysis underway

Cash, cash equivalents and marketable securities of **\$252.9M (unaudited)\*\*** as of December 31, 2024 are expected to fund operations into at least the **second half of 2026**

\*Formerly VTX002. Available for partnering or non-dilutive financing.

\*\*Preliminary cash, cash equivalents and marketable securities balance as of December 31, 2024 (unaudited), subject to adjustments resulting from, among other things, the completion of our end-of-period reporting processes and related activities, including the audit by our independent registered public accounting firm of our financial statements.