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Virtual Investor Event

March 11, 2024

Forward Looking Statements

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Ventyx Virtual Investor Event

Speakers and Participants

Ventyx Team

- **Raju Mohan, PhD** | Founder & CEO
- **John Nuss, PhD** | Chief Scientific Officer
- **Martin Auster, MD** | Chief Financial Officer
- **Chris Krueger, JD** | Chief Business Officer
- **Matt Cascino, MD** | VP, Clinical Development

Guest Speakers and KOLs

- **Marty Pomper, MD, PhD** | Chair, Dept of Radiology, UT Southwestern
- **Ted Dawson, MD, PhD** | Professor of Neurology, John Hopkins University

Disclosures:

Ted M. Dawson, MD, PhD: Consulting: T.M.D. is compensated for his role as a consultant, advisor, or Director for FBIO Acquisition Corp L, a subsidiary of Fortress Biotech Inc.; Aevum Therapeutics, Inc.; Inhibikase Therapeutics Inc.; and Valted Seq Inc. Stock Ownership: T.M.D. owns stock, stock options, or royalty interests in Aevum Therapeutics, Inc.; American Gene Technologies International Inc.; FBIO Acquisition Corp L, a subsidiary of Fortress Biotech Inc.; AbbVie; Inhibikase Therapeutics Inc; Valted, LLC; Neuraly, Inc.; D & D Pharmatech; and Valted Seq Inc. Research Sponsorship: T.M.D has a sponsored research agreement with Sun Pharma Advanced Research and Aevum Therapeutics, Inc.

Marty Pomper, MD, PhD: University of Texas Southwestern Medical Center (employee); D&D Pharmatech (equity, research, royalties, consulting); PlenaryAI, Inc. (equity); z-alpha (equity, consulting); Lantheus Holdings (research, royalties); Novartis (consulting); Earli (equity, consulting)

Internally Discovered Clinical-Stage Pipeline

Addressing Major Autoimmune and Inflammatory Diseases with High Unmet Need

Target	Program	Preclinical	Phase 1	Phase 2	Phase 3	Next Anticipated Milestones
NLRP3 *CNS-Penetrant*	VTX3232	Parkinson's disease, obesity, and other neuroinflammatory diseases				Initiate Ph 2a Parkinson's trial **H2 2024** Initiate Ph 2a Obesity trial **H2 2024**
NLRP3 *Peripheral*	VTX2735	Cardiovascular and other systemic inflammatory diseases				Phase 2 ready for CV indications
S1P1R	VTX002	Ulcerative colitis				Identify partner for Phase 3 trial
TYK2	VTX958	Crohn's disease				Phase 2 Crohn's data **mid 2024**

VTX958

Phase 2 Crohn's Disease Program Update

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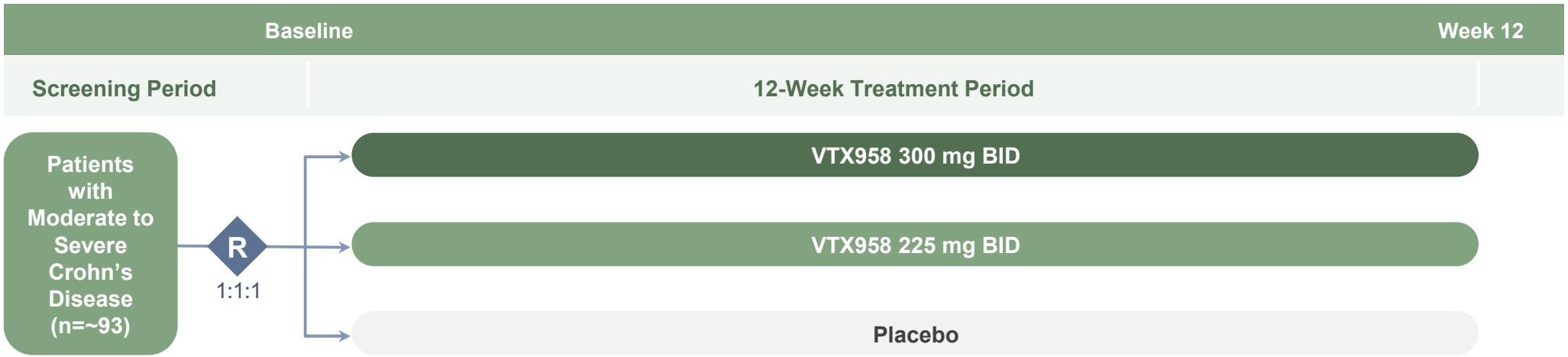
VTX958 Phase 2 Crohn's Disease Trial

Randomized, Placebo-Controlled Trial in Patients with Moderate to Severe Crohn's Disease



- **Protocol amendment implemented to streamline detection of a potential efficacy signal**
- **Primary Endpoints:** Change from baseline in mean CDAI score at Week 12
- **Secondary endpoints:** Proportion of patients achieving endoscopic response per SES-CD; Change in mean SES-CD score; proportion of patients achieving clinical remission and clinical response per CDAI; proportion of patients achieving PRO-2 remission
- Target enrollment changed to ~93 participants (previously ~132 participants); trial now closed to enrollment
- Randomization expected to complete in **Q1 2024; Topline data expected in mid 2024**
- Future capital commitment for VTX958 will be dependent on identification of a positive efficacy signal in the Phase 2 trial

SES-CD: Simple Endoscopic Score for Crohn's Disease; CDAI: Crohn's Disease Activity Index; PRO-2: Patient-Reported Outcome 2.

VTX002

Phase 2 OLE and Program Update

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VTX002 Phase 2 Study in Moderate-to-Severe UC

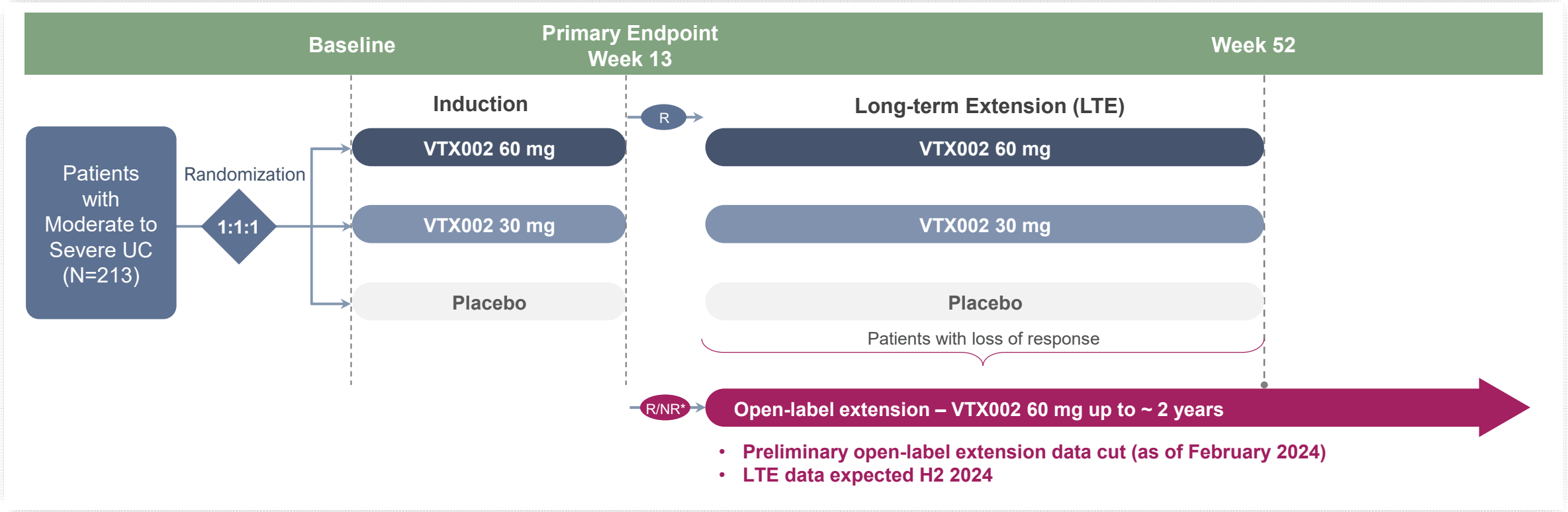
Designed to Serve as the First of Two Pivotal Trials

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



* Protocol version 1 study design. All patients had the option to roll-over regardless of response status. Subsequent protocol versions had patients with NR or loss of response only enter OLE
Note: NCT05156125. MMS: Modified Mayo Score; R: responder; NR: non-responder

Overview of VTX002 Induction Data

Robust Week 13 Clinical Remission with Differentiated Complete Endoscopic Remission

Key Takeaways from VTX002 Week 13 Data

Competitive week 13 clinical remission with differentiated endoscopic remission (MES=0)

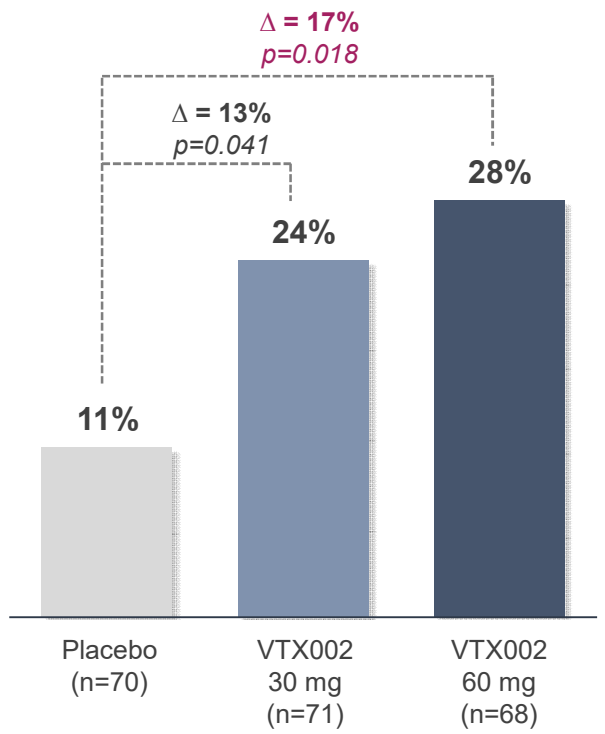
Deep remission (endoscopic and clinical remission), **symptomatic remission** and **histologic endoscopic mucosal improvement** rates further support clinical profile

Subgroup analysis demonstrated **differentiated clinical remission and endoscopic remission in patients with prior exposure to advanced therapies**

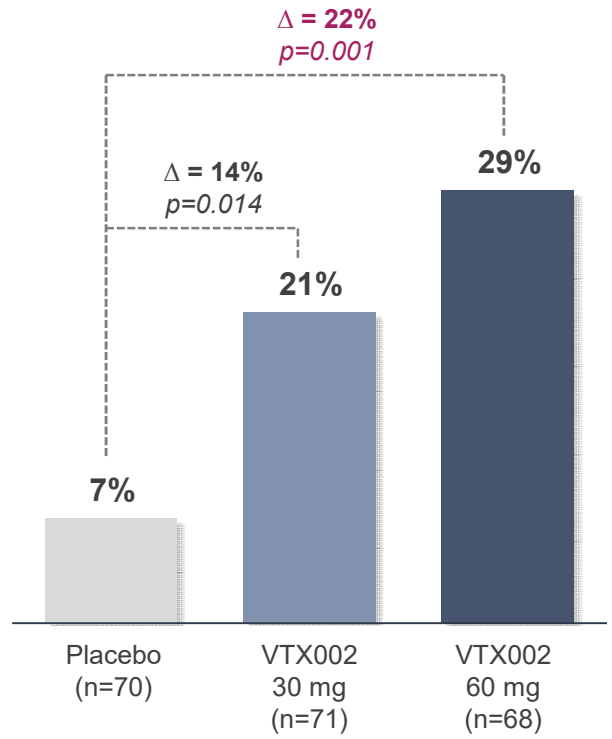
Zero cases of atrioventricular block, bradycardia, serious or opportunistic infections, or macular edema

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

Clinical Remission (Primary)



Endoscopic Remission (MES=0)



