UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 26, 2023

VENTYX BIOSCIENCES, INC.
(Exact name of Registrant as Specified in Its Charter)

Delaware	001-40928	83-2996852
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(IRS Employer Identification No.)

662 Encinitas Blvd
Suite 250
Encinitas, California 92024
(Address of Principal Executive Offices, Including Zip Code)

Registrant's Telephone Number, Including Area Code: (760) 593-4832

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	VTYX	The NASDAQ Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On January 26, 2023, Ventyx Biosciences, Inc. ("Ventyx") hosted an Investor R&D Day highlighting key aspects of its clinical-stage and discovery programs. During the webcast, Ventyx presented the slides attached as Exhibit 99.1 to this Current Report on Form 8-K, which are incorporated herein solely for purposes of this Item 7.01 disclosure.

Also on January 26, 2023, Ventyx issued a press release announcing the pipeline updates and strategic priorities presented at the Investor R&D Day. The press release is attached hereto as Exhibit 99.2 to this Current Report on Form 8-K and incorporated herein solely for purposes of this Item 7.01 disclosure.

In accordance with General Instruction B.2. of Form 8-K, all of the information furnished in this Item 7.01 and Item 9.01 (including Exhibit 99.1 and Exhibit 99.2) shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and shall not be incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except as shall be expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Corporate Presentation – January 26, 2023
99.2	Press Release, dated January 26, 2023
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

VENTYX BIOSCIENCES, INC.

Date: January 26, 2023

By: /s/ Raju Mohan
Raju Mohan, Ph.D.
Chief Executive Officer

Exhibit 99.1

Ventyx Biosciences 2023 R&D Day

January 26, 2023

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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 potential of Ventyx's product candidates and the anticipated continued progression of the development pipeline for such product candidates; and the anticipated timing of commencement, enrollment and completion of clinical trials for Ventyx's product candidates, including anticipated milestones for Ventyx's product candidates; and the expected timeframe for funding Ventyx's operating plan with current cash, cash equivalents and marketable securities. 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; disruption to our operations from the ongoing global outbreak of the COVID-19 pandemic, or from the ongoing military conflict in Ukraine, including clinical trial delays; 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; and other risks described in Ventyx's prior 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 quarterly period ended September 30, 2022 filed on November 4, 2022, 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.

Ventyx Biosciences 2023 R&D Day

Logistics

- The event is scheduled to end at approximately 11:30AM ET
- Lunch will be served at the conclusion of the session
- Please hold questions until the moderated Q&A session at the end of the event
  - Microphones will be circulated for those attending in person; virtual attendees can submit questions via chat box in the webcast platform
  - In the interest of time, please limit questions to one per analyst
- At the conclusion of the event, materials from today's presentations will be posted under the Investors section of our website (www.ventyxbio.com)

Ventyx Biosciences 2023 R&D Day

Speakers and Participants

Raju Mohan, PhD

CHIEF EXECUTIVE OFFICER, FOUNDER & DIRECTOR

William Sandborn, MD

PRESIDENT, CHIEF MEDICAL OFFICER

Martin Auster, MD

CHIEF FINANCIAL OFFICER

John Nuss, PhD

CHIEF SCIENTIFIC OFFICER

James Krueger, MD, PhD

ROCKEFELLER UNIVERSITY ADVISOR*

*Consultant/honoraria: AbbVie, Aclaris, Allergan, Almirall, Amgen, Artax Biopharma, Arena, Aristea, Asana, Aurigene, Biogen Idec, Boehringer Ingelheim, Bristol-Myers Squibb, Escalier, Galapagos, Janssen, Kyowa Kirin, Lilly, MoonLake Immunotherapeutics, Nimbus, Novartis, Pfizer, Sanofi, Sienna Biopharmaceuticals, Sun Pharma, Target-Derm, UCB, Valeant, Ventyx

*Grant support (to The Rockefeller University): AbbVie, Akros, Allergan, Amgen, Avillion, Biogen, Botanix, Boehringer Ingelheim, Bristol-Myers Squibb, Exicure, Innovaderm, Incyte, Janssen, Kyowa Kirin, Lilly, Nimbus Lackshmi, Novan, Novartis, PAREXEL, Pfizer, Regeneron, UCB, Vitae Pharmaceuticals.

Ventyx Biosciences 2023 R&D Day

Agenda

Time	Topic	Speaker
9:00 – 9:05AM	**Welcome**	**Martin Auster, M.D.** Chief Financial Officer
9:05 – 9:15AM	**Introductory Remarks**	**Raju Mohan, Ph.D.** Founder and CEO
9:15 – 9:50AM	**VTX958 Phase 2 Program and Strategy**	**Raju Mohan, Ph.D.** **William J. Sandborn, M.D.** President and CMO
9:50 – 10:00AM	**VTX958 ER Formulation Update**	**Raju Mohan, Ph.D.**
10:00 – 10:20AM	**VTX002 Phase 2 Update and Strategy**	**William J. Sandborn, M.D.**
10:20 – 10:40AM	**NLRP3 Portfolio**	**William J. Sandborn, M.D.** **John Nuss, Ph.D.** Chief Scientific Officer
10:40 – 10:50AM	**Discovery Update**	**John Nuss, Ph.D.**
10:50 – 11:30AM	**Q&A Session**	**All**

Introduction

Raju Mohan, Ph.D.
Founder and Chief Executive Officer

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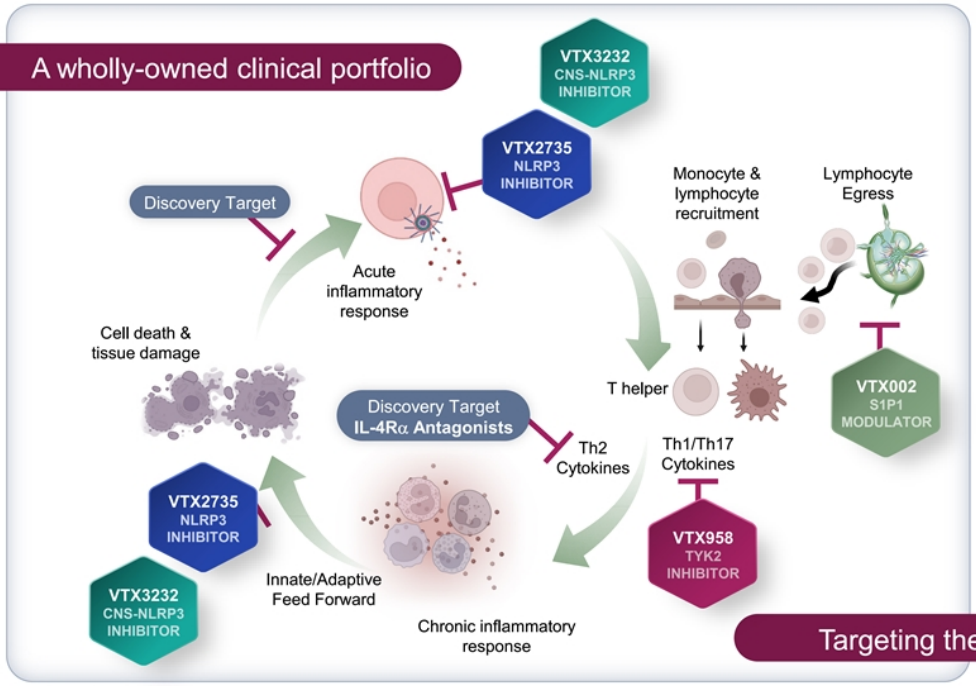
Ventyx's Chemistry-Driven, Efficient & Productive R&D Engine

A wholly-owned clinical portfolio



Validated Targets

Unmet Need

Differentiated Molecules

Improved Safety and Efficacy*

Targeting the cycle of chronic inflammation

*Represents target clinical profile for pipeline candidates.

Clear Strategy to Drive Value with Wholly-Owned Pipeline

Differentiated Clinical-Stage Assets Targeting Large Markets

Validated Targets	**TYK2**	Clinically validated in **PsO, PsA, SLE**; IL-23 pathway validated in **UC** and **CD**
	S1PR1	Only safe and effective oral mechanism in **moderate/severe UC**
	NLRP3	Strong **biologic rationale**; IL-1β validated by biologics
Differentiated Molecules	**VTX958**	**Class-leading** target coverage and safety in Phase 1; broad therapeutic window
	VTX002	Targeting potential **best-in-class** pharmacodynamic effect and efficacy in UC
	NLRP3	Potential best-in-class NLRP3 inhibitors for **peripheral and CNS** applications
Established Markets	**Large TAM**	Targeting established immunology markets totaling **>$50B** in annual WW sales and growing[1] Large indications dominated by injectable biologics with high demand for **safe and effective oral agents**

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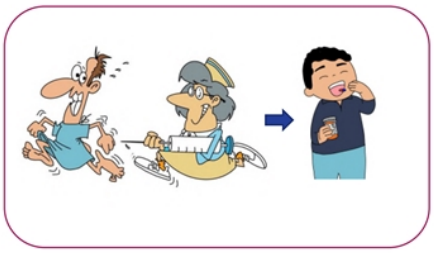
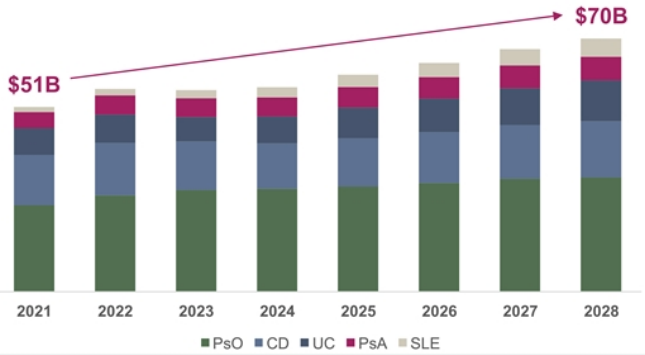
PsO: psoriasis; PsA: psoriatic arthritis; SLE: systemic lupus erythematosus; UC: ulcerative colitis; CD: Crohn's disease; TAM: total addressable market.
1. 2021 total WW indication sales in PsO, PsA, SLE, UC, and CD per EvaluatePharma estimates sourced in December 2022.

Disrupting Biologic-Dominated Immunology Markets

With Differentiated Safe and Effective Oral Agents

- Target indications remain underpenetrated
- Paucity of oral agents with attractive risk/benefit profiles
- Chronic disease populations - patients commonly cycle through therapies:
  - **Suboptimal response rates** in many autoimmune diseases (IBD, PsA, lupus)
  - **Loss of response** to biologic therapies over time (e.g. anti-drug antibodies)
  - Aversion to administration profile of available biologic therapies





- **>11 million** US patients[2]
- Dominated by injectable biologics
- **High demand** for oral agents

PsO: plaque psoriasis; PsA: psoriatic arthritis; SLE: systemic lupus erythematosus; UC: ulcerative colitis; CD: Crohn's disease.
1. 2021 total WW sales in PsO, PsA, SLE, UC, and CD per EvaluatePharma sourced in December 2022. 2. Epidemiology from CCFA, National Psoriasis Foundation, Lupus Foundation of America.

Wholly-Owned and Internally-Discovered Small Molecule Portfolio

With Multiple Near-Term Clinical Catalysts

S1P1R Modulator

Candidate	Indication	IND-Enabling	Phase 1	Phase 2	Phase 3	Anticipated Catalysts
VTX002	Ulcerative Colitis					Phase 2 data **H2 2023**

TYK2 Inhibitor

Candidate	Indication	IND-Enabling	Phase 1	Phase 2	Phase 3	Anticipated Catalysts
VTX958	Plaque Psoriasis					Phase 2 data **Q4 2023**
VTX958	Crohn's Disease					Phase 2 data **2024**
VTX958	Psoriatic Arthritis					Phase 2 data **H1 2024**

Peripheral NLRP3 Inhibitor

Candidate	Indication	IND-Enabling	Phase 1	Phase 2	Phase 3	Anticipated Catalysts
VTX2735	CAPS					Initiate Phase 2 **Q1 2023**

CNS-Penetrant NLRP3 Inhibitor

Candidate	Indication	IND-Enabling	Phase 1	Phase 2	Phase 3	Anticipated Catalysts
VTX3232	Parkinson's Disease					Initiate Phase 1 **H1 2023**

TYK2 Inhibitor VTX958

Raju Mohan, Ph.D.
Founder and CEO

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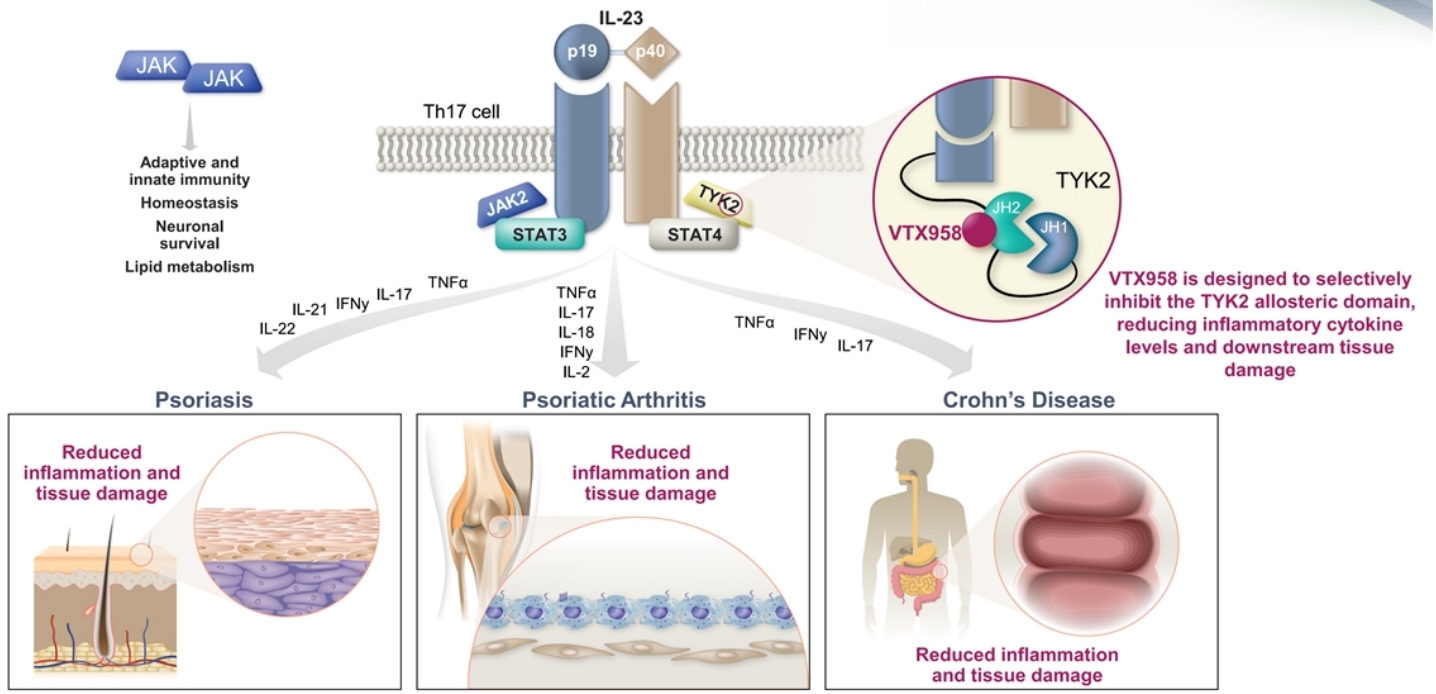
VTX958 Is a Potential Best-in-Class Allosteric TYK2 Inhibitor



1. Rendon A, Schäkel K. *Int J Mol Sci*. 2019;20(6):1475; 2. Carvalho AL, et al. *Front Mol Biosci*. 2021;8:662047; 3. Waszczykowski M et al. *Postepy Dermatol Alergol*. 2020;37(6):1001-1008; 4. Schmitt H, et al. *Front Immunol*. 2021;12:622934; 5. Ventyx Biosciences. Data on File. 2022.