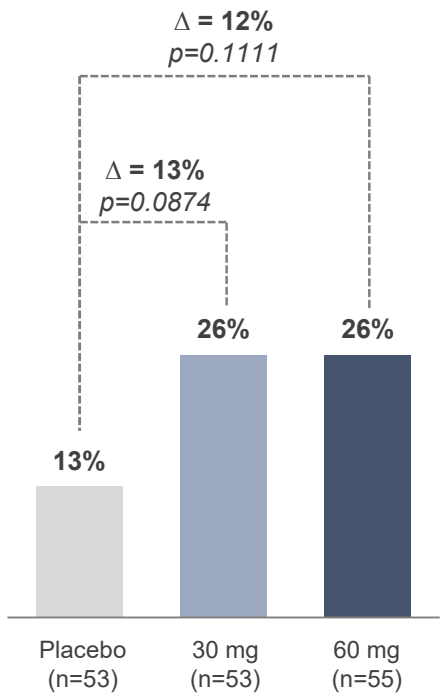
Clinical remission by modified Mayo Score (MMS) is defined as stool frequency subscore = 0 or 1, rectal bleeding subscore = 0, and endoscopic subscore ≤ 1 (excluding friability). Endoscopic remission is defined as a Mayo endoscopic subscore of 0. P-value for testing the treatment difference is based 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

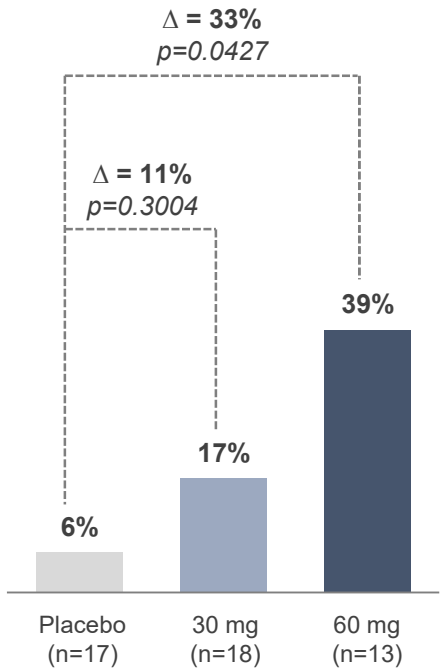
Clinical Remission and Endoscopic Remission at Week 13

Clinical Remission

Advanced Therapy Naïve

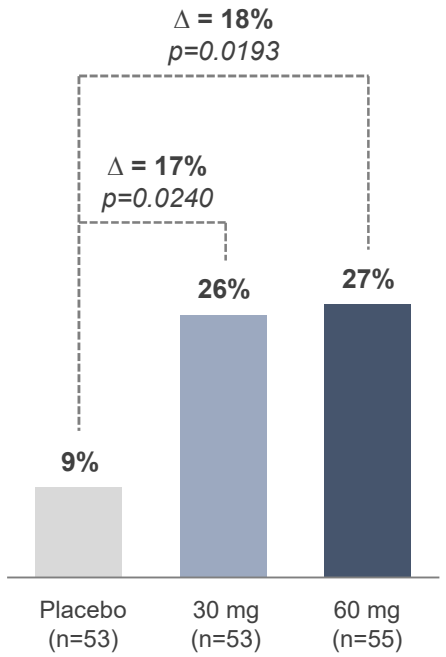


Advanced Therapy Experienced

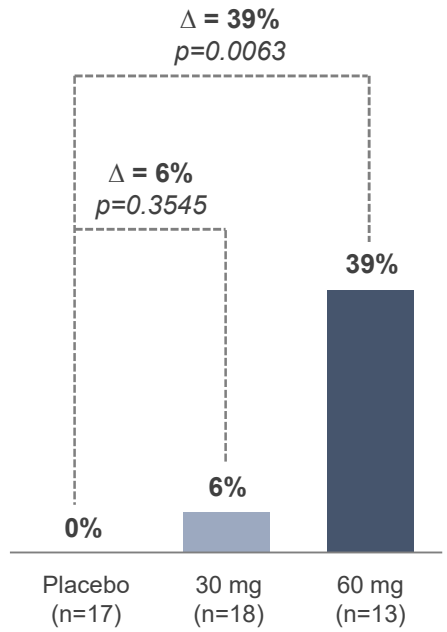


Endoscopic Remission

Advanced Therapy Naïve



Advanced Therapy Experienced



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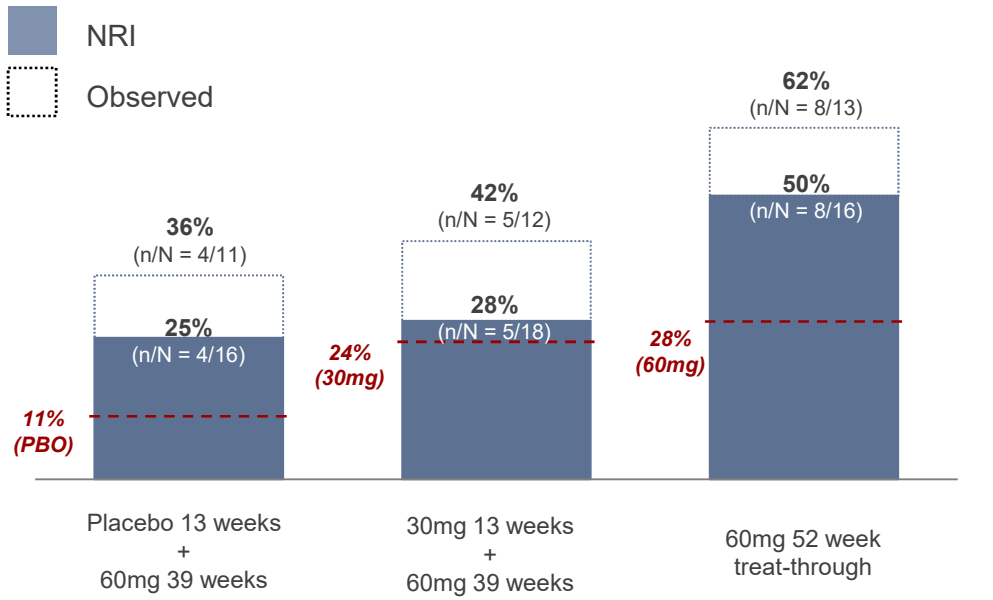
Preliminary Open-Label Extension Data

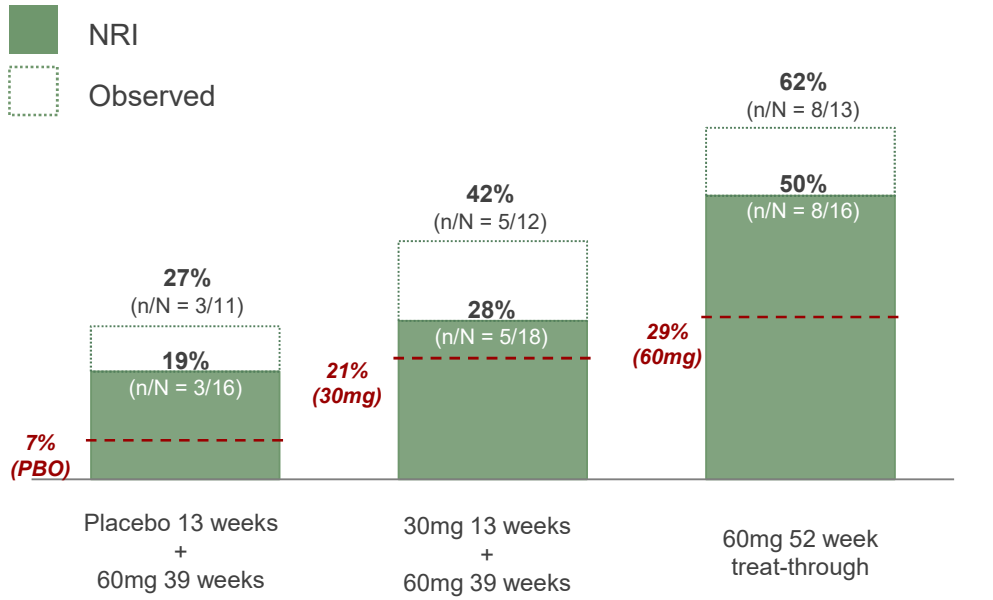
Further improvement in clinical and endoscopic remission rates at OLE week 39

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

% Clinical Remission at OLE Week 39[1] by Induction Dose Arm



% Endoscopic Remission[2] at OLE Week 39[1] 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: VTX002 has demonstrated the potential to set a new bar

Current Endoscopic Remission Outcomes

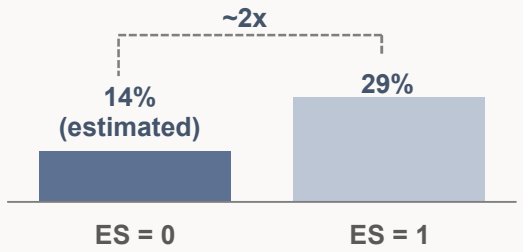
1 **The Vast Majority of Patients on Advanced Therapy Fail to Reach Endoscopic Remission, Particularly Within the Induction Period[1]:**

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[2]:**

12-month risk of clinical relapse
(meta-analysis of 17 studies):



3 **Achievement of Endoscopic Remission (MES=0) is Recognized in STRIDE II[3] Guidelines as an Aspirational Target of Long-Term Treatment:**

MES=0

- **Lower risk of disease recurrence**
- **Decreased steroid use**
- **Lower rate of surgical intervention & hospitalization**
- **Superior patient-reported outcomes**

VTX002 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

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[1] Based on analysis of Phase 3 trials for biologic and oral approved advanced agents; [2] Source: Yoon et al. Gastroenterology 2020;159(4):1262-1275.e7; [3] Source: Turner et al. Gastroenterology 2021;160:1570–1583

VTX002 OLE Conclusions and Program Status

Ventyx to Identify Partner or Other Source of Nondilutive Financing for Phase 3

- **OLE data continue to support the differentiated profile of VTX002 in ulcerative colitis**
- **VTX002 is Phase 3 ready (clinical, CMC, regulatory)**
  - End of Phase 2 meeting scheduled in Q2 2024
  - Phase 2 trial expected to serve as the first of two pivotal trials; single Phase 3 required for registration*
- **Ventyx to identify partner or other source of nondilutive financing for Phase 3**
  - New capital allocation priorities favor NLRP3 programs
  - Currently no additional internal spend planned for VTX002 other than to support ongoing Phase 2 LTE/OLE

*Pending outcome of planned discussions with regulators.