Sotyktu Label Differentiates TYK2 from JAK Inhibitor Class

Clean Label Supports Broad Appeal of TYK2 Mechanism in Target Indications

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use SOTYKTU safely and effectively. See full prescribing information for SOTYKTU.

SOTYKTU™ (deucravacitinib) tablets, for oral use

Initial U.S. Approval: 2022

----------INDICATIONS AND USAGE ----------

SOTYKTU is a tyrosine kinase 2 (TYK2) inhibitor indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. (1)

Limitations of Use:

Not recommended for use in combination with other potent immunosuppressants.

---------- DOSAGE AND ADMINISTRATION ----------

- For recommended evaluation prior to SOTYKTU initiation, see Full Prescribing Information. (2.1)
- Recommended dosage is 6 mg orally once daily, with or without food. (2.2)

---------- DOSAGE FORMS AND STRENGTHS----------

Tablets: 6 mg (3)

----------CONTRAINDICATIONS----------

Known hypersensitivity to deucravacitinib or any of the excipients in SOTYKTU. (4, 5.1)

----------WARNINGS AND PRECAUTIONS ----------

- *Hypersensitivity:* Hypersensitivity reactions such as angioedema have been reported. Discontinue if a clinically significant hypersensitivity reaction occurs. (5.1)
- *Infections:* SOTYKTU may increase the risk of infection. Avoid use in patients with active or serious infection. If a serious infection develops, discontinue SOTYKTU until the infection resolves. (5.2)
- *Tuberculosis:* Evaluate for TB prior to initiating treatment with SOTYKTU. (5.3)
- *Malignancy:* Malignancies including lymphomas were observed in clinical trials with SOTYKTU (deucravacitinib) (5.4)
- *Rhabdomyolysis and elevated CPK.* (5.5)
- *Laboratory Abnormalities:* Periodically evaluate serum triglycerides. Evaluate liver enzymes at baseline and thereafter in patients with known or suspected liver disease. (5.6)
- *Immunizations:* Avoid use with live vaccines. (5.7)
- *Potential Risks Related to JAK Inhibition:* It is not known whether TYK2 inhibition may be associated with the observed or potential adverse reactions of JAK inhibition. Higher rates of all-cause mortality, including sudden cardiovascular death, major adverse cardiovascular events, overall thrombosis, deep venous thrombosis, pulmonary embolism, and malignancies (excluding non-melanoma skin cancer) were observed in patients treated with a JAK inhibitor compared to those treated with TNF blockers in rheumatoid arthritis (RA) patients. SOTYKTU is not approved for use in RA. (5.8)

----------ADVERSE REACTIONS ----------

Most common adverse reactions (≥1%) are upper respiratory infections, blood creatine phosphokinase increased, herpes simplex, mouth ulcers, folliculitis, and acne. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Bristol-Myers Squibb at 1-800-721-5072 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

----------USE IN SPECIFIC POPULATIONS ----------

SOTYKTU is not recommended in patients with severe hepatic impairment (Child-Pugh C). (2.3)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 9/2022

Source: Sotyktu prescribing information (FDA package insert).

Highly Selective for TYK2 JH2 Domain

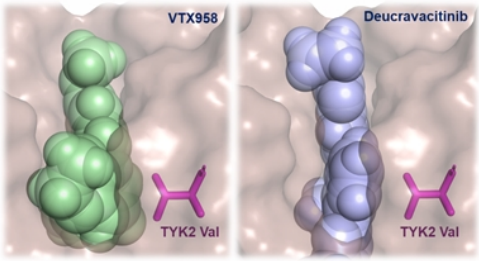
Inhibits TYK2 Pathways (IL-12, IL-23, IFNα) while Avoiding JAK1/2/3 Pathways

Structural Rationale for VTX958 Selectivity

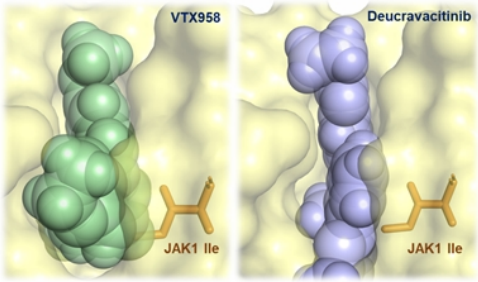
- Productive interaction for both VTX958 and Sotyktu (deucravacitinib) with valine residue in TYK2 JH2 domain
- VTX958 has a **steric clash** with the isoleucine residue (Ile) in the JAK1 JH2 domain – deucravacitinib does not
- Key determinant of the high TYK2 selectivity of VTX958

JH2 Binding (K_d)	Deucravacitinib	VTX958
TYK2	0.009 nM	0.058 nM
JAK1	0.43 nM	240 nM
Fold Selectivity for TYK2 vs. JAK1	48	**>4,000**

TYK2 JH2 domain



JAK1 JH2 domain



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Source: Ventyx internal data.

Selectively Inhibits IL-12, IL-23 and IFNα Signaling

Potently Inhibits TYK2 Pathways

Selective and potent inhibition of IL-12/23 and IFNα axis allows targeting pathways driving immune-mediated diseases

PROINFLAMMATORY INNATE & TH1/TH17 CYTOKINES

Psoriasis Patient PBMC

DRUG	IL-12 IC_{50} (nM)	IL-23 IC_{50} (nM)	IFNα IC_{50} (nM)
VTX958	**35**	**5**	**12**
deucravacitinib	10	10	5

No Measurable Inhibition of JAK1-Mediated Pathways

Lack of inhibition of IL-6, IL-10, IL-22 and other protective cytokines may avoid potential adverse events associated with less selective inhibitors

PLEIOTROPIC CYTOKINES WITH PROTECTIVE FUNCTIONS

DRUG	IL-22 IC_{50} (nM)	IL-10 IC_{50} (nM)	IFNγ IC_{50} (nM)	IL-4 IC_{50} (nM)	IL-6 IC_{50} (nM)
VTX958	**>10,000**	**>10,000**	**>10,000**	**>10,000**	**>10,000**
deucravacitinib	114	20	350	249	464

KEY TAKEAWAYS

- Potent activity against IL-23, a key cytokine implicated in several large immune/inflammatory indications
- Broad therapeutic window of VTX958 may allow for **biologic-like** target coverage in Phase 2/Phase 3
- Selectivity advantages vs. Sotyktu expected to drive **differentiated clinical profile**

Source: Ventyx internal data; assays conducted in peripheral blood mononuclear cells (PBMC)

Class-Leading Target Coverage

Phase 1 MAD Exposure and Target Coverage Across All Cohorts

MAD Dose	Target Coverage* (hours)					
	IL-12		IL-23		IFNα	
	IC_{90}	IC_{50}	IC_{90}	IC_{50}	IC_{90}	IC_{50}
50 mg BID	0	5	0	5	0	7
250 mg QD	4	9	4	9	6	10
500 mg QD	6	14	6	14	7	16
175 mg BID	**16**	**24**	**16**	**24**	**17**	**24**
350 mg BID	**24**	**24**	**24**	**24**	**24**	**24**

*Data from Phase 1 MAD Day 10 (steady state); exposures used for target coverage calculations:

- IL-12 hWB IC_{90} = 865 ng/mL; IC_{50} = 130 ng/mL; IFNα hWB IC_{90} = 584 ng/mL; IC_{50} = 73 ng/mL
- IL-12 IC_{50} and IC_{90} values used for IL-23 IC_{50} and IC_{90} calibration (hWB assay not available for IL-23)
- IL-12 and IL-23 share TYK2-specific heterodimer IL-12Rβ1

KEY TAKEAWAYS

- **IC_{90} coverage up to 24 hours** for IL-12, IL-23 and IFNα
- Sotyktu 6mg QD achieves ~9 hours IC_{50} coverage (does not reach IC_{90})
- Exposures may approach **biologic-like suppression of IL-12/23 pathways**

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Source: Ventyx internal data.

Robust Dose-Dependent Validation of Target Coverage

Phase 1 MAD *In Vivo* and *Ex Vivo* Pharmacodynamic Assays

Complete suppression of IL-12 signaling

- Dose-dependent inhibition of IFNγ at all time-points in response to IL-12/IL-18 dual stimulation
- Implies **complete suppression of IL-23 signaling**
  - IL-12 and IL-23 share TYK2-specific heterodimer IL-12Rβ1

***Ex Vivo* IFNγ response (ELISA) to IL-12/IL-18 dual stimulation**

BL= baseline
**Geometric mean*

Robust inhibition of TYK2-responsive genes CXCL10, ISG20, IFI27

- Genes are direct downstream targets of IFNα and display diverse onset, amplitude and resolution kinetics
- Potent exposure-PD activity on all three genes
- Response is dose-related through all cohorts tested

***In Vivo* IFNα challenge - Impact on TYK2-mediated genes (% Inhibiton* 175 mg BID)**

Time post-challenge	4h	6h	8h	12h	16h	24h
CXCL10	97	82	42	95	95	63
ISG20	80	69	54	79	101	39
IFI27	78	68	62	60	71	84

**% inhibition shown as placebo adjusted geometric mean*

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Source: Ventyx internal data.

VTX958 Phase 2 Clinical Program

William J. Sandborn, M.D.
President and CMO

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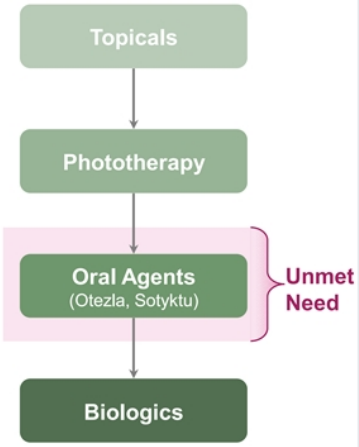
Moderate to Severe Plaque Psoriasis Landscape

High Unmet Need for Safe and More Effective Oral Agents



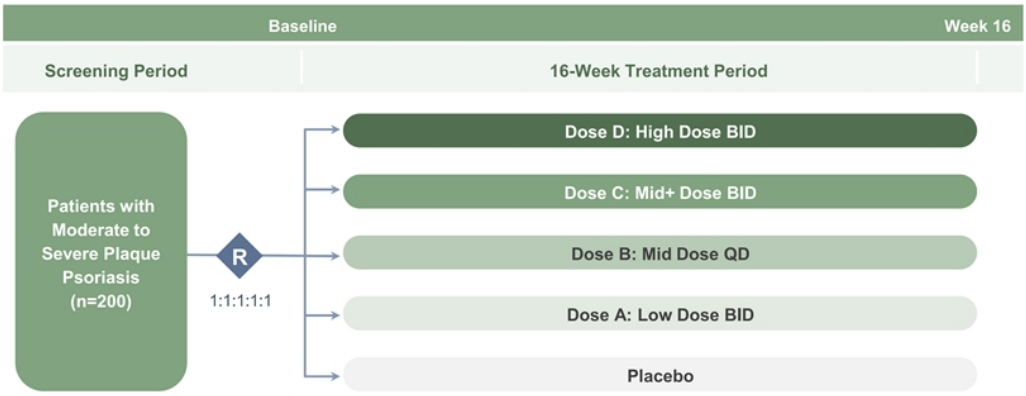
- WW psoriasis market **forecasted to surpass $31B in annual sales by 2028**; market expansion to be led by growth of IL-23 biologics and novel oral agents (i.e. Sotyktu)[1]
- Otezla has surpassed **$2B** annual sales despite modest efficacy and tolerability issues [1]
- Sotyktu's clean label supports **superior risk-benefit profile** of TYK2 class vs. other orals
- Sotyktu capturing early market share: **~25-30% of new oral prescriptions** in first few months of launch, with significant TRx contribution from Otezla and biologic-experienced patients [2]

Source: 1. Commercial data from EvaluatePharma sourced in December 2022. 2. BMY investor presentation January 2023.

Phase 2 SERENITY PsO Trial

Randomized, Placebo-controlled Trial in Patients with Moderate to Severe Plaque Psoriasis

- **Primary endpoint:** Proportion of patients achieving PASI-75 at Week 16
- **Secondary endpoints:** PASI-90/100; sPGA 0/1; change from baseline in PASI, DLQI, BSA
- First patient dosed in December; topline data expected in **Q4 2023**



Dose Selection

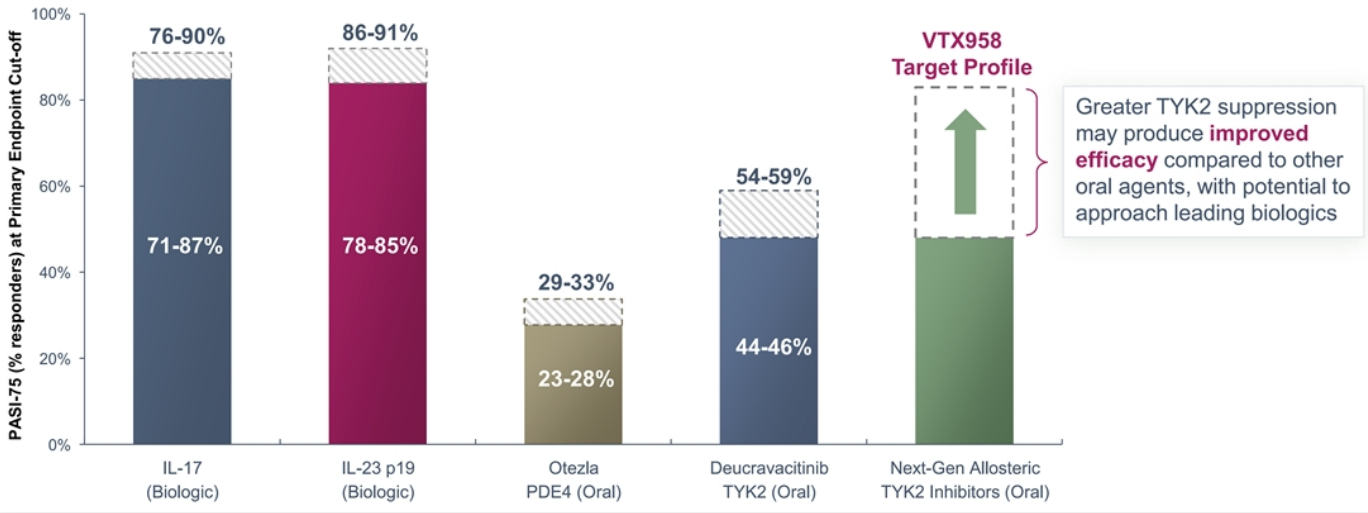
- Broad exposure range enables evaluation of **dose response and optimal Phase 3 dose selection**
- High dose expected to achieve **trough TYK2 IC_{90} coverage** (as measured by IL-12/IL-23)*

*Represents predicted TYK2 target coverage (as measured by IL-12/IL-23) based on VTX958 Phase 1 MAD data, relative bioavailability studies and internal PK modeling.
PASI: Psoriasis Area and Severity Index; sPGA: Static Physician Global Assessment; DLQI: Dermatology Life Quality Index; BSA: Body Surface Area.

Target Profile Expected to Drive Clinical Differentiation

Best-in-Disease Oral Potential in the ~$24B WW Annual Psoriasis Market

Psoriasis Competitive Landscape

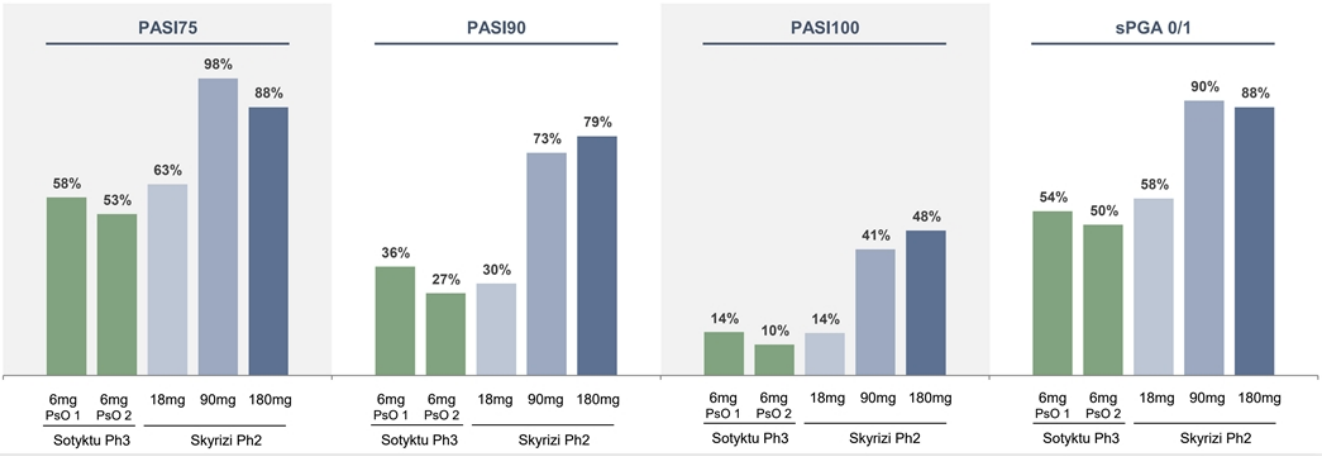


Note: Solid area represents placebo-adjusted response rate; dashed area indicates total observed response rate; primary endpoint cut-off ranges from Week 10 to Week 16.
Sources: Company reports and FDA labels for approved anti-IL-17 and anti-IL-23 biologics; market statistics sourced from EvaluatePharma.

Skyrizi Data Illustrate Dose Response of IL-23 Pathway in PsO

Comparing Partial to Full Pathway Inhibition

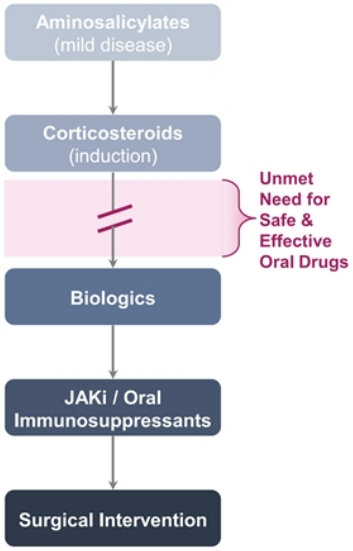
- Skyrizi (risankizumab) Phase 2 efficacy for 18mg dose at Week 12 is similar to Sotyktu approved 6mg dose at Week 16 (partial inhibition of IL-23 pathway)
- Robust dose response observed with fuller pathway inhibition at 90mg and 180mg doses (150mg approved dose); illustrates the potential for greater efficacy with a TYK2 inhibitor achieving ~trough IC_{90} coverage



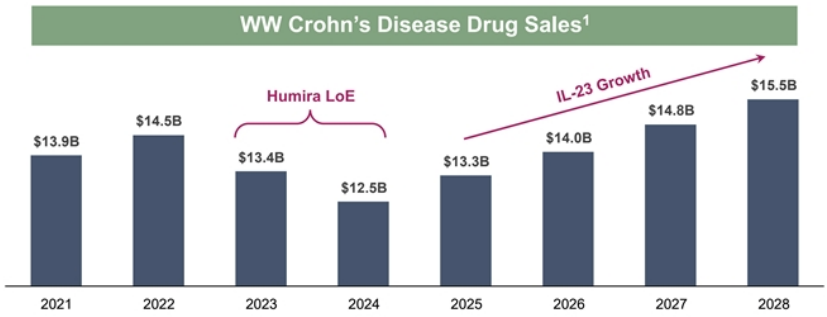
Source: Sotyktu prescribing information (FDA label); Papp et al. N Engl J Med 2017;376:1551-60. PASI: Psoriasis Area and Severity Index; sPGA: Static Physician Global Assessment.

Moderate to Severe Crohn's Disease Landscape

Significant Opportunity Due to Lack of Safe and Effective Oral Agents



- Crohn's disease is a **~$13-15B+ annual market** despite **lack of safe and effective oral agents** available to treat moderate/severe disease[1]
- IL-23 mechanism is considered most efficacious by KOLs (same pathway targeted by TYK2 inhibition)
- Highly attractive opportunity for VTX958 based on **broad therapeutic window** and **first-mover advantage**.
- Safe and effective oral agent could drive significant market expansion

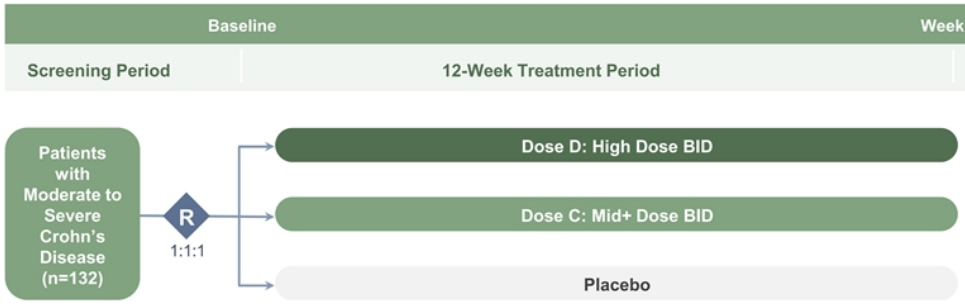


Source: 1. Commercial data from EvaluatePharma sourced in December 2022; Ventyx internal data.

Phase 2 HARMONY CD Trial

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

- **Co-Primary Endpoints:** Change from baseline in mean CDAI score and proportion of patients achieving endoscopic response per SES-CD (≥50% reduction from baseline) at Week 12
- **Secondary endpoints:** Change from baseline in mean SES-CD score; proportion of patients achieving clinical remission and clinical response per CDAI; proportion of patients achieving PRO-2 remission
- First patient dosed in January; topline data expected in **2024**



Dose Selection

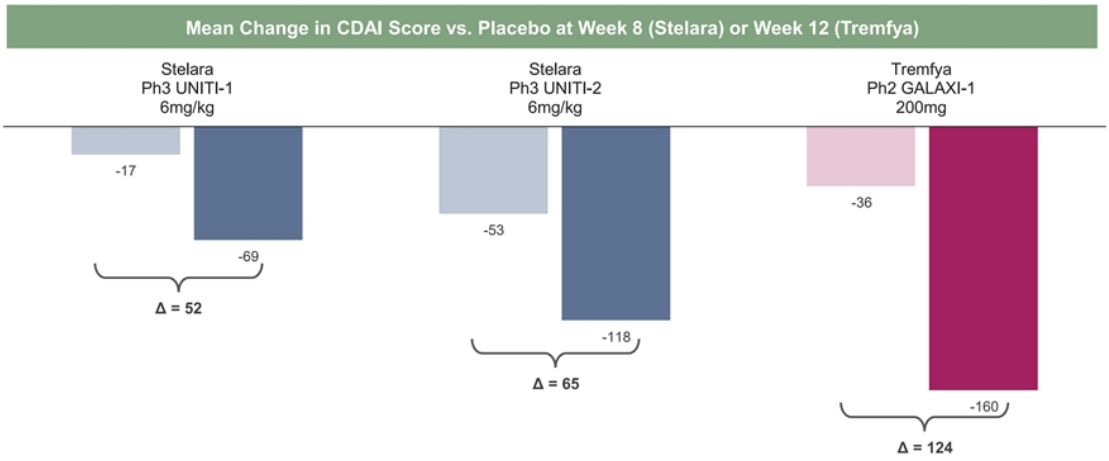
- High dose expected to achieve **trough TYK2 IC_{90} coverage** (as measured by IL-12/IL-23)*

*Represents predicted TYK2 target coverage (as measured by IL-12/IL-23) based on VTX958 Phase 1 MAD data, relative bioavailability studies and internal PK modeling.
SES-CD: Simple Endoscopic Score for Crohn's Disease; CDAI: Crohn's Disease Activity Index; PRO-2: Patient-Reported Outcome 2.

Phase 2 HARMONY CD Trial Designed to Detect Meaningful Signal

Co-Primary Endpoint: Mean Change from Baseline in CDAI Score

- Mean change from baseline in CDAI score is a sensitive endpoint to detect separation of drug arm from placebo
- Clinical remission and clinical response per CDAI included as ranked secondary endpoints

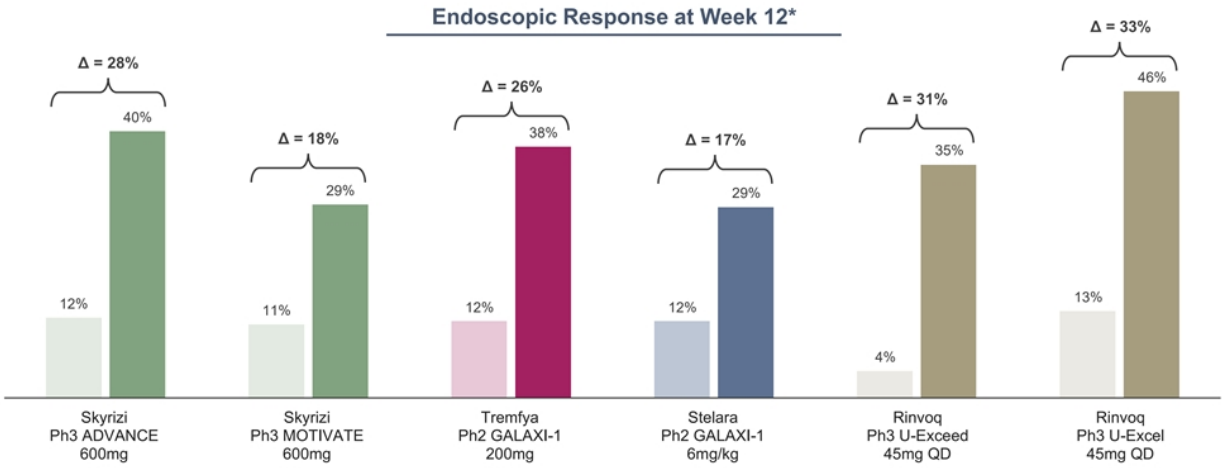


Source: Feagan *et al. N Engl J Med* 2016;375:1946-60. Sandborn *et al. Gastroenterology* 2022;162:1650–1664.

Phase 2 HARMONY CD Trial Designed to Detect Meaningful Signal

Co-Primary Endpoint: Endoscopic Response (SES-CD 50% Reduction)

- Endoscopic response per SES-CD (50% reduction from baseline) may exhibit less variable placebo response relative to other outcome measures



Note: Stelara data represent Stelara arm in Phase 2 GALAXI-1 study of Tremfya.
Source: Prescribing information (FDA labels); Rinvoq: Phase 3 CD topline results press releases (Abbvie); Tremfya/Stelara: Sandborn *et al. Gastroenterology* 2022;162:1650–1664.

Unlocking the Opportunity in IBD

Full Pathway Inhibition Required for Efficacy in Crohn's Disease

Agent	PsO Dose (Induction)	Crohn's Dose (Induction)
Skyrizi (IL-23)	**150 mg Wks 0, 4** Subcutaneous	**600 mg Wks 0, 4, 8** Intravenous
Tremfya (IL-23)	**100 mg Wks 0, 4** Subcutaneous	**200 mg Wks 0, 4, 8** Intravenous
Stelara (IL-12/23)	**45 mg/90 mg Wks 0, 4** Subcutaneous, Weight-based	**260 mg/390 mg/520 mg Wk 0** Intravenous, Weight-based

Greater TYK2 pathway inhibition may be needed for IBD efficacy

- Biologics data suggest **full pathway suppression** is required for optimal efficacy in Crohn's disease
- Deucravacitinib Phase 2 in UC failed (6 mg BID dose 0 hours IC_{90} coverage)
- Higher doses of VTX958 may approach biologic-like IL-12/23 pathway suppression
- Profile of VTX958 may unlock a major market opportunity in Crohn's, a **>$13B global market**

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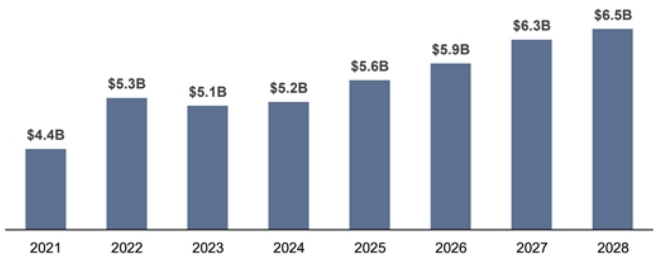
Source: FDA labels for approved drugs/indications, represents adult dosing schedules Tremfya Crohn's dose sourced from company data release (JNJ).

Psoriatic Arthritis Landscape

Unmet Need for Additional Safe and Effective Oral Agents

- Psoriatic arthritis (PsA) is a chronic, immune-mediated, inflammatory polyarthritis strongly associated with psoriasis (PsO)
- PsA can cause **significant physical disability**; clinical presentation is heterogeneous
- Many patients have uncontrolled disease despite available therapies
- Meaningful opportunity for TYK2 class based on modest efficacy of Otezla and safety risks of JAK inhibitors

WW Psoriatic Arthritis Drug Sales[1]



Epidemiology & Clinical Manifestations

~30% of PsO patients will develop PsA[2]

>800K American adults have PsA[3]

Symptom burden: joint pain & swelling; dactylitis; nail dystrophy; axial involvement; fatigue; psoriasis

Increased risk of **early mortality** and **serious comorbidities**

Treatments

Conventional DMARDs
- Methotrexate
- Sulfasalazine

Biologics
- Anti-TNFα
- Anti-IL-17
- Anti-IL-23

Novel Orals
- JAKi
- PDE4i
- TYK2 successful in Phase 2

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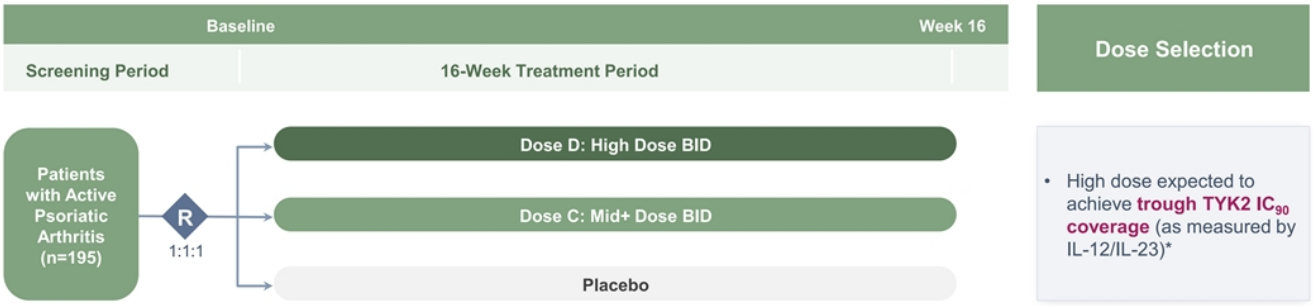
Source: 1. Commercial data from EvaluatePharma sourced in December 2022. 2. Mease PJ, *et al. J Am Acad Dermatol*. 2013;69(5):729-735. 3. Ogdie A, Weiss P. *Rheum Dis Clin North Am*. 2015;41(4):545-568. DMARD: Disease-modifying antirheumatic drug.