NLRP3 Inhibition

Broad Potential in Inflammatory Diseases

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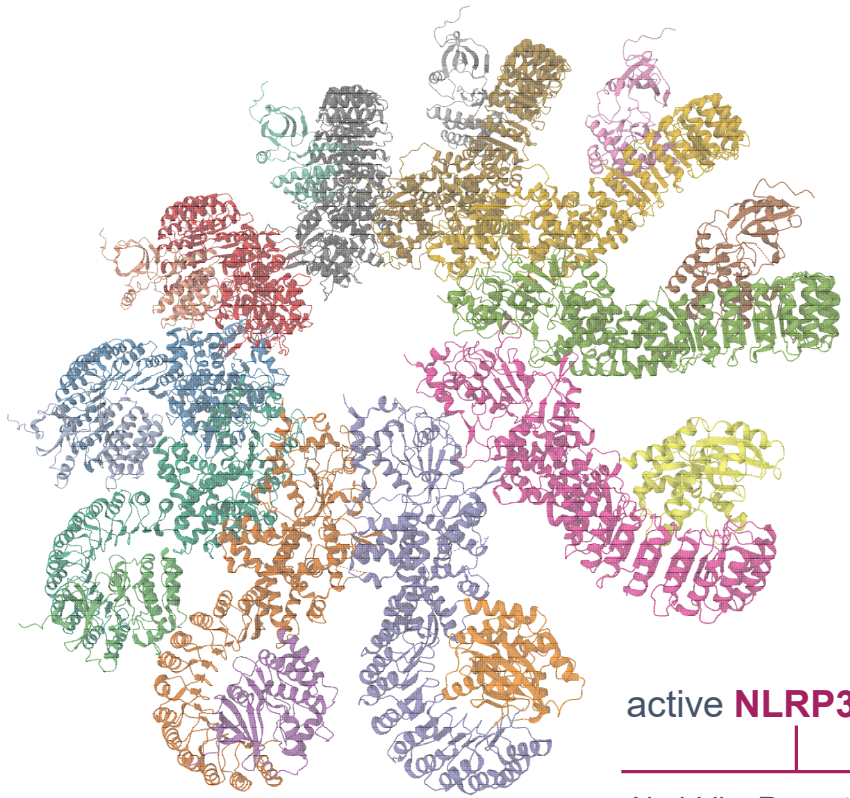
NLRP3 Inflammasome: A Key Component of Innate Immunity

Dysregulation Linked to a Broad Range of Inflammatory Diseases

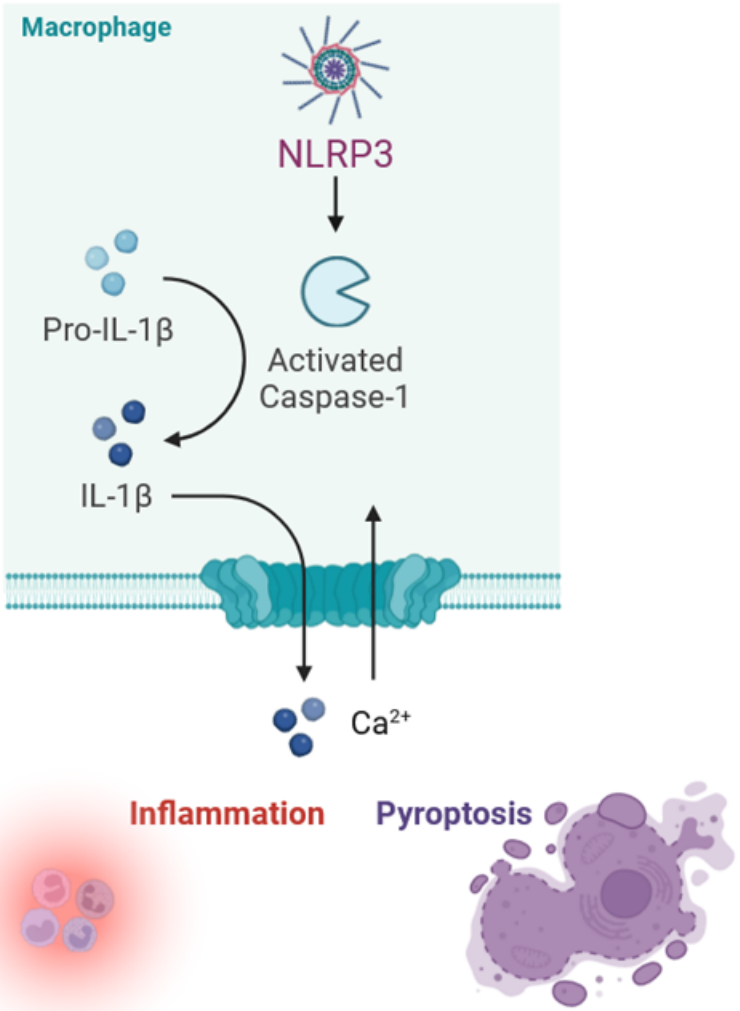


active **NLRP3** inflammasome disk

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-1β** 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-1β antibodies have demonstrated therapeutic benefit

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

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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
- Obesity

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CNS: Central nervous system. CAPS: Cryopyrin-associated periodic syndromes. FCAS: Familial cold autoinflammatory syndrome

VTX2735

Peripheral NLRP3 Inhibitor

Phase 2 CAPS (FCAS) Trial Results

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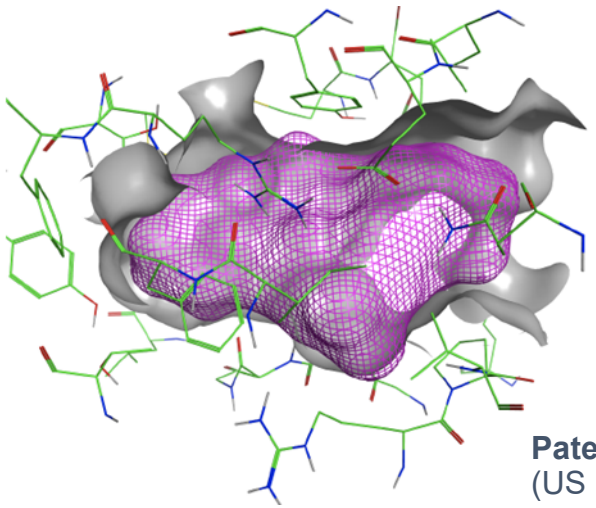
VTX2735: A Potent & Selective Peripheral NLRP3 Inhibitor

Phase 2 Ready for Systemic Inflammatory Diseases

Highly Potent & Selective

- hu WB IC_{50} (IL-1β) = 80 nM
- No inhibition of other inflammasomes



Patent granted
(US Pat. No. 11,603,375)

Nonclinical & Phase 1 Package

- Demonstrated PD and *in vivo* efficacy in rodent models
- High exposures & target coverage achieved in Phase 1
- Promising clinical safety profile
  - No signals that raise safety concerns that require further nonclinical study for genetox, safety pharmacology and phototoxicity
  - Chronic tox studies initiated, to finish EOY
  - Current tox data support 3 months of human dosing
- Potent inhibitor in PBMC from CAPS (FCAS) patients

Phase 2 proof-of-concept study in CAPS patients (FCAS) completed

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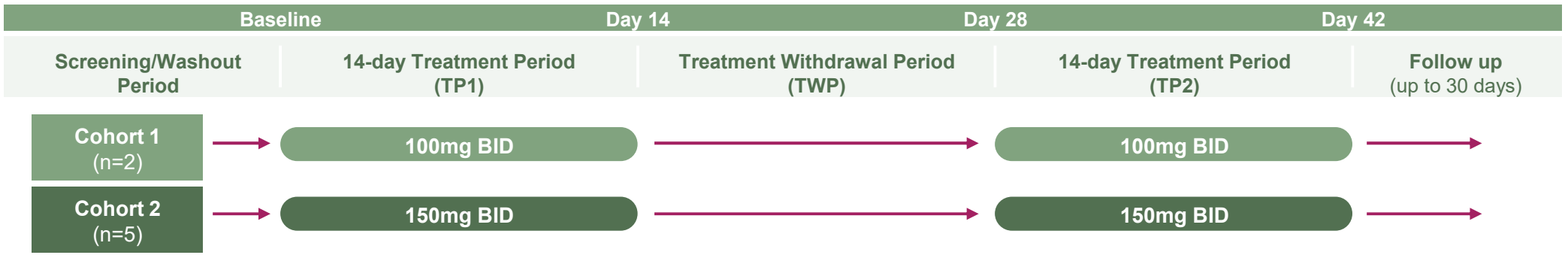
Source: Ventyx internal data. CAPS: Cryopyrin-associated periodic syndromes. FCAS: Familial cold autoinflammatory syndrome. WB: whole blood

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

Trial Design and Participants

- **CAPS** is an ultra rare condition driven by **excess NLRP3 activity; 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-1α, IL-1β, IL-6, and IL-18)
- **7 participants enrolled** (diverse NLRP3 mutations, prior SoC therapies, and symptoms)
  - 5 participants completed the trial; 1 withdrew consent after TP1 and 1 withdrew due to lack of efficacy



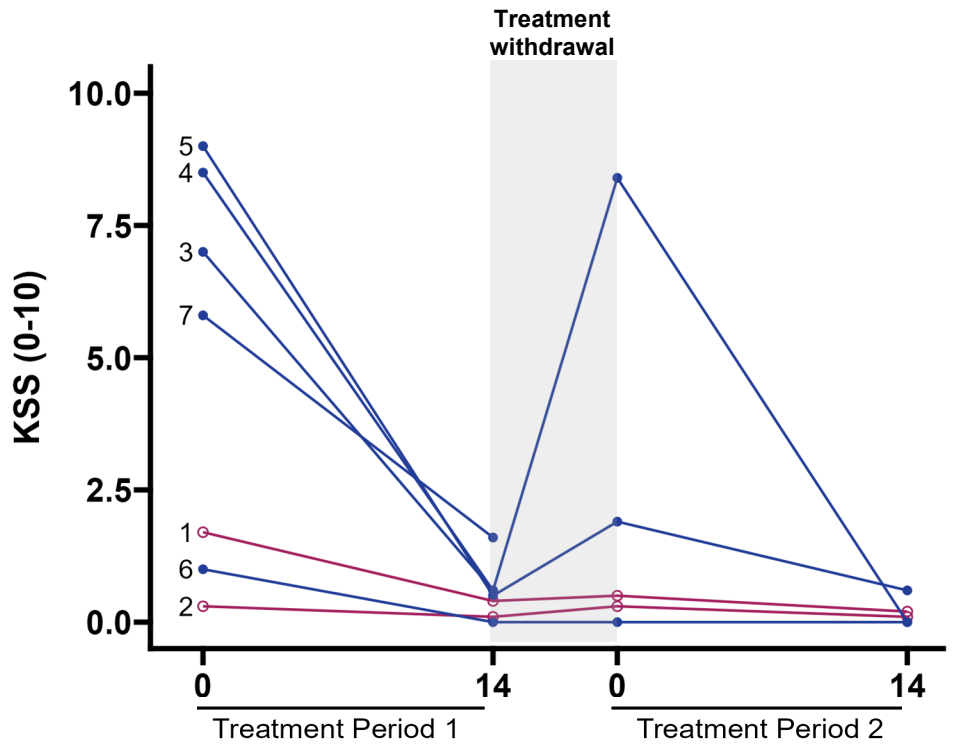
Source: Ventyx data on file.