Phase 2 TRANQUILITY PsA Trial

Randomized, Placebo-controlled Trial in Patients with Active Psoriatic Arthritis

- **Primary endpoint:** Proportion of patients achieving ACR20 response at Week 16
- **Secondary endpoints:** ACR50/70 response; change from baseline in HAQ-DI, SF-36 PCS
- Screening initiated in January; topline data expected in **H1 2024**



Dose Selection

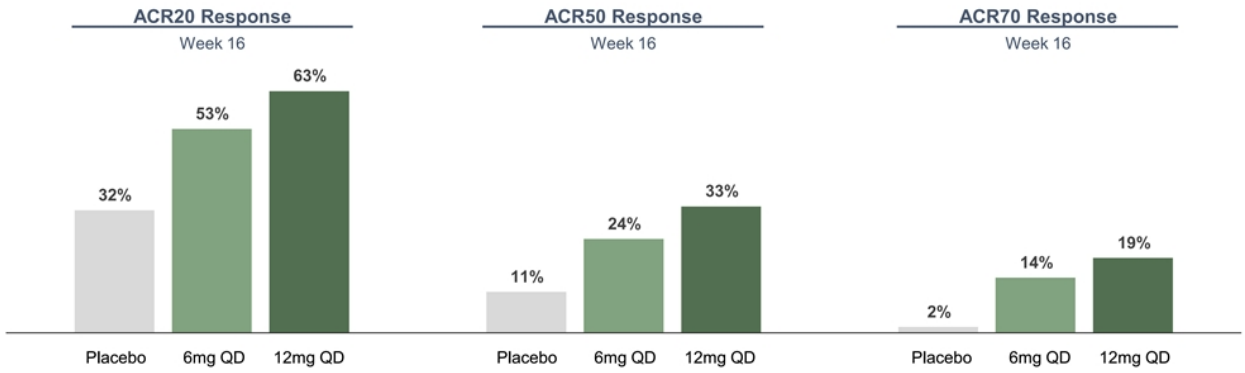
- High dose expected to achieve **trough TYK2 IC_{90} coverage** (as measured by IL-12/IL-23)*

*Represents predicted TYK2 target coverage (as measured by IL-12/IL-23) based on VTX958 Phase 1 MAD data, relative bioavailability studies and internal PK modeling.
ACR: American College of Rheumatology criteria; HAQ-DI: Health Assessment Questionnaire – Disability Index; SF-36 PCS: Short Form-36 Physical Component Summary.

Sotyktu Showed Strong Dose Response in Phase 2 PsA Trial

Sotyktu Phase 2 Data Demonstrate Dose Response on ACR20/50/70 Response

- In Phase 2, Sotyktu (deucravacitinib) achieved consistent dose response across ACR20/50/70
- Data suggest potential for VTX958 to **exceed efficacy of Sotyktu 6mg QD dose with superior target coverage**
- Achieving this profile with consistent safety may establish VTX958 as oral agent of choice in PsA

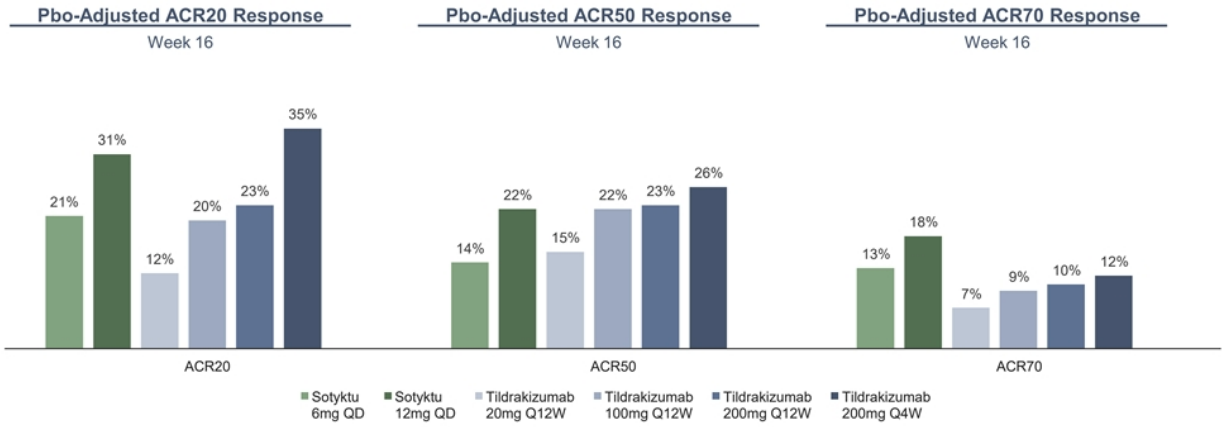


Source: Mease PJ, *et al. Ann Rheum Dis* 2022;81:815–822.

Sotyktu Showed Strong Dose Response in Phase 2 PsA Trial

Sotyktu Compared to Tildrakizumab Phase 2 Dose-Ranging Data

- Tildrakizumab (IL-23 p19) Phase 2 dose-ranging data further illustrate dose response of the IL-23 pathway in psoriatic arthritis

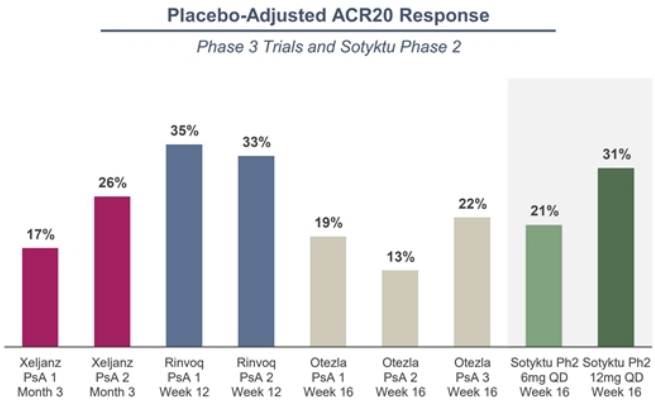


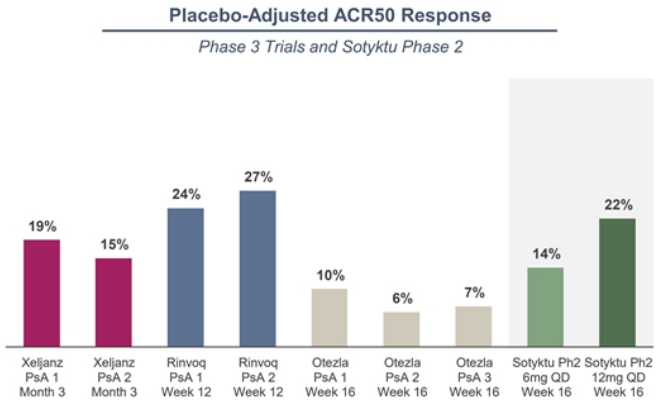
Source: Mease PJ, *et al. Ann Rheum Dis* 2022;81:815–822. Mease PJ, *et al. Ann Rheum Dis* 2021;80:1147–1157.

Sotyktu Phase 2 Efficacy (12mg) Competitive with Best Oral Agents

Psoriatic Arthritis Landscape (Oral Agents) – ACR20 and ACR50 Response

- Sotyktu 12mg QD dose achieved efficacy comparable to best available oral agents in Phase 2 (12mg QD achieves ~18 hours IC_{50} coverage; does not achieve IC_{90} coverage)
- Data suggest potential for VTX958 to achieve **best-in-disease oral efficacy** with greater pathway suppression (up to trough IC_{90} coverage)





Source: Prescribing information (FDA label) for each approved agent; Sotyktu: Mease PJ, *et al. Ann Rheum Dis* 2022;81:815–822.

VTX958 Extended Release (ER) Formulation Development

Raju Mohan, Ph.D.
Founder and CEO

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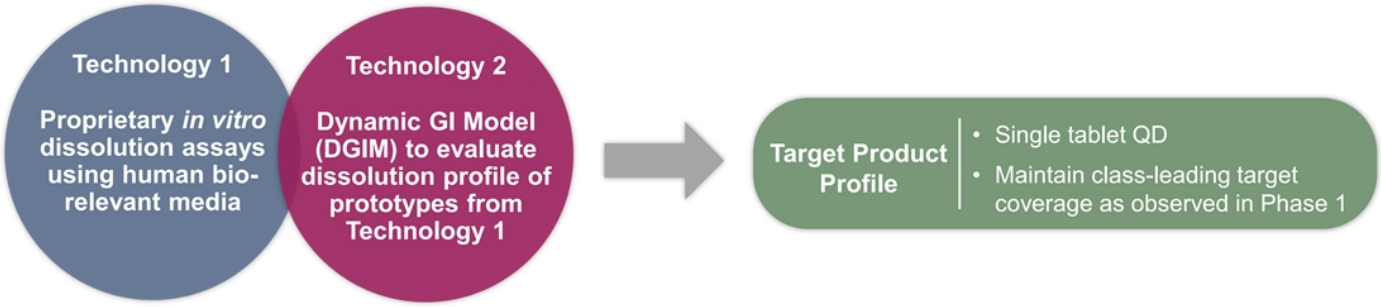
VTX958 ER Tablet Prototypes Developed for Human PK Studies

Coupling Static *In Vitro* Dissolution Assays with Dynamic Modeling for Clinical Formulation Selection



Status and Next Steps

- Prototype ER prototype tablets have been engineered to have the **desired release profile** in nonclinical testing/modeling
- First cycle of in-human testing to begin in **Q1 2023**; expect to provide formulation update **~mid 2023**
- Manufacturing for Phase 3 studies to begin in H2 2023

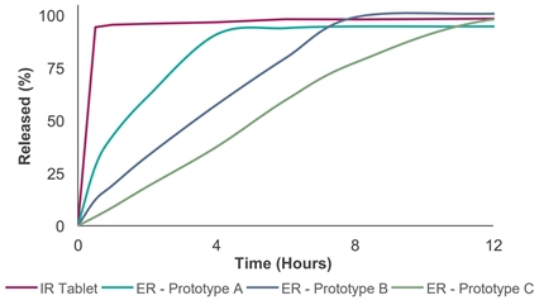
ER Prototype Formulations Exhibit Desired Release Profile

In-Human Testing to Begin in Q1 2023

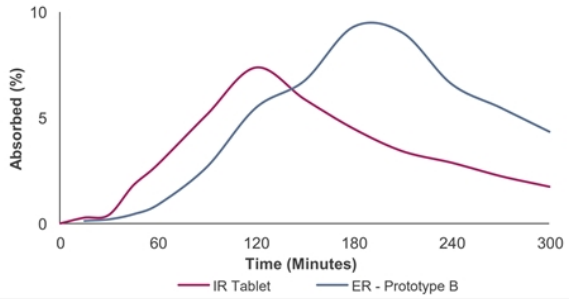
- *In vitro dissolution* assays and DGIM driven optimization affords ER tablets having ideal drug release kinetics per TPP:
  - Longer T_{max} and significant increases in bio-accessible drug release
- First formulations for in-human testing have been selected with dosing to begin in **Q1 2023**

	Bioaccessible Dose	T_{max}
IR Tablet	1.0	1.6h
ER Tablet Prototype B	**1.5x** **Greater Exposure**	**>3h** **Controlled Release**

Release Profile - IR Tablets vs. Prototype ER Tablets*



Rate of Absorption – IR Tablets vs. Prototype ER Tablets*

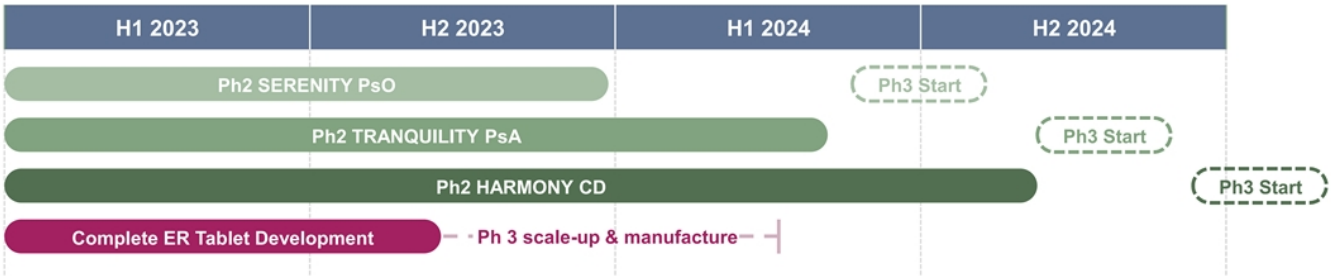


Source: Ventyx internal data. *Data represent internal ER prototype models based on *in vitro* testing.

VTX958 Program Summary

Phase 2 Program Expected to Establish Potential Best-in-Class Profile

- Phase 1 data suggest a potential **best-in-class therapeutic window** (safety and target coverage)
- Three Phase 2 trials underway in plaque psoriasis, psoriatic arthritis and Crohn's disease
- Trials designed to explore a **broad range of exposures** and target coverage, including **trough TYK2 IC_{90} coverage** at high dose
- Phase 2 readouts expected to begin in **Q4 2023** (psoriasis); PsA and CD to follow in 2024
- ER tablet development on track with human testing to begin Q1 2023; Phase 3 manufacturing beginning in H2 2023; update planned for **~mid 2023** after completion of initial in-human testing



Source: Ventyx internal data and projections.

VTX002 Development and Strategy

William J. Sandborn, M.D.
President and CMO

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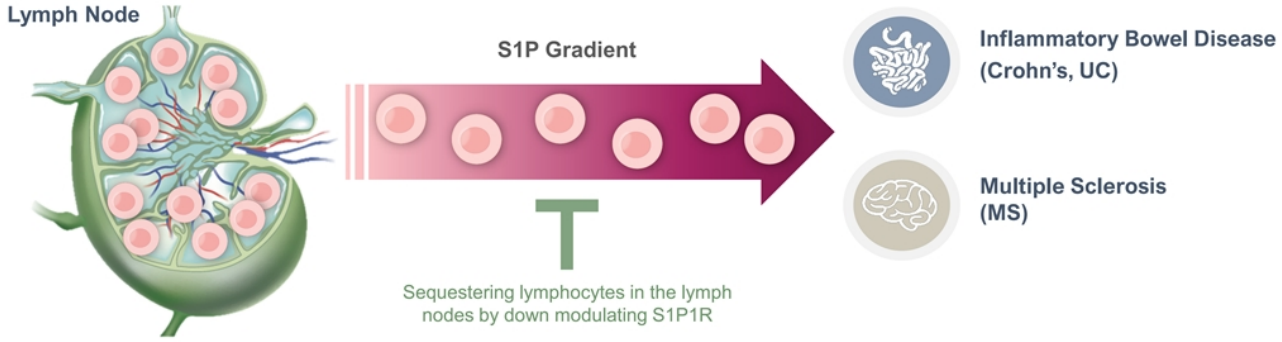
S1P1 Receptor Modulation Is a Validated Mechanism

Established Efficacy and Safety Across Agents in UC and MS

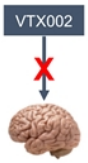
- Gilenya (fingolimod, a *non-selective* S1PR modulator) approved in 2010 – first oral disease-modifying therapy for relapsing forms of MS
- Long-term safety and efficacy of S1P receptor modulation has been established with **>870K patient years of exposure** for fingolimod alone[1]
- Receptor subtype selectivity for S1P1R and an improved understanding of fingolimod's MoA and safety profile have led to development of more selective second-generation S1PR modulators
- Zeposia (ozanimod) became the first S1PR modulator approved for UC in May 2021



Source: 1. Sullivan *et al. Neurol Neuroimmunol Neuroinflamm* Jan 2022, 9 (1) e1092.

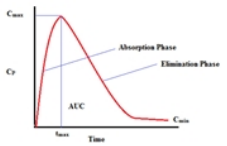
VTX002 Is Engineered for Maximal Safety, PD and Efficacy

Peripherally Restricted



Potential to Avoid Macular Edema

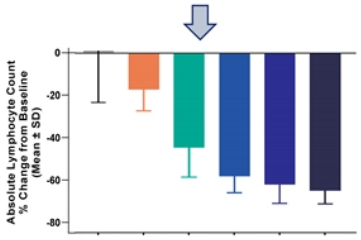
Optimal $T_{1/2}$ (~20 hours)



Rapid Steady-State and Fast Offset of Action

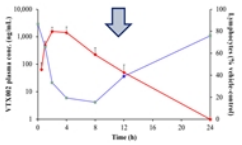
No Dose-Limiting Toxicity

No SAEs, elevated LFTs, abnormal PFTs or macular edema



Potent and Sustained Lymphocyte Reduction

No Phosphate Metabolites



Fast Onset of Action

Dose Titration

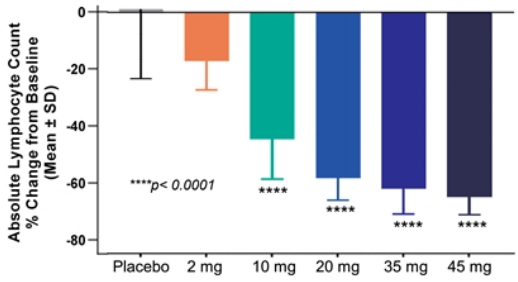
Mitigates CV Concerns

Potential for Differentiated Clinical Profile in UC Patients

Phase 1 Trials Informed Phase 2 Dose Selection

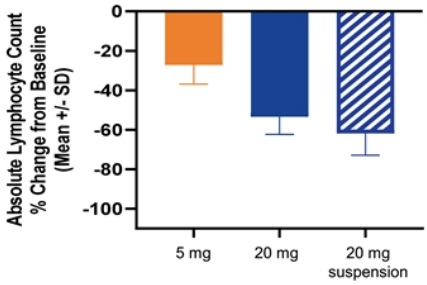
Dose-Dependent Lymphocyte Suppression Observed

Pharmacodynamics - Suspension



- Demonstrated consistent, sustained reduction of lymphocytes up to 65% across multiple dose groups
  - Steady state % lymphocyte change on final day of dosing

Pharmacodynamics – Tablet



- Tablet exhibits **86%** relative bioavailability vs. suspension
  - Acute lymphocyte Δ (max % reduction following single dose)

KEY TAKEAWAYS

- 30mg and 60mg tablets in Phase 2 are equivalent to ~26mg and ~52mg suspension, respectively
- 60mg tablet targets **best-in-class pharmacodynamic effect** (>70% ALC reduction from baseline)

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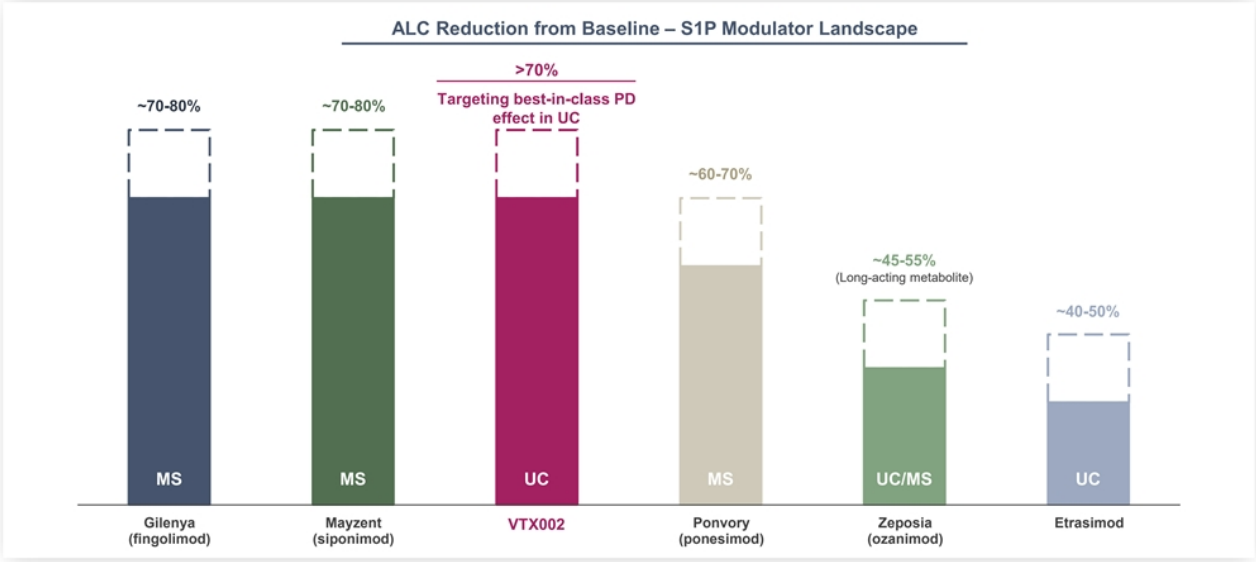
Source: Ventyx internal data. ALC: absolute lymphocyte count.

Targeting Best-in-Class PD Effect in Ulcerative Colitis

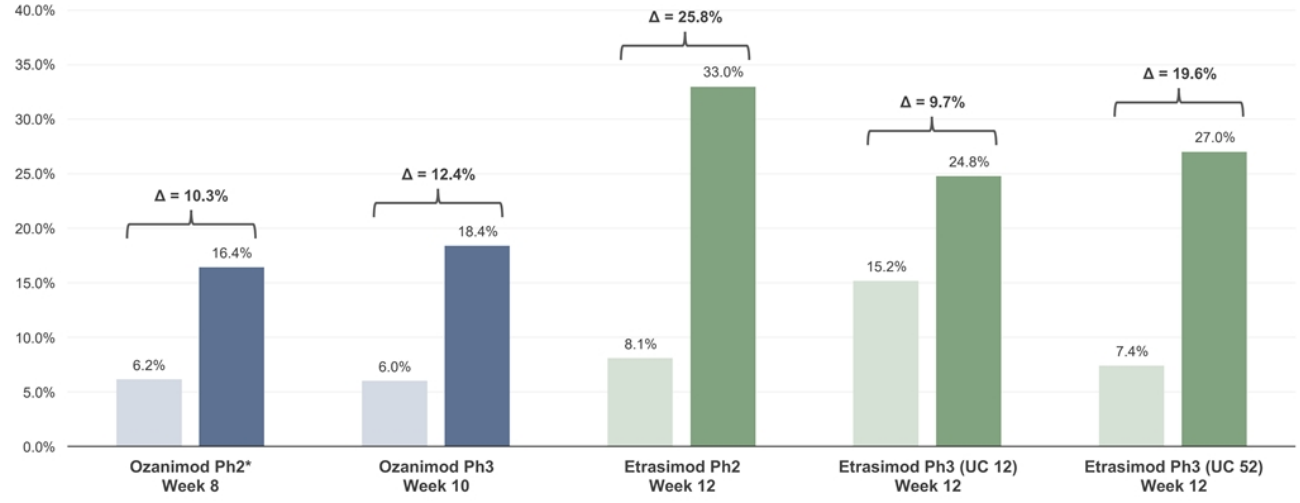
S1P Receptor Modulator Landscape in UC and MS



Source: FDA labels and review docs for approved agents; etrasimod: Phase 2 data and approximation from Phase 3 etrasimod ELEVATE 12 and ELEVATE 52 studies; Ventyx internal data. UC: ulcerative colitis; MS: Multiple Sclerosis; ALC: absolute lymphocyte count.

S1P Receptor Modulators in Ulcerative Colitis

Placebo-Adjusted Clinical Remission (Induction)



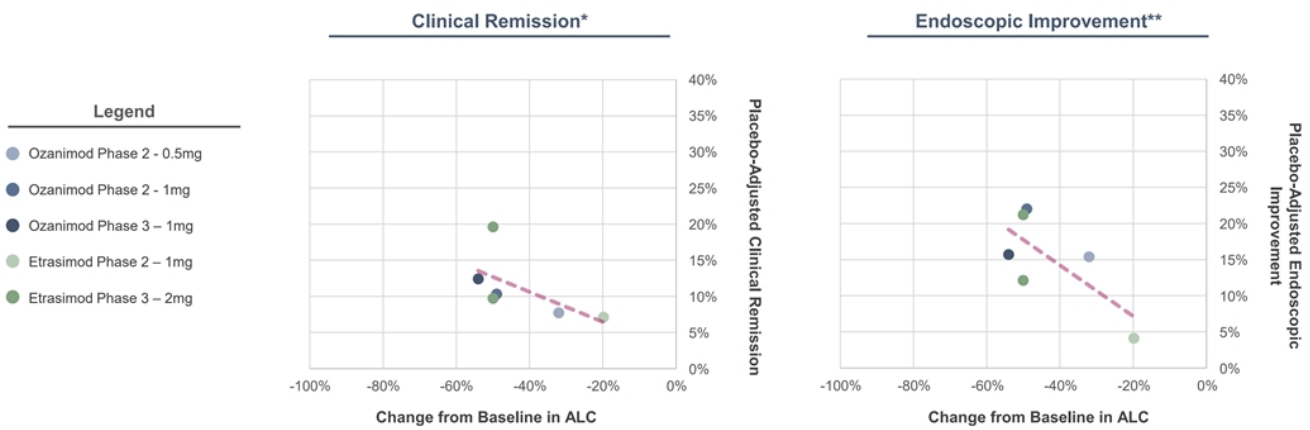
VTX002: Potential for class-leading efficacy with placebo-adjusted clinical remission in the 15-25% range

*Ozanimod Phase 2 clinical remission defined as total MCS ≤ 2 points with no individual sub score > 1 point; in all other trials, clinical remission was based on the 3-component Mayo score.

Source: Sandborn *et al. N Engl J Med* 2016;374:1754-62. Sandborn *et al. N Engl J Med* 2021;385:1280-91. Sandborn *et al. Gastroenterology* 2020;158:550–561. Pfizer etrasimod Phase 3 data presentation (DDW 2022).

S1P Modulator Efficacy Correlates with PD Effect

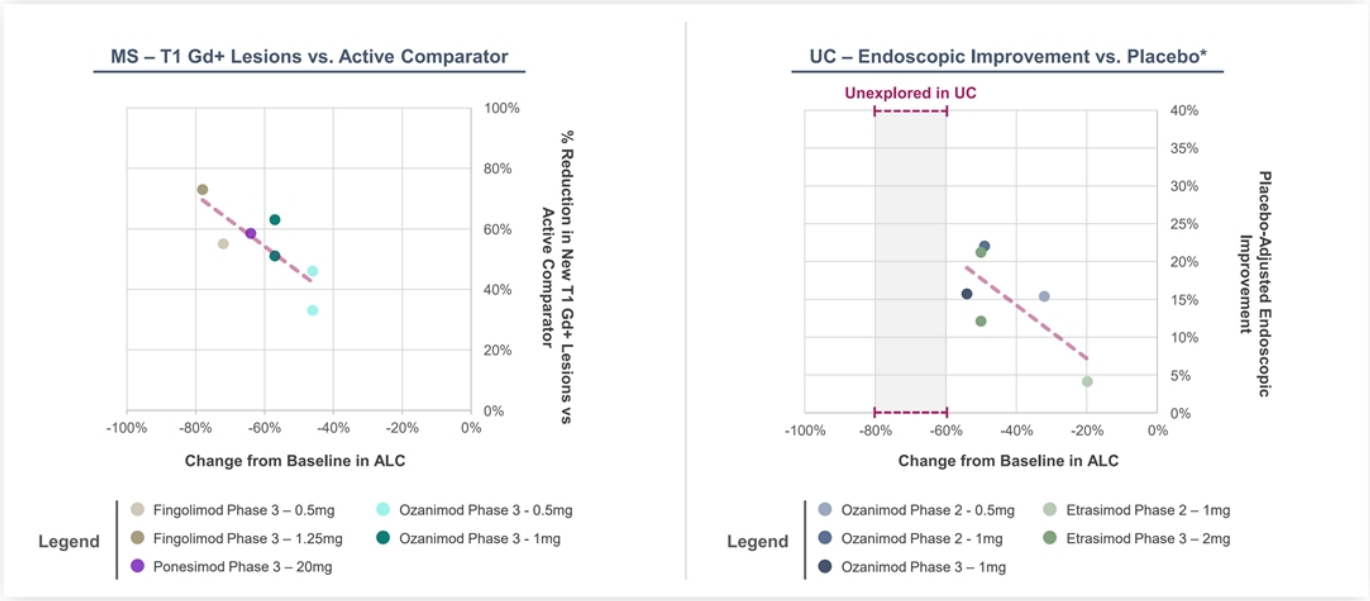
Efficacy Outcomes and Lymphocyte Suppression in UC



*Ozanimod Phase 2: clinical remission defined as total Mayo Clinic score (4-component) ≤2 with no individual sub-score >1; in all other trials, clinical remission was based on the 3-component Mayo score.
**Etrasimod Phase 2: endoscopic improvement defined as Mayo endoscopic subscore (ES) ≤1; Ozanimod Phase 2: showing mucosal healing, defined as ES ≤1; in all other trials, endoscopic improvement defined as ES ≤1 with the absence of friability.
Source: Sandborn *et al. N Engl J Med* 2016;374:1754-62. Sandborn *et al. N Engl J Med* 2021;385:1280-91. Sandborn *et al. Gastroenterology* 2020;158:550–561. Etrasimod Phase 3 data presentation (DDW 2022).

S1P Modulator Efficacy Correlates with PD Effect

Established Correlation in UC and MS

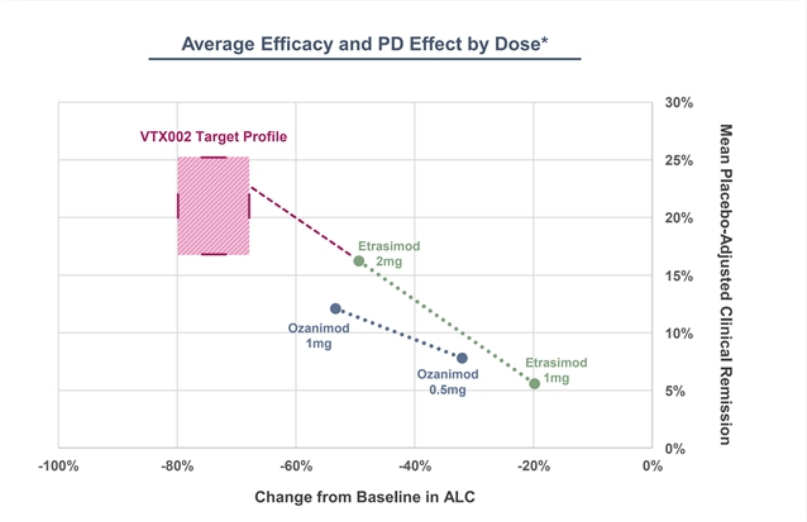


*Etrasimod Phase 2: endoscopic improvement defined as Mayo endoscopic sub-score (ES) ≤1; Ozanimod Phase 2: showing mucosal healing, defined as ES ≤1; in all other trials, endoscopic improvement defined as ES ≤1 with the absence of friability.