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)*

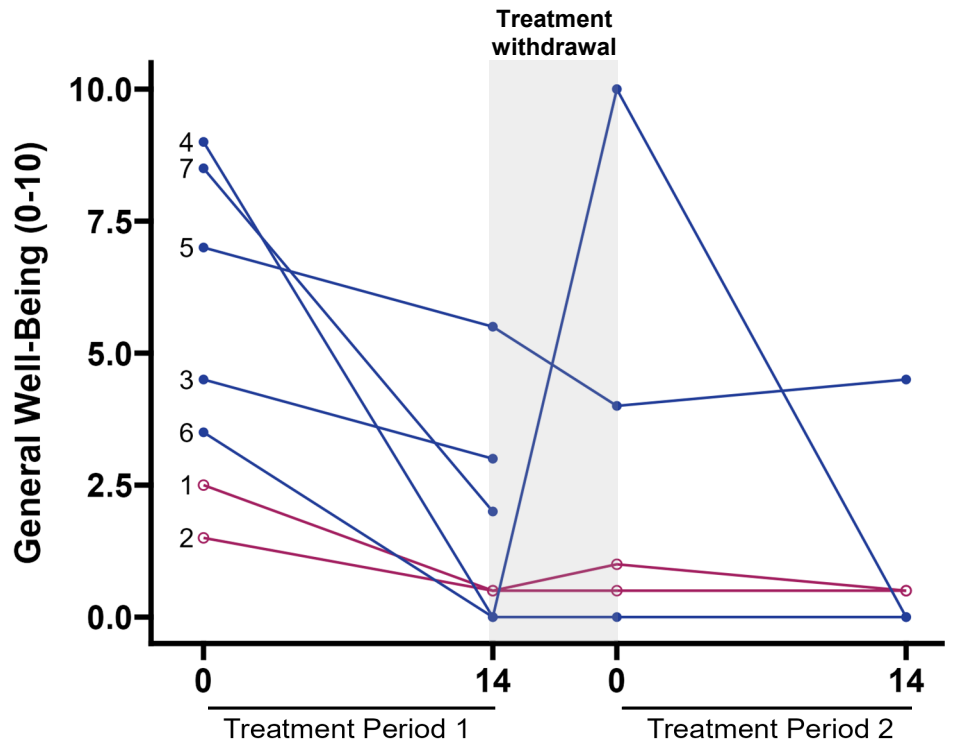
Daily mean of five symptom scores



Mean 85% reduction during Treatment Period 1

General Well-Being (0-10)*

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



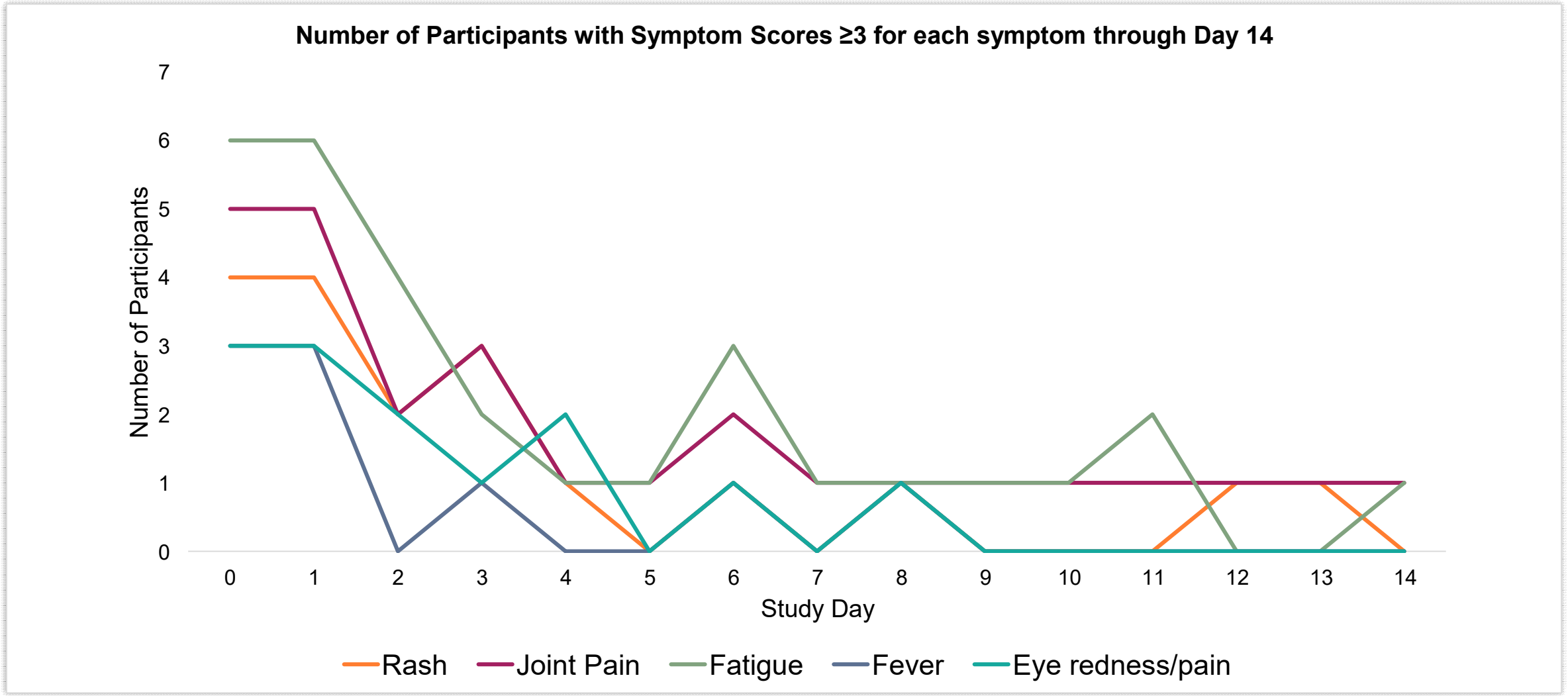
Mean 68% reduction during Treatment Period 1

100 mg BID — 150 mg BID

Source: Ventyx data on file (07 March 2024). *Note: One participant did not complete Treatment Period 1; the final measurement prior to study discontinuation is reported.

VTX2735 Effects on Disease Activity

Improvement in All CAPS Symptoms During First Week of Treatment with VTX2735



Source: Ventyx data on file (07 March 2024).

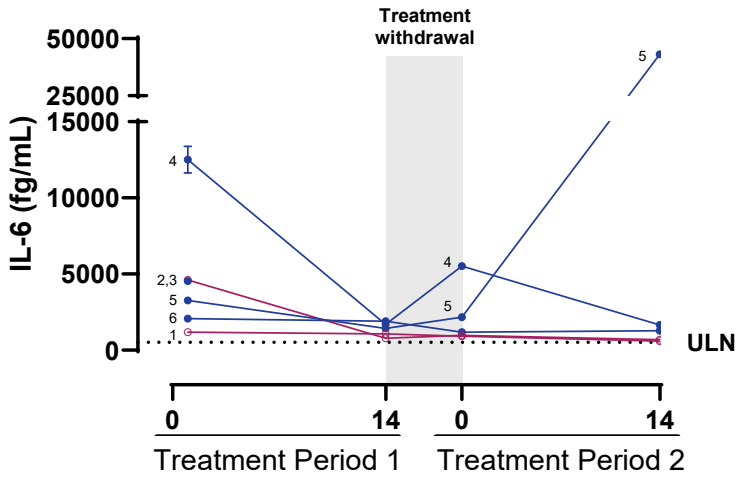
VTX2735 Biomarker Changes

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 antibodies (canakinumab)

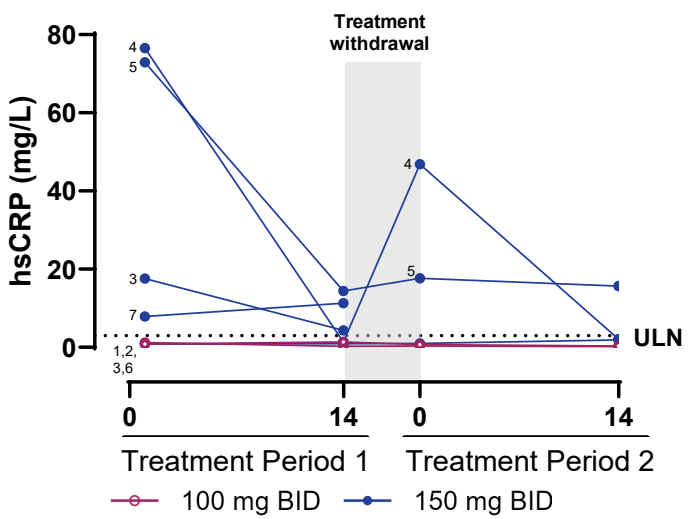
IL-6

Interleukin 6



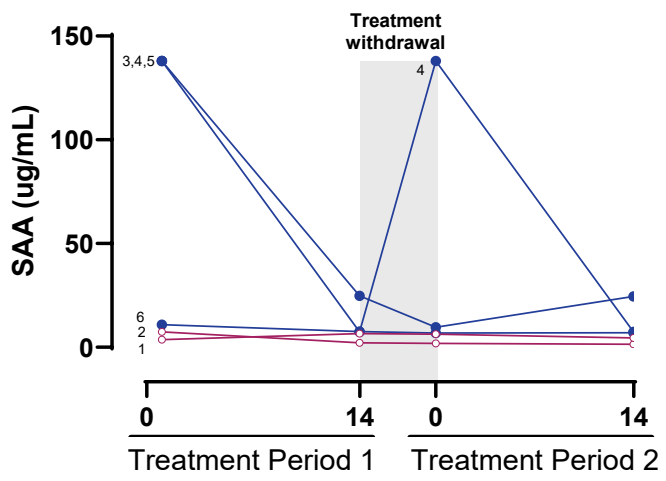
hsCRP

High-sensitivity C-reactive Protein



SAA

Serum amyloid A



Source: Ventyx data on file. *Note: 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

VTX2735 Was Well Tolerated

All Adverse Events Were Mild or Moderate and Resolved Without Treatment Interruption

Related AEs

AE	Grade	Relationship	Action	Outcome	SAE
Activated partial thromboplastin time prolonged	Grade 1	Related	Dose not changed	Recovered/Resolved	No
Anxiety	Grade 1	Related	Dose not changed	Recovered/Resolved	No
Blood phosphorus increased	Grade 1	Related	Dose not changed	Recovered/Resolved	No
Prothrombin time/INR prolonged	Grade 1	Related	Dose not changed	Recovered/Resolved	No
Pyrexia	Grade 1	Related	Dose not changed	Recovered/Resolved	No

Grade 2 or Higher AEs

AE	Grade	Relationship	Action	Outcome	SAE
Gastroenteritis	Grade 2	Not related	Dose not changed	Recovered/Resolved	No
Left rotator cuff tear	Grade 2	Not related	Dose not changed	Recovered/Resolved	No

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Source: Ventyx data on file.

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 were mild or moderate and resolved without treatment interruption
- **These data represent a major milestone for VTX2735 and for NLRP3 inhibition**
  - **Dr. Hal Hoffman (UCSD):** “Results similar to what we have seen in IL-1 inhibition studies” (Ilaris, Kineret, etc.); 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

Biologic-like Activity in CAPS Trial

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

Promising Safety Profile

- No CYP, hERG or transporter interactions
- No toxicological signals of concern
- Well-tolerated in all SAD/MAD dose groups and Phase 2 CAPS trial

Phase 2 Ready

- IP position secure; patent issued (US Pat. No. 11,603,375)
- Multi-kilo API production completed
- Extended-release dosing form expected Q3 2024

VTX3232

CNS-Penetrant NLRP3 Inhibitor

Phase 1 Trial Results

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VTX3232: Designed to Achieve Disease-Modifying CNS Exposures

Phase 2 Ready for Neuroinflammatory Diseases

Highly Potent and Selective

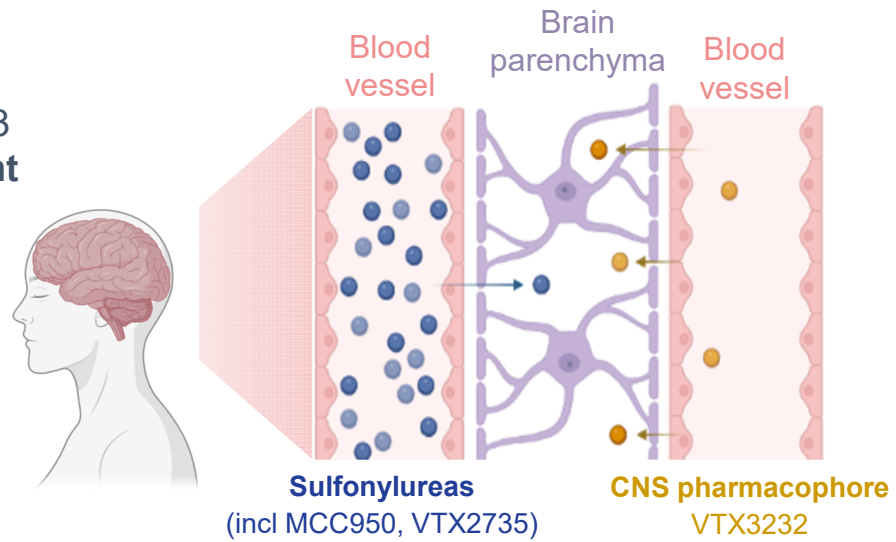
- hu WB IC_{50} (IL-1β) = **15 nM**
- hu Microglia IC_{50} (IL-1β) = **2.7 nM**
- No inhibition of other inflammasomes

Optimal CNS-drug properties in Phase 1

- Promising safety & tolerability through 14-day MAD
- Near-equal CNS partitioning; **human Kp,uu = 0.5**
- T½ = ~17 h with high free-drug fraction
- **20-40 mg QD exceeds CSF IL-1β IC_{90} for 20-24 h**
- Robust effects on inflammatory biomarkers