Sources (UC): Sandborn *et al. N Engl J Med* 2016;374:1754-62. Sandborn *et al. N Engl J Med* 2021;385:1280-91. Sandborn *et al. Gastroenterology* 2020;158:550–561. Etrasimod Phase 3 data presentation (DDW 2022).
Sources (MS): Cohen *et al. N Engl J Med* 2010;362:402-15. Cohen *et al. Lancet Neurol* 2019;18: 1021–33. Comi *et al. Lancet Neurol* 2019;18: 1009–20 Kappos *et al. JAMA Neurol.* 2021;78(5):558–567.

Targeting Best-in-Class Efficacy in UC

Strong Rationale for Differentiation with Superior PD Effect



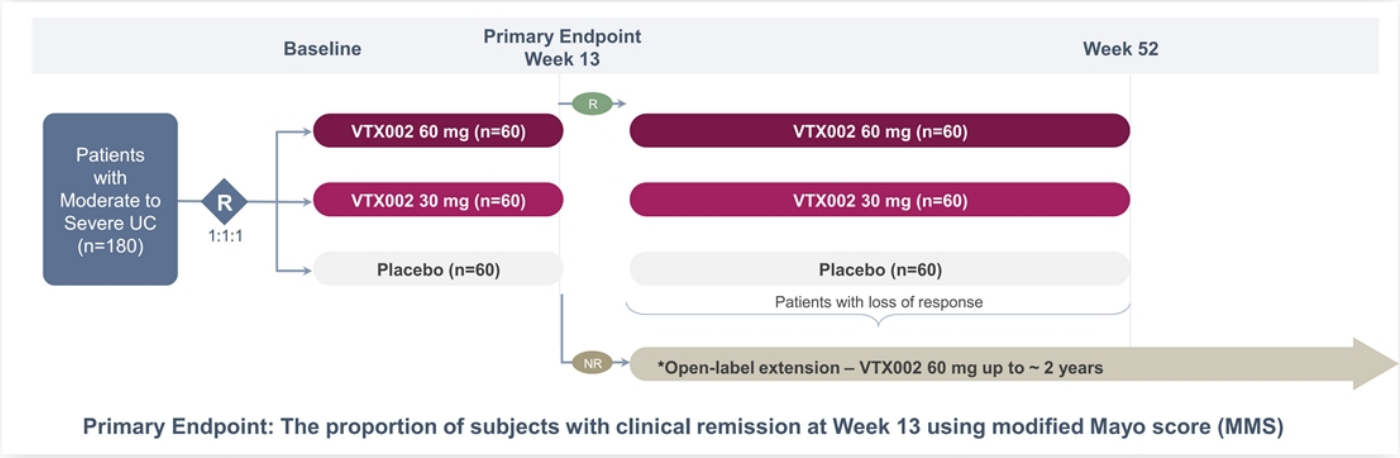
Key Takeaways

- Targeting best-in-class efficacy with placebo-adjusted clinical remission in the 15-25% range
- PD / efficacy correlation supports hypothesis that **superior lymphocyte suppression** may result in **improved efficacy**
- Preliminary lymphocyte data from the ongoing Phase 2 OLE suggest potential achievement of target PD profile

*Data represent weighted average calculations of placebo-adjusted clinical remission and reduction from baseline in absolute lymphocyte count by dose across Phase 2 and Phase 3 trials. Chart is illustrative of VTX002 target profile with caveats of cross-trial comparison and data aggregation.

Phase 2 Ulcerative Colitis Trial

Trial Design Recap and Target PD Effect



Primary Endpoint: The proportion of subjects with clinical remission at Week 13 using modified Mayo score (MMS)

Dose Selection: Target PD Effects

- **VTX002 30 mg:** lymphocyte suppression similar (or superior) to predecessor S1P receptor modulators in UC (**~45-60%** from baseline)
- **VTX002 60 mg:** lymphocyte suppression similar to first-generation S1P receptor modulators in MS (**>70%** from baseline)

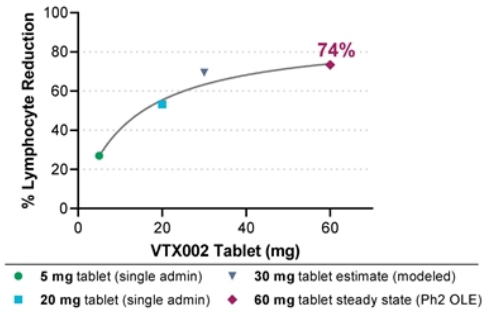
Preliminary OLE Data Suggest Superior Lymphocyte Suppression

Superior ALC Reduction May Drive Improved Efficacy in UC

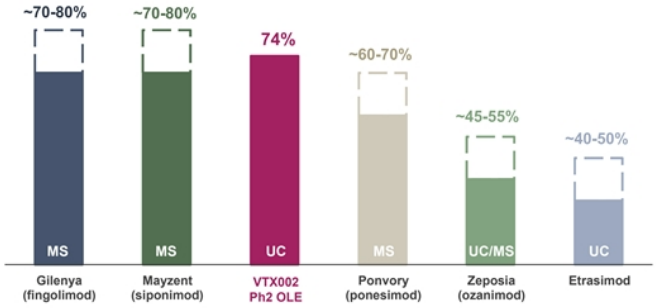
Preliminary PD Data Phase 2 OLE

- Absolute lymphocyte count (ALC) taken at **week 26** (after 13-week randomized period + 13 weeks open-label treatment with **60mg** dose)
- As of January 15th, average **ALC reduction from baseline of ~74%** observed at Week 26
- Preliminary data suggest pharmacodynamic differentiation of VTX002 vs. etrasimod and ozanimod in UC

ALC Reduction from Baseline by Dose*



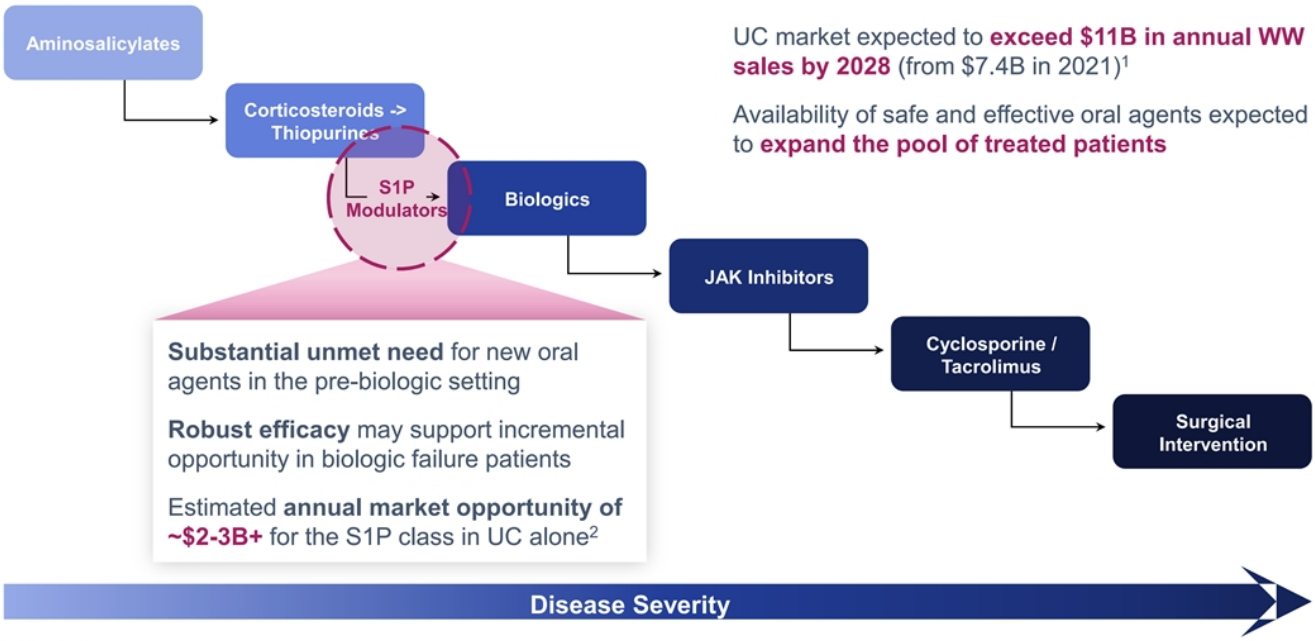
Potential Differentiation from Existing S1P Modulators in UC



Source: Ventyx internal data. *5mg and 20mg data observed from Phase 1 RelBA trial; 30mg modeled based on RelBA data; 60 mg tablets data from ongoing extension of Phase 2 trial (steady state); 3-parameter regression curve fits data.

Substantial Market Opportunity for a Potential Best-in-Class S1P Modulator

Treatment Paradigm and Unmet Need in Ulcerative Colitis



UC market expected to **exceed $11B in annual WW sales by 2028** (from $7.4B in 2021)[1]

Availability of safe and effective oral agents expected to **expand the pool of treated patients**

Substantial unmet need for new oral agents in the pre-biologic setting

Robust efficacy may support incremental opportunity in biologic failure patients

Estimated **annual market opportunity of ~$2-3B+** for the S1P class in UC alone[2]

Source: [1]Market data from EvaluatePharma sourced in December 2022; [2]Ventyx internal estimates based on market research.

VTX002 Program Summary

Phase 2 Ulcerative Colitis Topline Data Expected in H2 2023

- Phase 2 trial may serve as the first of two pivotal trials required for registration in UC
- Enrollment progressing well – expected to complete in **~mid-2023**
  - Supports topline (induction) data readout **H2 2023**
- Phase 2 doses selected to establish differentiation and identify optimal Phase 3 dose:
  - **30mg:** Targeting lymphocyte reduction similar to (or better than) etrasimod and ozanimod (**~45-60%**)
  - **60mg:** Targeting best-in-class lymphocyte reduction in UC (**>70%**)
- Preliminary open-label extension (OLE) data suggest **achievement of target PD effect** at 60mg dose:
  - As of January 15th, **average ALC reduction from baseline of ~74%** observed at Week 26 (patients completing 13 weeks open-label treatment with VTX002 60mg)

Source: Ventyx internal data and projections.

NLRP3 Inhibitor Portfolio

William J. Sandborn, M.D.
President and CMO

John Nuss, Ph.D.
Chief Scientific Officer

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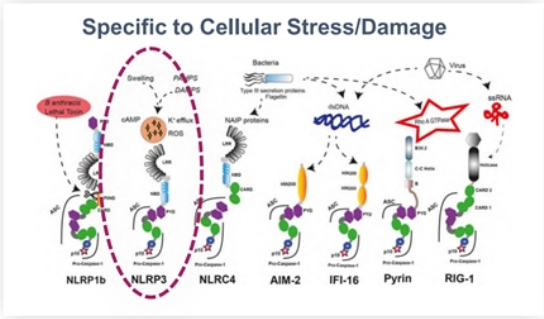
Advantages of NLRP3 Inhibition vs. IL-1β Antibody Approach

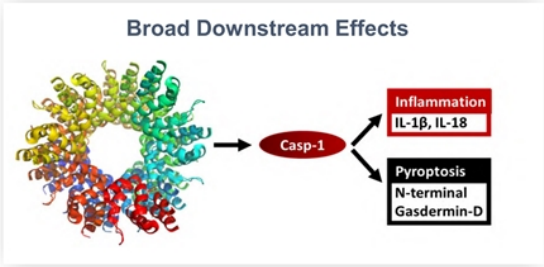
Specific to cellular stress and damage:

- All inflammasome family members release IL-1β for host protection, with different specializations
- NLRP3 specializes in detecting cell stress and danger signals

Inhibition of multiple key inflammatory mediators:

- Inhibition of **IL-1β**
- Inhibition of **IL-18**
  - IL-18 enhances NK cell functions, drives Th1 skewing and stimulates TNF/IL-6/CRP production
  - Strong association between IL-18 and atherosclerosis
- Inhibition of **pyroptosis**
  - Pyroptosis is essential for rapid release of a myriad of other mediators (alarmins and DAMPs)
  - Pyroptosis can have greater impact on tissue damage than IL-1β release in certain cases (myocardial infarction)





Source: Ventyx EMBO2021 Poster; Bahrami et al., 2021 *Curr Med Chem.* Man et al., 2017 *Immunol. Rev.* DAMP: Damage-associated molecular pattern; PAMP: Pathogen-associated molecular pattern..

Targeting a Broad Range of Major Inflammatory Diseases

NLRP3

Systemic Diseases

Peripheral NLRP3 inhibitors are designed to treat cardiovascular, dermatologic, rheumatic and rare genetic diseases

- Cardiovascular
- Dermatologic
- Rheumatic
- Rare Genetic Diseases

Our solution: VTX2735

Neuroinflammatory Diseases

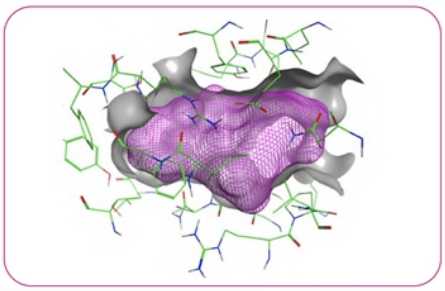
CNS-directed NLRP3 inhibitors are designed to treat a range of neuro-degenerative disorders, such as Alzheimer's and Parkinson's disease

- Alzheimer's Disease
- Parkinson's Disease
- ALS
- Multiple Sclerosis

Our solution: VTX3232

Potent and Selective Peripheral NLRP3 Inhibitor VTX2735

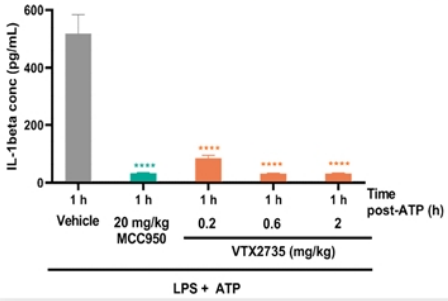
- Highly potent, novel & selective inhibitor of IL-1β
- Potent inhibitor in PBMC derived from CAPS patients
- Demonstrated PD and *in vivo* efficacy in rodent models
- **High exposures and target coverage achieved in Phase 1**
- **Excellent clinical safety profile in Phase 1**
- Phase 2 proof-of-mechanism study in CAPS initiating in **Q1 2023**



In Vitro Potency & Selectivity

		IL-1β IC_{50} (nM)
On Target	human monocytes	2
	human whole blood	**80**
Off Target	AIM2	>10000
	NLRC4	>10000
	NF-kb	>10000

Mouse Pharmacodynamic Assay



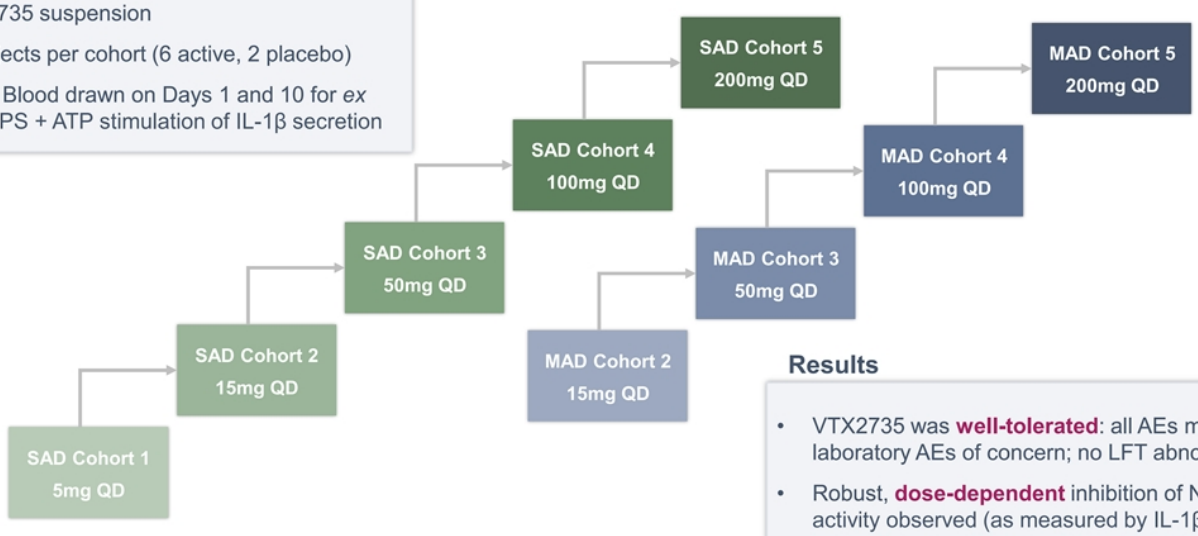
Source: Ventyx internal data. CAPS: Cryopyrin-Associated Periodic Syndromes.

VTX2735 was Safe and Well-Tolerated in Phase 1

Phase 1 SAD/MAD Trial in Healthy Volunteers

Design

- VTX2735 suspension
- 8 subjects per cohort (6 active, 2 placebo)
- MAD: Blood drawn on Days 1 and 10 for *ex vivo* LPS + ATP stimulation of IL-1β secretion



Results

- VTX2735 was **well-tolerated**: all AEs mild, no laboratory AEs of concern; no LFT abnormalities
- Robust, **dose-dependent** inhibition of NLRP3 activity observed (as measured by IL-1β)

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Source: Ventyx internal data.

Excellent Target Coverage

Target Coverage in MAD Phase and Calibration to Modeled Tablet Human Exposure

- VTX2735 exhibited dose-proportionate increases in C_{max} and AUC; PK consistent with repeat dosing
- Robust coverage of IL-1β IC_{50} and IC_{90} achieved (Day 10 steady state exposures)
- Tablet developed for Phase 2 studies; excellent relative bioavailability vs. suspension
- 100mg BID tablet dose predicted to **cover IL-1β IC_{90} for ~20 hours**

		MAD Dose (Suspension)				Tablet	
Target Coverage (hours) IL-1β		15mg QD	50mg QD	100mg QD	200 mg QD	100mg BID	150mg BID
	IC_{50}	6	10	12	**15**	**24**	**24**
	IC_{90}	3	5	6	**9**	**20**	**22**

*Data from Phase 1 MAD Day 10 (steady state); exposures used for target coverage calculations:
Human whole blood IL-1β assay: IC_{50} = 76.4 nM or 34 ng/mL; IC_{90} = ~400 nM or 175 ng/mL

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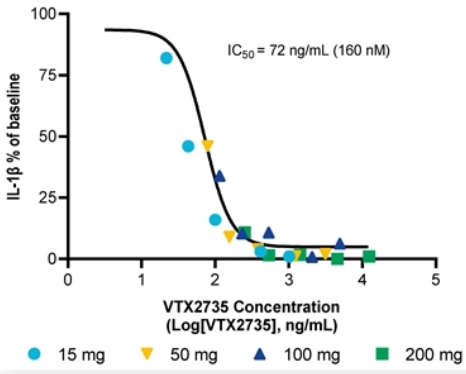
Source: Ventyx internal data.

Robust Dose-Dependent Pharmacodynamic Activity

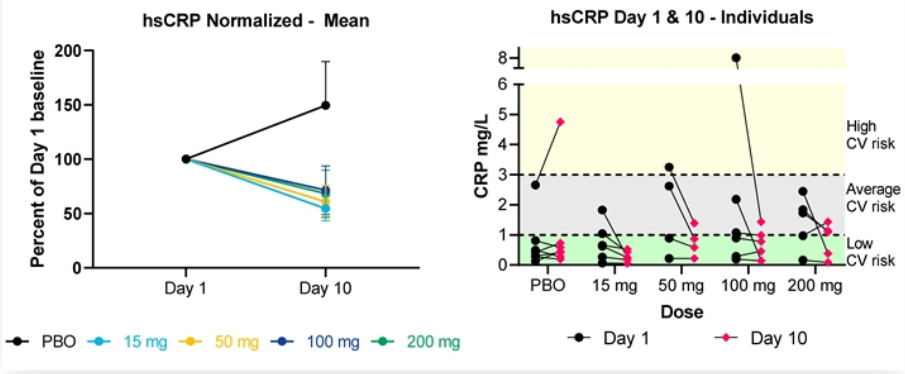
Ex Vivo IL-1β Stimulation Assay and *In Vivo* hsCRP Biomarker Assessment

- VTX2735 demonstrated robust dose- and concentration-dependent inhibition of IL-1β *ex vivo*
- Statistically significant inhibition of normalized hsCRP at all 4 doses (cardiovascular risk factor)

Concentration-Dependent Suppression of IL-1β *Ex Vivo*[1]



Strong Inhibition of High Sensitivity CRP (hsCRP)[2]



Source: Ventyx internal data. 1. *Data from Day 10 of Phase 1 MAD, 1 to 8h post-dose *ex vivo* LPS plus ATP-mediated IL-1β release assay. 2. hsCRP measured on Day 1 (pre-dose) and Day 10 (pre-dose) in normal healthy volunteers.

Broad Activity Against Multiple NLRP3 Mutations

Potential for Differentiation in CAPS Setting

What is CAPS?

An ultra-orphan auto-inflammatory disease caused by various mutations in NLRP3 and characterized by inappropriate release of IL-1β and symptoms of recurrent systemic inflammation

KEY TAKEAWAY

VTX2735 blood assay data from CAPS patients suggest inhibitory activity across several mutations: FCAS, MWS and NOMID subset of CAPS patients

IC_{50} in Blood Monocyte Assay (nM)

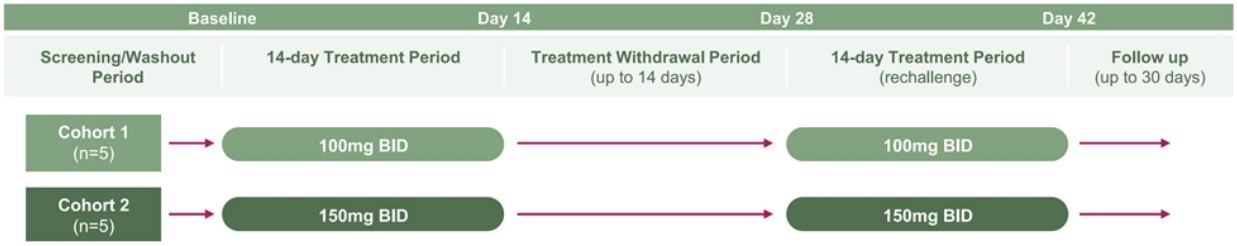
		75% of all CAPS patients In North America					Most Severe
CPD	Challenge	FCAS1 L353P	FCAS2 (L353P)	FCAS3 (L353P)	FCAS4 A439V/G564R	FCAS.MWS E525K/V198M	NOMID F309Y
VTX2735	LPS	117	56	166	14	24	17
MCC950	LPS	>10K	>10K	>10K	1,264	>10K	>10K

Source: UCSD (Dr. Hal Hoffman's lab) and Ventyx internal data. CAPS: Cryopyrin-Associated Periodic Syndromes; FCAS: Familial Cold Autoinflammatory Syndrome NOMID: Neonatal Onset Multisystem Inflammatory Disease; MWS: Muckle-Wells Syndrome.

Phase 2 CAPS Trial Designed to Efficiently Establish Proof-of-Mechanism

Anticipated Phase 2 CAPS PoM Trial Design

- Phase 2 proof-of-mechanism trial will enroll up to 10 familial cold autoinflammatory syndrome (**FCAS**) patients
- **Anticipated Endpoints:** Change from baseline in Key Symptom Score (KSS); achievement of KSS 30/50/75% response (change from baseline); change in symptom severity and CGI-S from baseline; time to resolution of flare
- Trial expected to initiate in **Q1 2023**



Source: Ventyx internal data. CGI-S: clinical global impression-severity. CAPS: Cryopyrin-Associated Periodic Syndromes.

VTX2735 Program Summary

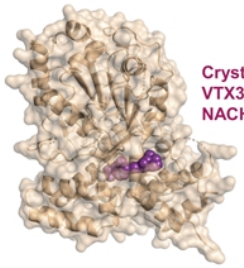
Opportunities in a Broad Range of Indications

- **Potential best-in-class NLRP3 inhibitor**
  - Highly potent and selective in IL1β release human whole blood assays
- **Excellent safety and target coverage in Phase 1**
  - Data suggest a wide therapeutic window; safely achieved robust IL-1β IC_{50}/IC_{90} coverage
  - All AEs mild – **no drug-related LFT abnormalities**
- **Ability to maximize exposures in Phase 2**
  - Safety profile supports broad range of exposures in Phase 2
  - CAPS study expected to efficiently establish PoM in patients
  - **NLRP3 mechanistic rationale in multiple large cardiovascular, rheumatic and dermatologic indications**

Potency & Selectivity	Differentiated from competitor/ reference compounds ✓
Target Coverage	Strong coverage of IL-1β IC_{50}, IC_{90} in Phase 1 Robust suppression of IL-1β *ex vivo* ✓
Safety	Excellent Phase 1 safety Good preclinical safety margins ✓
Markets/ Indications	Large populations in cardio, rheumatic and dermatologic diseases ✓

Novel CNS-Penetrant NLRP3 Inhibitor VTX3232

- Potential **highly potent brain-penetrant** inhibitor of NLRP3
- **Structurally unique** to other compounds in this space
- Excellent CNS exposures in rodent, dog, and monkey
- IND filing and Phase 1 trial initiation expected in **H1 2023**
- **Well positioned to target NLRP3-mediated neuroinflammatory diseases, including Parkinson's disease**

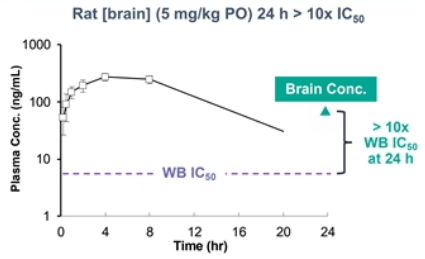


Crystal structure of VTX3232 with NLRP3 NACHT domain

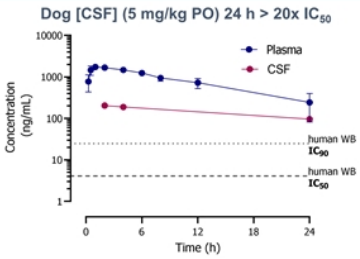
In Vitro Potency & Selectivity

		VTX3232
On Target	hWB IL-1β IC_{50} (nM)	13
Off Target	AIM2	>10000
	NLRC4	>10000
	NF-kb	>10000

Rat PK (PO, 5mg/kg)



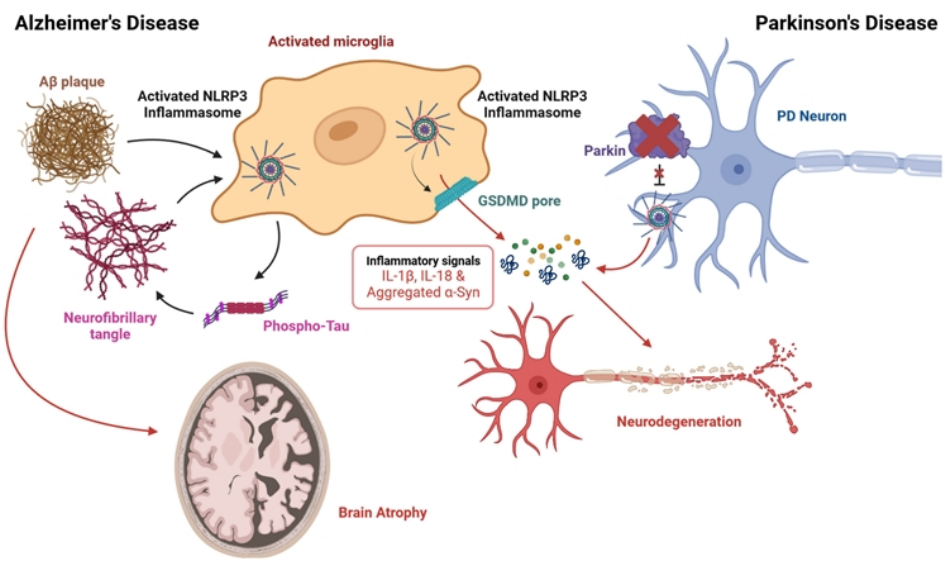
Dog PK (PO, 5 mg/kg)



Source: Ventyx internal data. hWB: Human whole blood.

NLRP3 Is Implicated in Multiple Neuroinflammatory Diseases

Robust Opportunity for a CNS-Penetrant NLRP3 Inhibitor



NLRP3 in Neuroinflammatory Diseases

- NLRP3 activation has been **directly implicated** in major neurodegenerative diseases
- Growing body of preclinical evidence for NLRP3 inhibition as a **potential disease-modifying approach**
- NLRP3 knockout prevents both amyloid and tau plaques
- NLRP3 inhibition prevents α-synuclein pathology and dopaminergic neuro-degeneration in murine Parkinson's models

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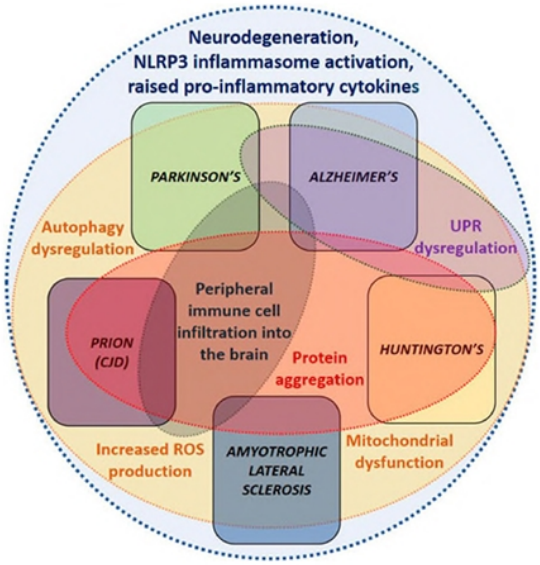
Source: Liang T *et al.* 2022 *Front. Pharmacol.* 13:845185. Ising, C *et al. Nature* 575, 669–673 (2019). Panicker *et al. Neuron.* 2022;110(15):2422-2437.e9.