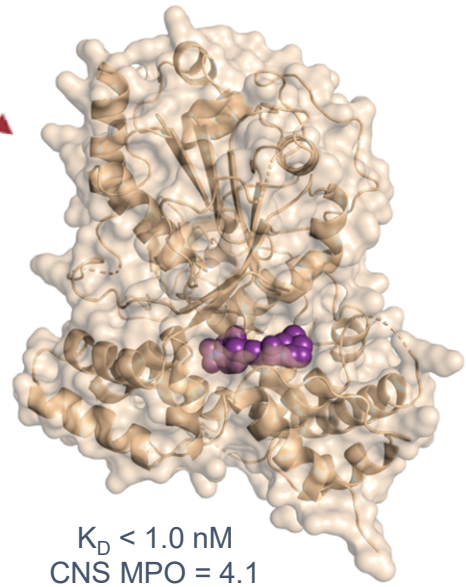
Sulfonylurea class of NLRP3 inhibitors have **poor inherent BBB permeability**

High systemic doses required to achieve CNS efficacy



VTX3232 is rationally-designed for **CNS efficacy** without high peripheral exposures

Rapid equilibration across BBB to reach microglial target cells

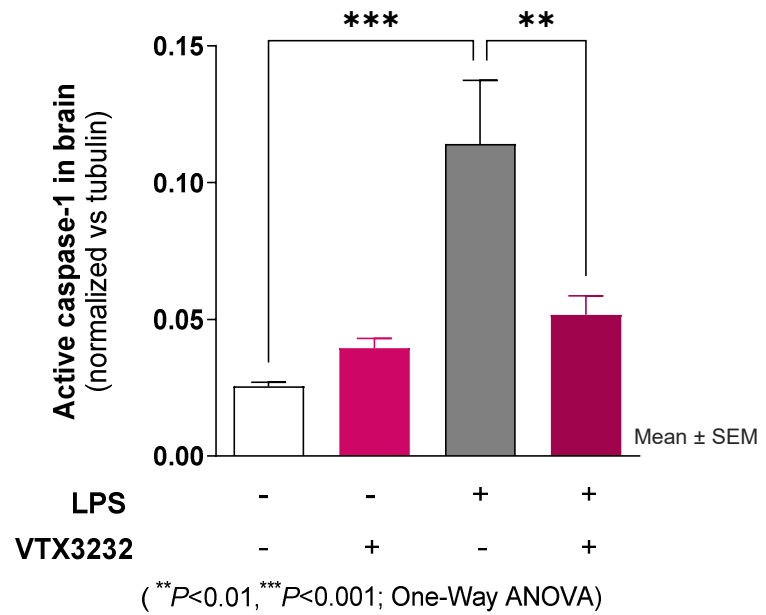


K_D < 1.0 nM
CNS MPO = 4.1

Source: Ventyx internal data. BBB, blood brain barrier; CNS, central nervous system, Kp,uu, partition coefficient; MPO, multiparameter optimization. Images created with BioRender.

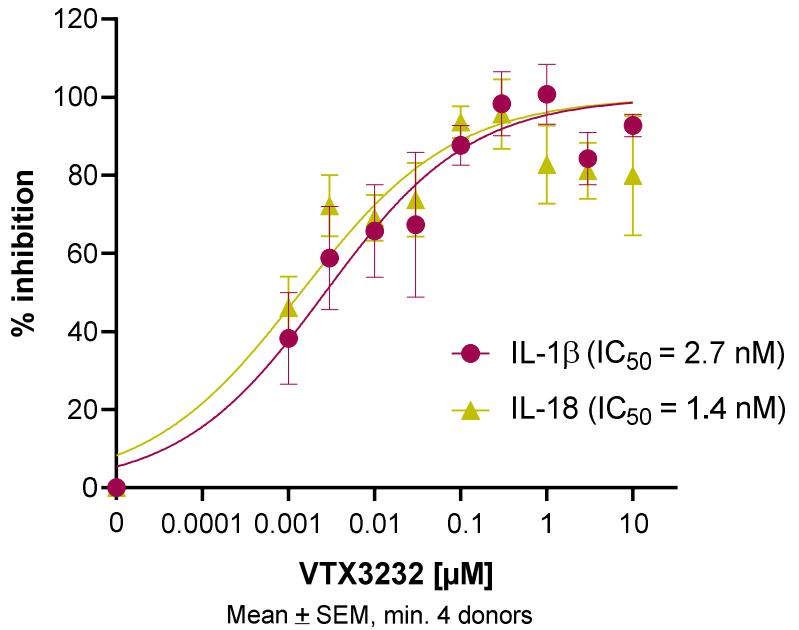
VTX3232 Efficacy In Neuroinflammation Models

Mouse Neuroinflammation Model



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

LPS-Primed Human Microglia



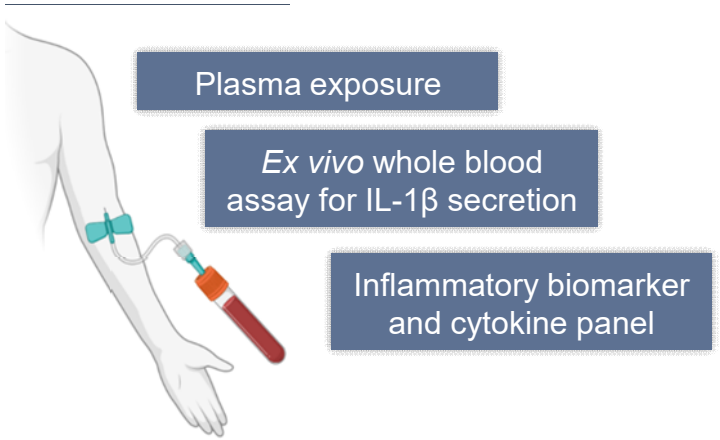
Potent inhibition of induced IL-1β & IL-18, selective vs TNFα

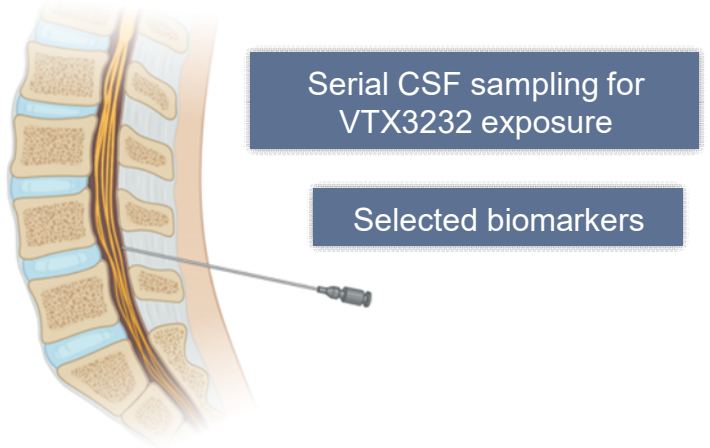
VTX3232 activity translates to CNS-relevant assays and models

Source: Ventyx internal data. CNS: central nervous system.

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

Phase 1 SAD and MAD Study Goals	Status
SAD and MAD to assess safety, tolerability and exposure	**Complete**
Ex vivo pharmacodynamic assessment of IL-1β inhibition*	**Complete**
Separate cohorts for VTX3232 exposure in CSF**	**Complete**
Plasma and CSF biomarkers	Ongoing
Relative bioavailability of VTX3232 tablets	**~100%**
Food effect study	**No food effect**





*LPS/ATP stimulation of huWB from treated subjects in MAD
**CSF exposure is a surrogate for drug free-fraction in the brain

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VTX3232 Safety Assessment

All Adverse Events Considered Mild or Moderate (Phase 1 MAD Cohorts)

		VTX3232 (MAD)				
Treatment Emergent AEs	**Placebo** (n=10)	**1 mg** (n=6)	**3 mg** (n=6)	**10 mg** (n=6)	**20 mg** (n=6)	**40 mg** (n=6)
Vomiting	1 (10%)	-	-	-	-	-
Conjunctivitis	1 (10%)	-	-	-	-	-
Constipation	1 (10%)	1 (16.7%)	-	-	-	-
Covid-19	1 (10%)	-	-	-	-	1 (16.7%)
Viral Syndrome	1 (10%)	-	-	-	-	-
Gastroenteritis	-	-	-	1 (16.7%)	-	-
Contact dermatitis	-	-	-	-	1 (16.7%)	-
Dry skin on legs	-	-	-	-	1 (16.7%)	-
Lightheaded	-	-	-	-	-	1 (16.7%)
Headache	-	-	-	-	-	1 (16.7%)
Nausea	-	-	-	-	-	1 (16.7%)
Drowsiness	-	-	-	-	-	1 (16.7%)

Note: MAD CSF cohorts are excluded in the table above as the safety profile in these cohorts is obscured by AEs related to indwelling spinal catheters.

Safety Findings

- VTX3232 was **well tolerated** in Phase 1 SAD/MAD trial
- All treatment emergent AEs considered mild or moderate (CTCAE Grade 1 or 2)
- **No dose-limiting toxicities** observed
- Safety profile supports wide therapeutic window

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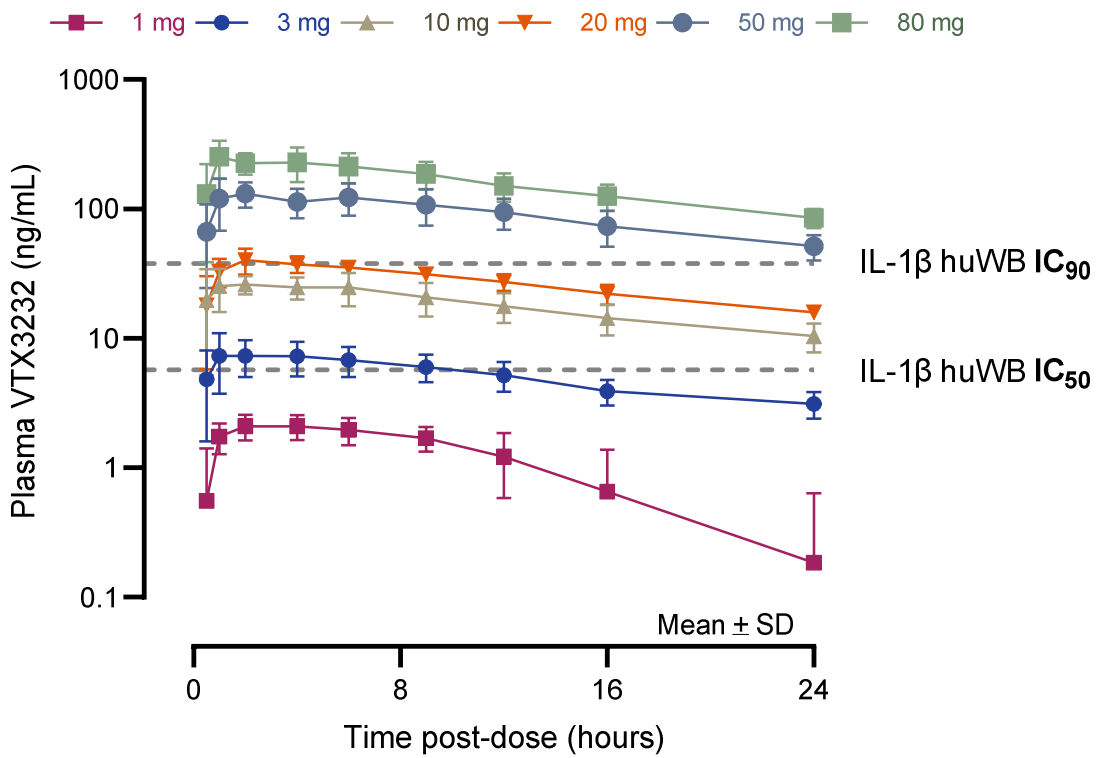
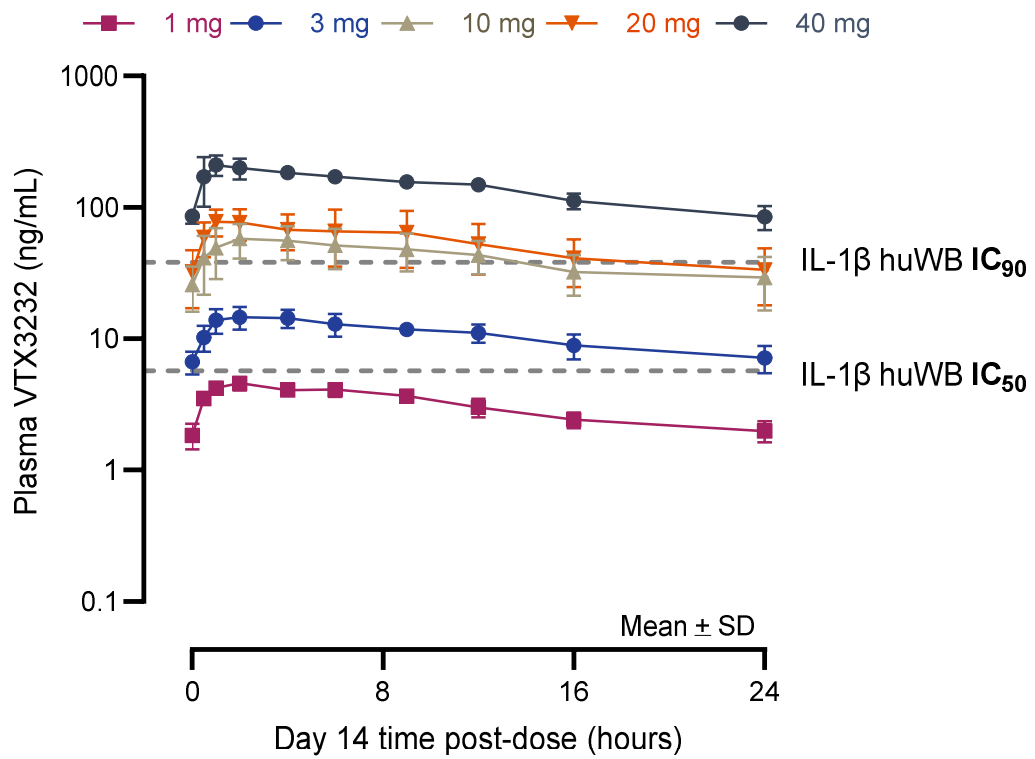
Source: Ventyx internal data.

VTX3232 Phase 1 SAD and 14 Day MAD Pharmacokinetics

Single Ascending Dose



Multiple Ascending Dose



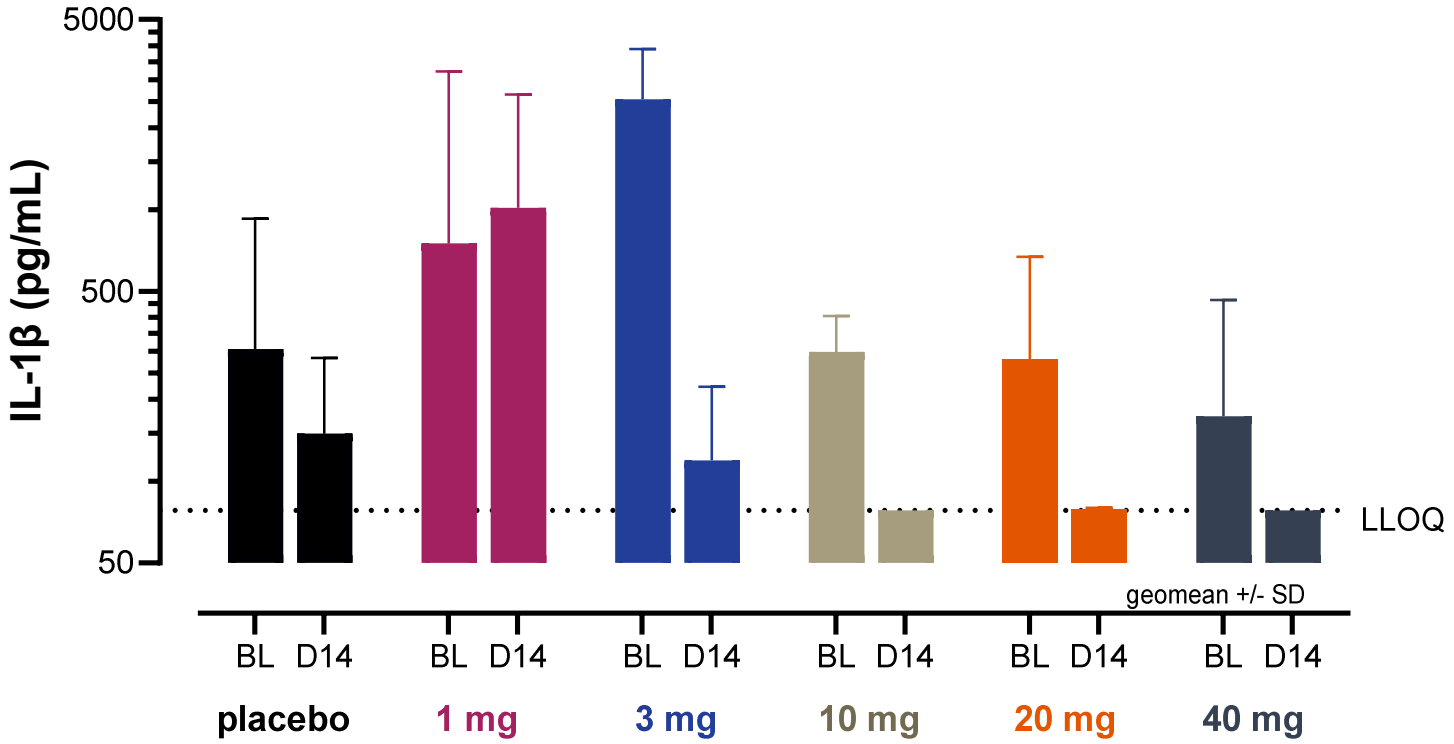
Dose-related, linear exposure from 1 mg to 80 mg

3 mg QD achieves **24 h IL-1β IC_{50}** coverage

Source: Ventyx internal data.

VTX3232 Whole Blood *Ex Vivo* Stimulation Assay

Potent Target Engagement Demonstrated At and Above 3 mg QD



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).

Data Summary

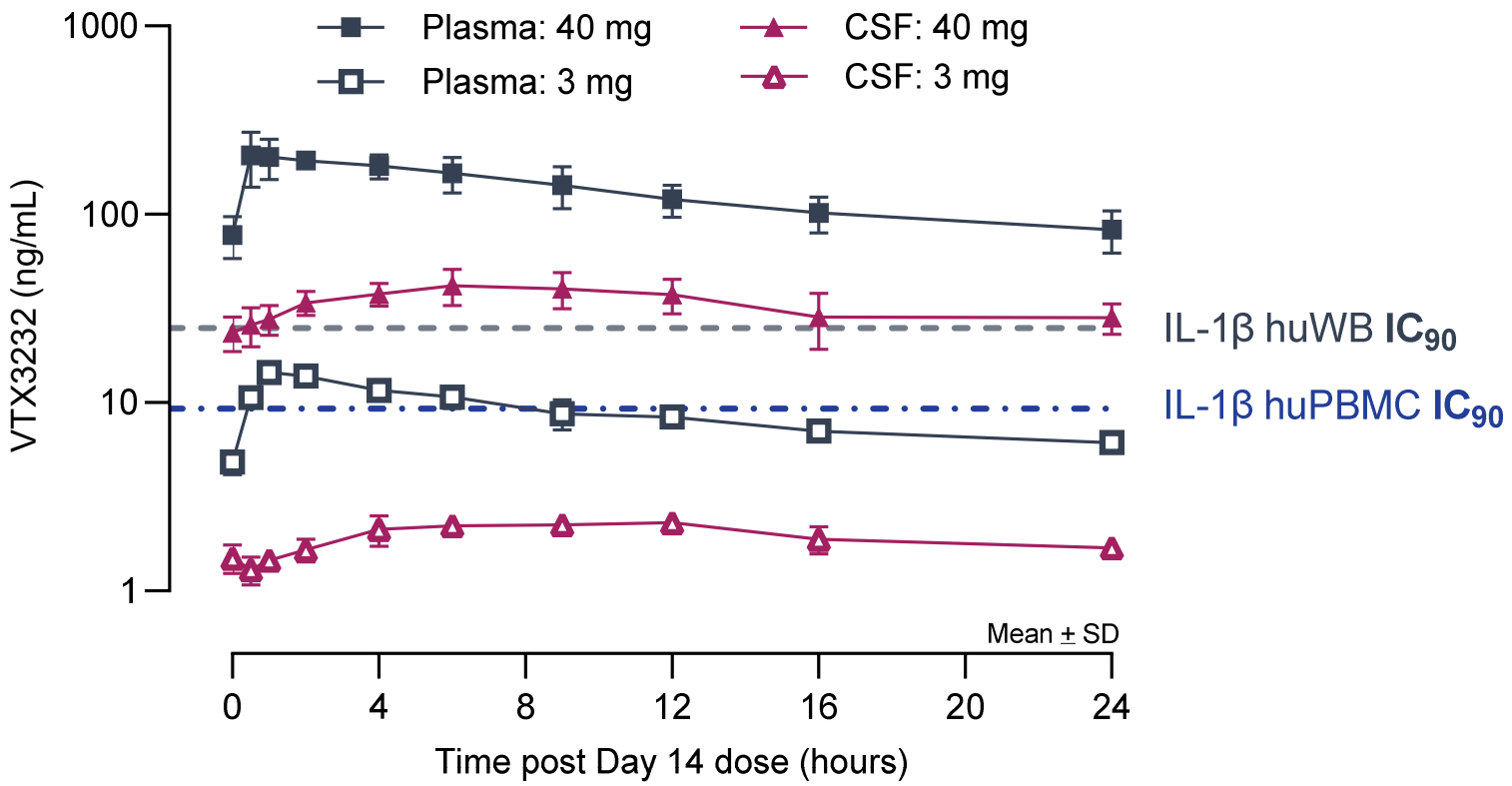
Blockade of NLRP3 mediated IL-1β is maintained at Day 14 with repeat dosing

Maximal inhibition achieved at doses of 10 mg QD and higher

Source: Ventyx internal data.

VTX3232 Pharmacokinetics in Cerebrospinal Fluid (CSF)

Matched Plasma & CSF Exposure in MAD Cohorts



Data Summary

VTX3232 achieves comparable exposures in both plasma and CSF

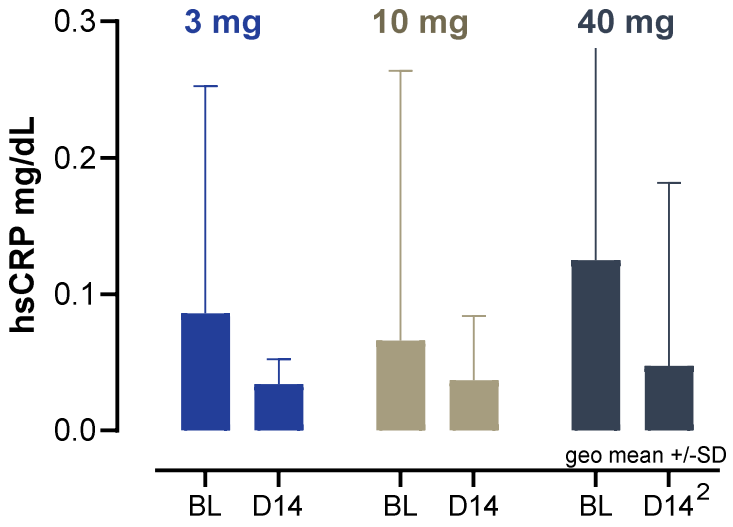
40 mg QD **exceeds CSF IC_{90} for 24 h**, achieving robust target coverage for NLRP3 in microglia for neuroinflammatory conditions

Source: Ventyx internal data.

VTX3232 Effects on Inflammatory Biomarkers

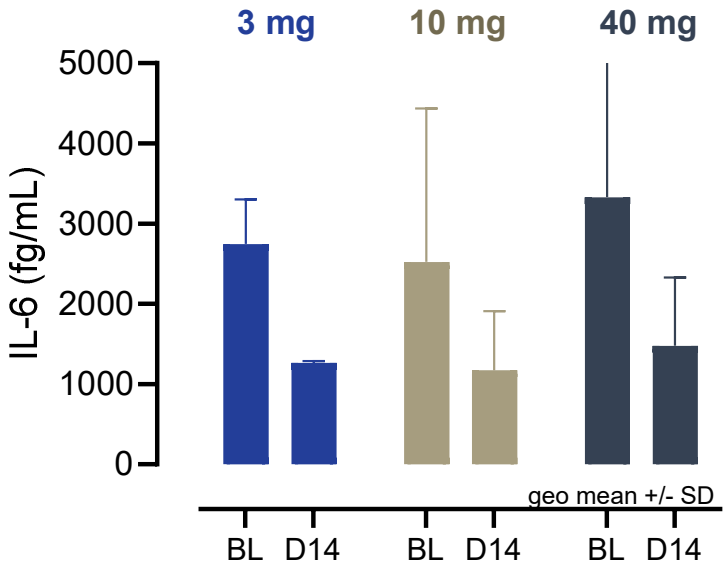
Reduction in hsCRP and IL-6 Comparable to that Achieved by Canakinumab* (IL-1β mAb)

Plasma hsCRP

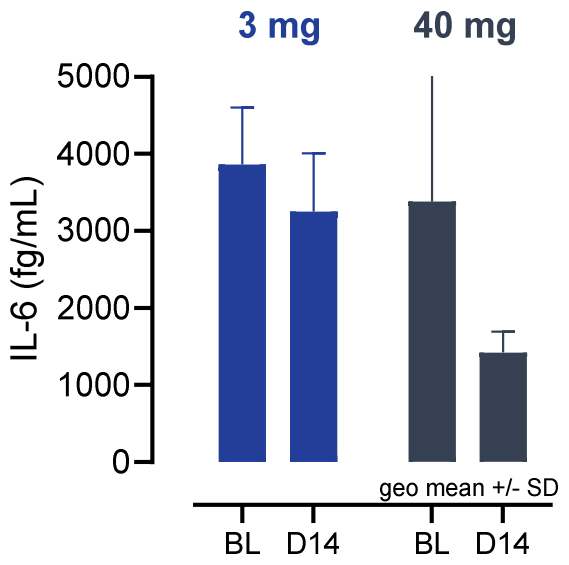


Systemic inflammation biomarker hsCRP lowered by as much as 55%

Plasma IL-6



CSF IL-6



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

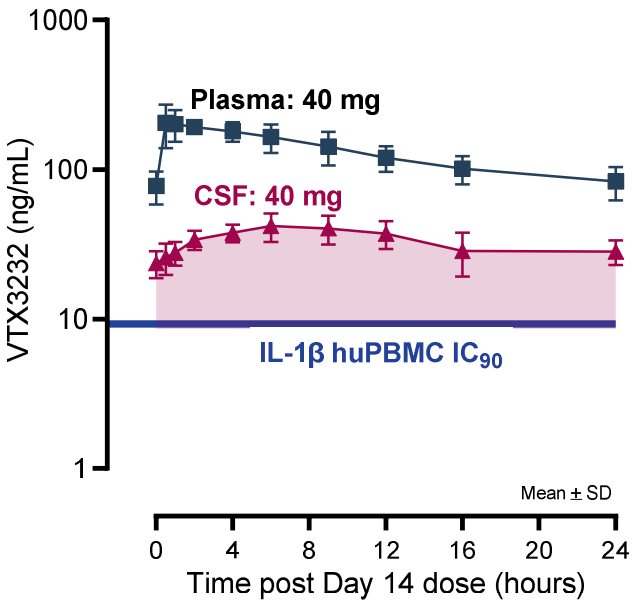
*Canakinumab: 35-40% hsCRP and IL-6 reduction based on literature reported values for canakinumab[1]

1. Ridker PM, MacFadyen JG, Everett BM *et al.*. *Lancet* 2018; 391:319-28; Ridker PM, Libby P, MacFadyen JG *et al. Eur Heart J.* 2018; 39:3499-507.
2. Day 14 pre dose samples not available for 40mg cohort. Data 2hr post dose displayed.
Source: Ventyx internal data. BL: pre-dose baseline. D14: Day 14 pre-dose samples, unless otherwise noted.

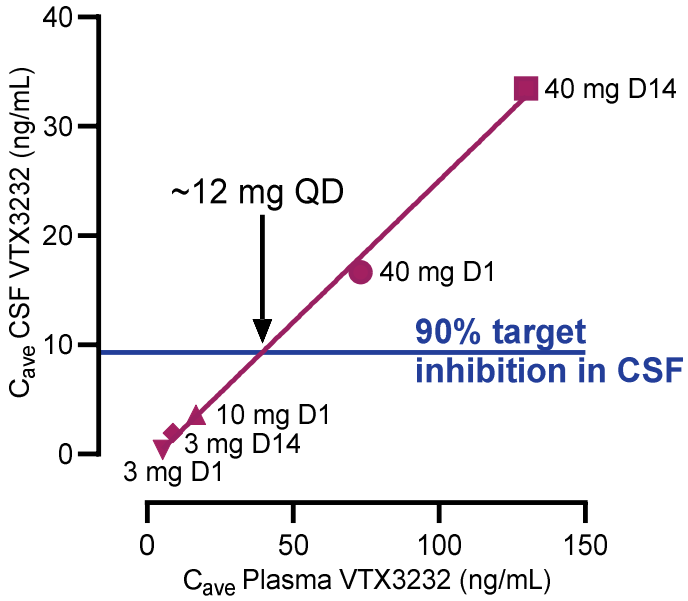
Conclusions from the Phase 1 Trial of VTX3232 in NHV

Potentially Class-leading Safety and Efficacy Profile for Neuroinflammatory Diseases

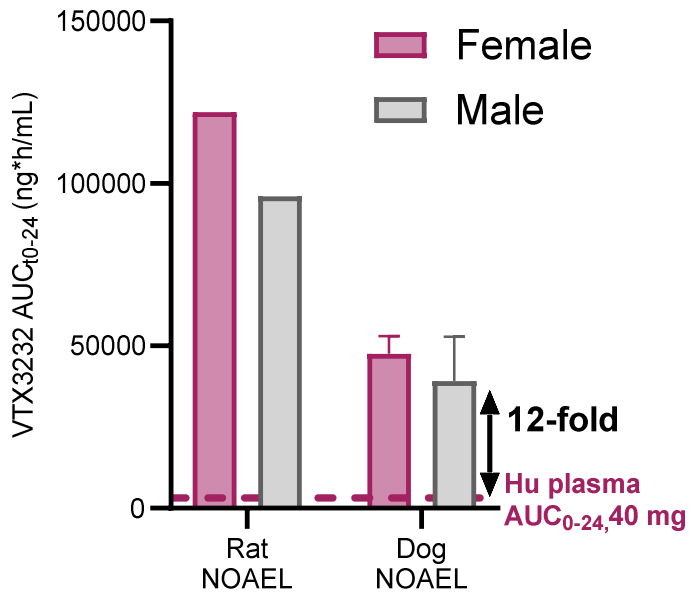
40 mg QD Dose: Target Coverage



Data Predict Low Efficacious Doses



Toxicology Safety Margin



- **Well-tolerated** in healthy volunteers
- **Robust target coverage achieved in the plasma and CNS**
- **Potent, dose-dependent PD effect** in *ex vivo* IL-1β assay and on inflammatory biomarkers
- **CSF IL-1β IC_{90} coverage for 24h at 40 mg QD**
- **Data predict target coverage ≥ IC_{90} at doses ≥ 12 mg**

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Source: Ventyx internal data.

VTX3232: Potential First-Mover Position in NLRP3-Mediated Neuroinflammation

Highly Potent & Selective

- Structurally unique, unrelated to MCC-950
- 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-1β release for >24 h

High CNS Target Coverage

- T½ = ~17 h with high free fraction
- High CNS penetration; human Kp,uu = 0.5
- 3 mg QD repeat dosing maintains CSF IC_{50} coverage
- 40 mg QD repeat dosing exceeds CSF IC_{90} coverage

Promising Safety Profile

- No CYP, hERG, or transporter interactions
- No toxicological signals for further non-clinical study
- Well-tolerated in all SAD/MAD dose groups

Phase 2 Ready

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

NLRP3 Inhibitor Portfolio

Clinical Development Strategy

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Building a Diversified Pipeline in Inflammatory Disease

Broad Potential in Systemic Inflammatory and Neuroinflammatory Conditions

Ventyx NLRP3 Inhibitors

VTX2735

Systemic Inflammatory Diseases

- ❖ **Secondary prevention of MACE**
- ❖ **Recurrent pericarditis**
- Metabolic diseases
- Rheumatic diseases
- Dermatologic diseases
- Rare genetic diseases

VTX3232

Neuroinflammatory Diseases

- ❖ **Parkinson's disease**
- ❖ **Obesity**
- Multiple sclerosis (MS)
- Alzheimer's disease
- Amyotrophic lateral sclerosis (ALS)
- Other neurodegenerative diseases

MACE: Major adverse cardiovascular event.

VTX2735 in Cardiovascular Disease

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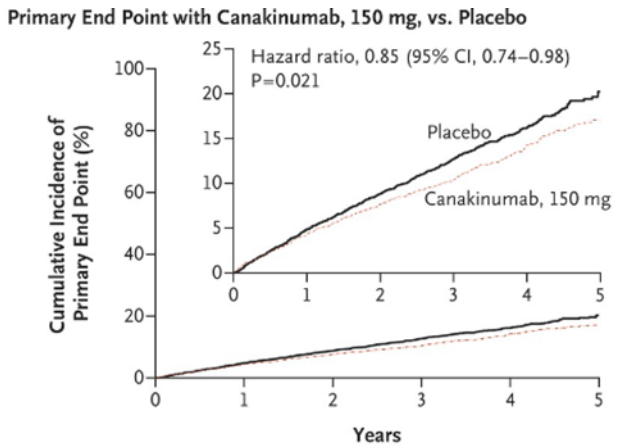
Attractive Opportunities for VTX2735 in Cardiovascular Disease

Leading Opportunities – Secondary Prevention of MACE and Recurrent Pericarditis

MACE Prevention

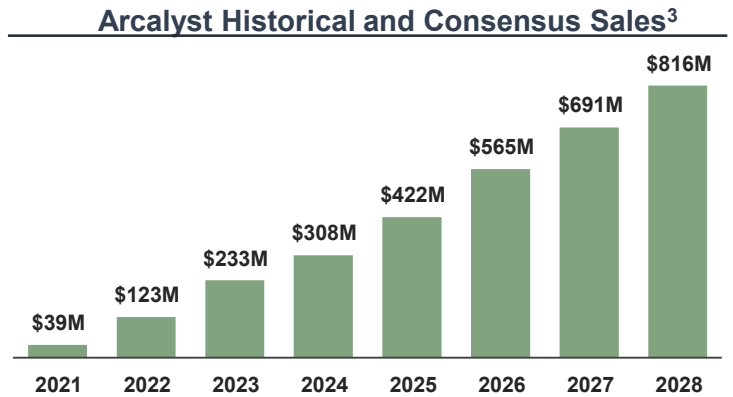
- **CANTOS trial of canakinumab validates IL-1β approach in reduction of MACE risk**
  - Reductions in MACE associated with inflammatory biomarker reductions (hsCRP, IL-6, IL-18)[1]



- **A safe, oral peripheral NLRP3 inhibitor may be an ideal approach for secondary prevention of MACE**
  - Blockbuster opportunity with multiple targetable populations

Recurrent Pericarditis

- **2021 approval of Arcalyst (rilonacept) validates IL-1α/β approach**
  - ~40,000 patient U.S. prevalent population with RP[2]
  - Arcalyst generated $233M in 2023 sales in 2nd full year of commercial availability; consensus sales **>$800M** in 2028



- **Regulatory precedent for efficient path to market**
  - Open-label Phase 2 followed by a single registrational Phase 3 trial

Source: 1. Ridker et al., *N Engl J Med* 2017; 377:1119-1131 DOI: 10.1056/NEJMoa1707914; 2. Klein et al., *J Am Heart Assoc.* 2021 Aug 3;10(15):e018950. doi: 10.1161/JAHA.120.018950;
3. Historical sales from Kiniksa investor presentation; consensus sales (2024+) from Evaluate Pharma.

VTX3232 Phase 2a Trial in Parkinson's Disease

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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[1]
- Estimated **~$10-$15B+ annual TAM** for first disease-modifying therapy[2]

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

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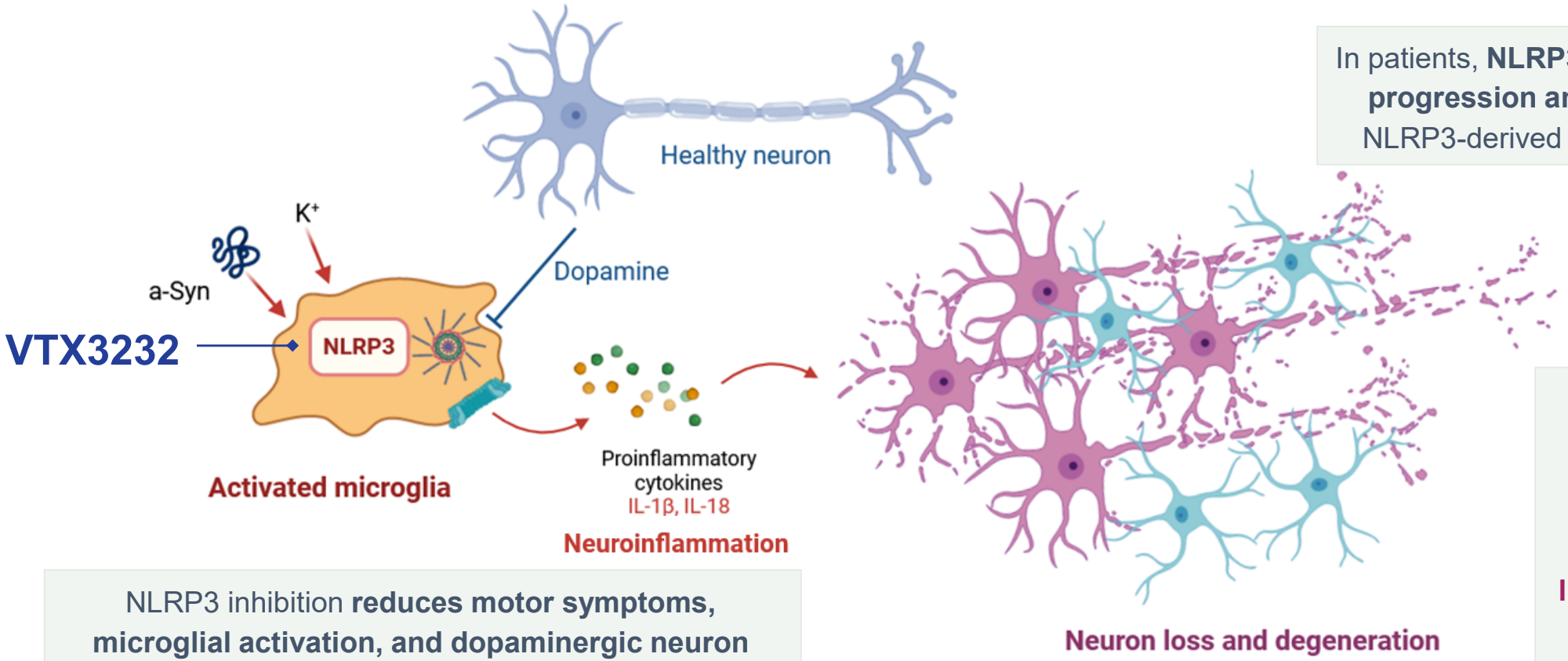
Source: 1. Grand View Research Parkinson's disease market report; 2. ClearView Healthcare Partners market research for internal use.

NLRP3 Is a Promising Therapeutic Target in Parkinson's Disease

Neuroinflammation Plays a Central Role in Parkinson's 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



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

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

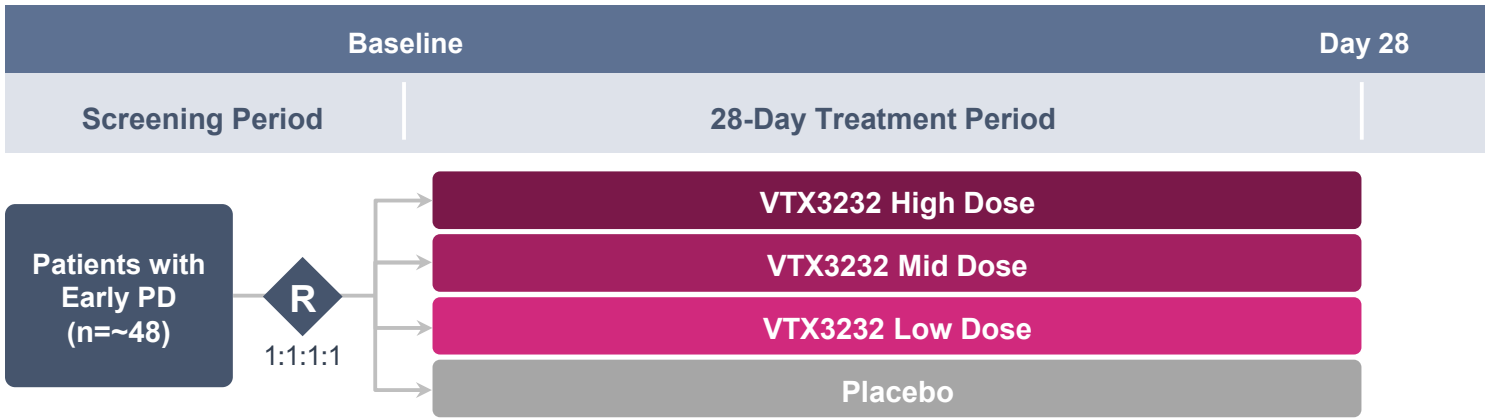
Neuroinflammation through excess NLRP3 activity may be the mechanistic link driving neuronal cell death in PD

Source: Liang T et al. 2022 Front. Pharmacol. 13:845185. Ising, C et al. Nature 575, 669–673 (2019). Panicker et al. Neuron. 2022;110(15):2422-2437.e9. Grotemeyer, A. et al., *J Neuroinflammation* 20, 79 (2023). Huang et al., *J Nueroimmunology*, Volume 354, 2021, 577543. Gordon et al., *Sci. Transl. Med.* 10,eaah4066(2018).

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

Disease-Relevant Biomarkers and Neuroimaging

- **A Phase 2a trial in participants with early Parkinson's disease is expected to initiate in H2 2024**
  - Impact on relevant plasma and CSF biomarkers: IL-1β, IL-18, α-synuclein, NfL, GFAP, NGAL, Aβ40/42
  - Impact on microglial inflammation via neuroimaging
- **Test of therapeutic hypothesis that CNS NLRP3 inhibition will result in reduced inflammation and disruption of PD pathophysiology**



Objectives

- Disease and NLRP3-related biomarkers in plasma and CSF
- Pharmacokinetics
- Neuroimaging for microglial inflammation

Note: preliminary trial design, subject to change pending regulatory feedback.

VTX3232 Phase 2a Trial in Obesity

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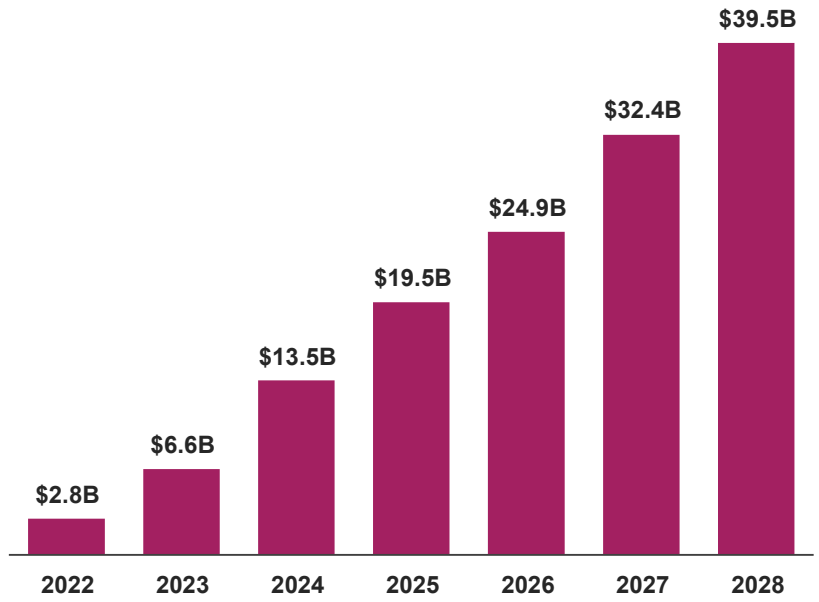
NLRP3 Is Emerging as an Important Target in Obesity

The NLRP3 Inflammasome in Obesity and Related Metabolic Disease

- **The NLRP3 inflammasome is emerging as an important axis in obesity and obesity-related metabolic disease**
  - Obesity is a chronic inflammatory condition associated with release of NLRP3-related cytokines such as IL-1β 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 in obese individuals is associated with reduced expression of NLRP3 and decreased systemic inflammation[1]
- **NLRP3 inhibition drives weight loss in diet-induced obesity (DIO) mouse model[2]**
  - Weight loss effect similar in magnitude to semaglutide (GLP-1)
  - Brain exposure appears necessary for weight-loss effect
  - Inhibition of reactive gliosis (inflammation) in the hypothalamus proposed as potential mechanism

Projected Growth in the Obesity Market[3]

Driven by expected adoption of GLP-1s



Blockbuster opportunity for novel mechanisms in obesity and related metabolic impairment

Source: 1. Vandanmagsar et al., *Nat Med.* 2011 Feb;17(2):179-88. doi: 10.1038/nm.2279; 2. Thornton et al., *Journal of Pharmacology and Experimental Therapeutics* Feb 9, 2024, JPET-AR-2023-002013; DOI: https://doi.org/10.1124/jpet.123.002013 3. EvaluatePharma market projections.

Phase 2a Trial of VTX3232 in Obese Participants with Elevated CV Risk

Measuring Key Inflammatory Biomarkers and Changes in Body Composition

- **A randomized, placebo-controlled trial of VTX3232 in obese participants with elevated CV risk is expected to initiate in H2 2024**
  - Adult participants with obesity, elevated CRP, and at least one additional risk factor of atherosclerotic cardiovascular disease
- **Trial intended to efficiently identify a potential efficacy signal and support path forward in obesity**
  - Biomarkers to assess CV risk reduction in obese population; potential to measure other markers of metabolic impairment

Endpoints

- Change from baseline in CRP (**primary**)
- Inflammatory biomarkers
- Change from baseline in weight and body composition

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Note: preliminary trial design, subject to change pending regulatory feedback.

Internally Discovered Clinical-Stage Pipeline

Addressing Major Autoimmune and Inflammatory Diseases with High Unmet Need

Target	Program	Preclinical	Phase 1	Phase 2	Phase 3	Next Anticipated Milestones
NLRP3 *CNS-Penetrant*	VTX3232	Parkinson's disease, obesity, and other neuroinflammatory diseases				Initiate Ph 2a Parkinson's trial **H2 2024** Initiate Ph 2a Obesity trial **H2 2024**
NLRP3 *Peripheral*	VTX2735	Cardiovascular and other systemic inflammatory diseases				Phase 2 ready for CV indications
S1P1R	VTX002	Ulcerative colitis				Identify partner for Phase 3 trial
TYK2	VTX958	Crohn's disease				Phase 2 Crohn's data **mid 2024**

Cash, cash equivalents and marketable securities of $252.2M* as of December 31, 2023, are expected to fund operations into at least the second half of 2026

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* Does not include $100 million gross proceeds raised in PIPE financing announced on March 7, 2024

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