NLRP3 Is Implicated in Multiple Neuroinflammatory Diseases

Robust Opportunity for a CNS-Penetrant NLRP3 Inhibitor



NLRP3 in Neuroinflammatory Diseases

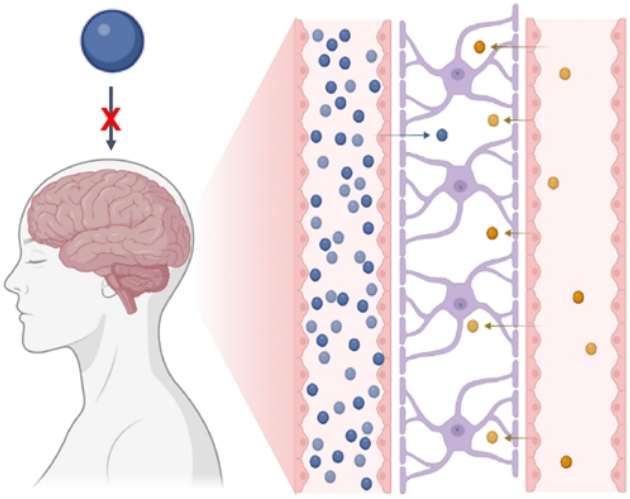
Inflammasomes can be activated in the CNS in response to acute injury, autoimmune-mediated injury, and/or accumulation of misfolded or aggregated proteins in the brain

- Several large neuroinflammatory conditions with high unmet medical need share **overlapping disease mechanisms:**
  - Parkinson's disease
  - Alzheimer's disease
  - Huntington's disease
  - ALS

Source: Holbrook *et al.* (2021) *Front. Pharmacol.* 12:643254.

VTX3232 Exhibits Optimal CNS Drug Characteristics

Rationally Designed for CNS Bioavailability



VTX3232

Species	Kp,uu (CSF/plasma)
Rat	**0.27**
Mouse	**0.58**
Dog	**1.28**
Monkey	**0.37**

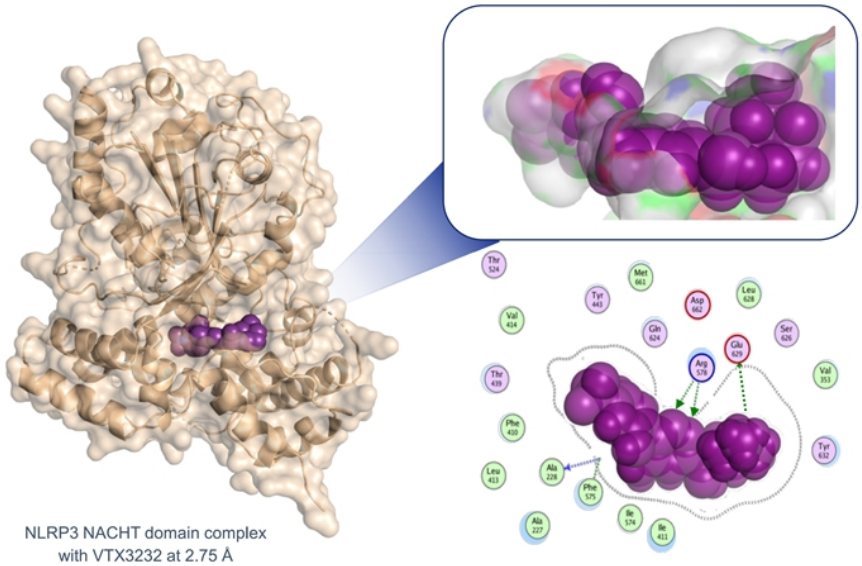
Preclinical Profile

- VTX3232 is a novel next-generation NLRP3 inhibitor combining **excellent potency with high BBB permeability**
- Preclinical evaluation in 4 species demonstrated **near-equal partitioning** between CSF, brain and plasma
- Therapeutically-relevant concentrations in microglia are reached with low peripheral exposure

Source: Loryan, I. *et al. Pharm Res* 39, 1321–1341 (2022).

X-Ray Crystal Structure Illuminates Key NLRP3 Interactions

VTX3232 Mechanism of Action



NLRP3 NACHT domain complex with VTX3232 at 2.75 Å

Mechanism of Action

- VTX3232 inhibits NLRP3 by functioning as a 'molecular glue'
- Binding site is the pocket formed by all four NACHT subdomains, close to ADP
- VTX3232 **stabilizes an inactive form** of NLRP3, preventing ADP/ATP exchange and the conformational change required for activation and subsequent NLRP3 assembly

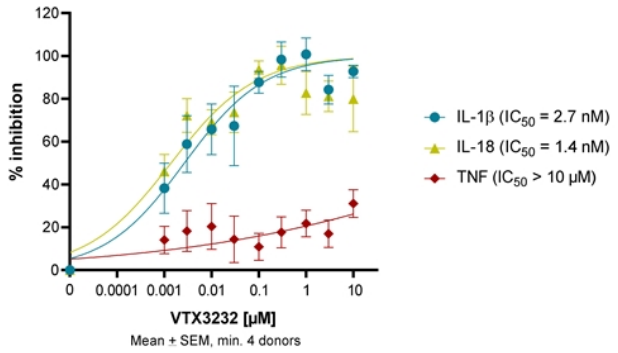
Source: Dekker *et al. J Mol Biol.* 2021 Dec 3;433(24):167309.

Inhibiting Neuroinflammation in Preclinical Models

Efficacy Demonstrated In *In Vitro* and *In Vivo* Neuroinflammation Models

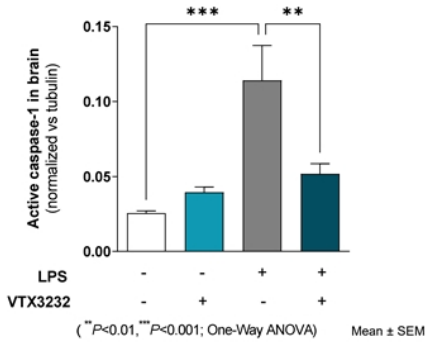
- Specific inhibition of IL-1β and IL-18 release in **human monocyte-derived microglia** and in rat neuron-microglia coculture following NLRP3 activation
- **Potent *in vivo* inhibition** of brain caspase-1 activation, immediately downstream of NLRP3

Inhibition of BzATP-induced IL-1β, IL-18 and TNF in LPS-primed human microglia



Mean ± SEM, min. 4 donors

Inhibition of caspase-1 activation in mouse neuroinflammation model

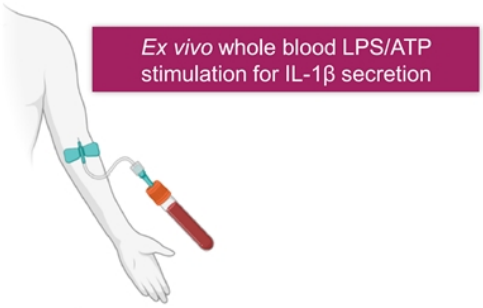


Source: Ventyx internal data.

Phase 1 Trial to Explore CNS Drug Exposure and PD Effect

Anticipated Phase 1 Trial Approach in Healthy Volunteers

- **Anticipated design*:** Phase 1 SAD/MAD trial with safety, tolerability, PK and PD endpoints
  - One cohort in each of the SAD and MAD portions with CSF sampling for PK and CNS drug exposure
  - Pharmacodynamic assessment with LPS/ATP *ex vivo* stimulation of IL-1β secretion in whole blood samples
- **IND submission and Phase 1 trial initiation expected in H1 2023**
- Potential for cohort of Parkinson's disease patients to explore impact on relevant CSF/blood biomarkers:
  - α-synuclein, lysosomal enzymes, markers of amyloid/tau pathology and neurofilament light chain



*Pending IND submission and alignment with FDA.

Discovery Update

John Nuss, Ph.D.
Chief Scientific Officer

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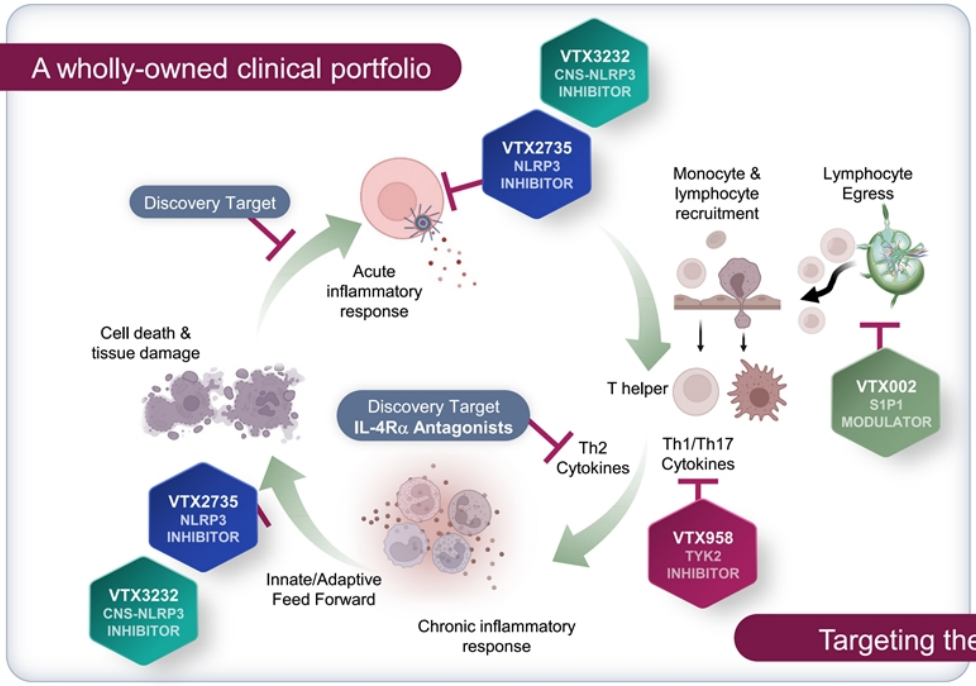
Chemistry-Driven, Efficient & Productive R&D Engine



Validated Targets

Unmet Need

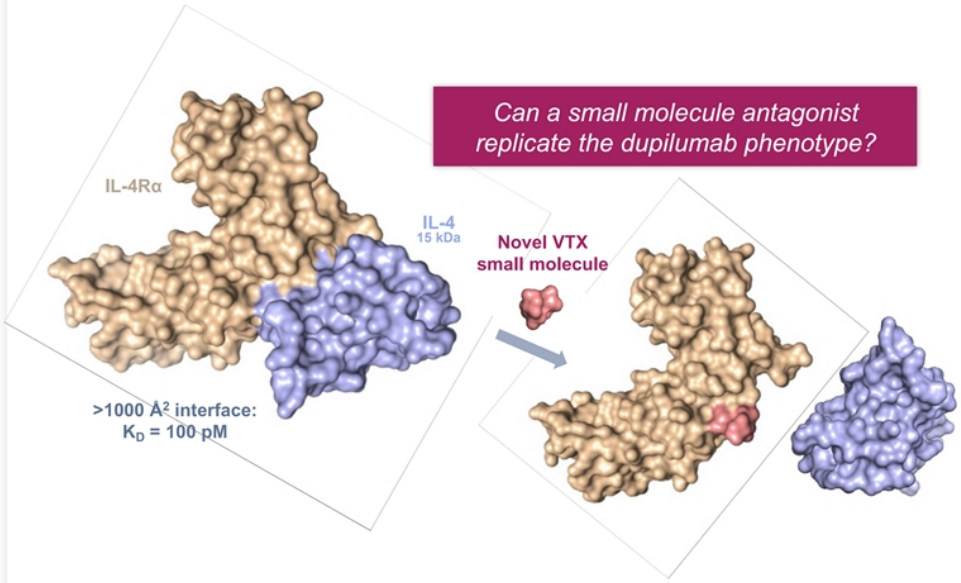
Differentiated Molecules

Improved Safety and Efficacy*

*Represents target clinical profile for pipeline candidates.

Targeting IL-4Rα with Small Molecule Antagonists

IL-4Rα Blockade Is Validated in Multiple Large Autoimmune Indications



IL-4Rα Blockade

- IL-4Rα blockade prevents **both IL-4 and IL-13 signaling**, key Th2 effector cytokines that drive inflammation
- Dupilumab (anti-IL4Rα) approved for:
  - atopic dermatitis
  - asthma
  - eosinophilic esophagitis
  - chronic rhinosinusitis
  - prurigo nodularis
- **No oral small molecule IL-4Rα-targeted antagonists** have entered clinic to date

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Source: Ventyx internal data.

Optimizing Small Molecule IL-4Rα Antagonists

Progressing Through Lead Optimization Towards *In Vivo* Proof-of-Concept

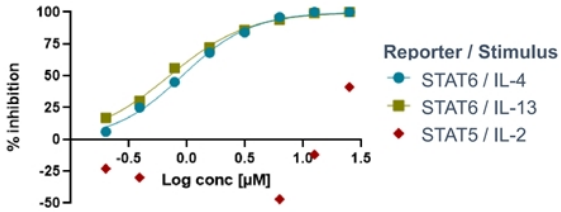
Attractive Chemical Properties

- "Fragment-like" size and lipophilicity
- Non-covalent, reversible binders
- Ro5 compliant, no structural flags

Validated Target Engagement

- Inhibition of STAT6 phosphorylation in cells upon IL-4 and IL-13 stimulus
- Selective for IL-4 *vs.* IL-2 signaling
- IL-4Rα interaction confirmed by **5 orthogonal biophysical methods**

Full Antagonist Efficacy



Internally-Discovered IL-4Rα Antagonists

- Multiple novel chemical series discovered in-house
- Compounds replicate dupilumab phenotype: **selective sub-µM inhibition of IL-4/IL-13 signaling**
- Currently enabling structure-based design (X-ray crystal and ligand-/ target-based NMR)
- **Next Steps:** Lead optimization towards functional efficacy in *ex vivo* assays and *in vivo* proof-of-concept in 2023

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Source: Ventyx internal data.

Wholly-Owned and Internally-Discovered Small Molecule Portfolio

With Multiple Near-Term Clinical Catalysts

S1P1R Modulator

Candidate	Indication	IND-Enabling	Phase 1	Phase 2	Phase 3	Anticipated Catalysts
VTX002	Ulcerative Colitis					Phase 2 data **H2 2023**

TYK2 Inhibitor

Candidate	Indication	IND-Enabling	Phase 1	Phase 2	Phase 3	Anticipated Catalysts
VTX958	Plaque Psoriasis					Phase 2 data **Q4 2023**
VTX958	Crohn's Disease					Phase 2 data **2024**
VTX958	Psoriatic Arthritis					Phase 2 data **H1 2024**

Peripheral NLRP3 Inhibitor

Candidate	Indication	IND-Enabling	Phase 1	Phase 2	Phase 3	Anticipated Catalysts
VTX2735	CAPS					Initiate Phase 2 **Q1 2023**

CNS-Penetrant NLRP3 Inhibitor

Candidate	Indication	IND-Enabling	Phase 1	Phase 2	Phase 3	Anticipated Catalysts
VTX3232	Parkinson's Disease					Initiate Phase 1 **H1 2023**

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Ventyx Biosciences Announces Pipeline Updates and Highlights Strategic Priorities at Investor R&D Day

Phase 2 clinical trials of VTX958 (TYK2 inhibitor) in plaque psoriasis, Crohn's disease and psoriatic arthritis are ongoing with topline Phase 2 data in plaque psoriasis expected in Q4 2023

The Phase 2 trial of VTX002 (S1P1R modulator) in ulcerative colitis is on track to complete enrollment by mid-2023; new pharmacodynamic data support best-in-class potential

Releases new data highlighting attractive profiles of NLRP3 inhibitors VTX2735 and VTX3232

Discloses new small molecule discovery program targeting IL-4Rα

Webcast of investor R&D Day to begin at 9:00 AM ET

ENCINITAS, Calif., January 26, 2023 (GLOBE NEWSWIRE) – Ventyx Biosciences, Inc. (Nasdaq: VTYX) ("Ventyx"), a clinical-stage biopharmaceutical company focused on advancing novel oral therapies that address a broad range of inflammatory diseases with significant unmet medical need, is hosting an investor R&D Day today highlighting key aspects of Ventyx's clinical-stage and discovery programs.

"I am thrilled to highlight progress across our diverse, wholly-owned pipeline of differentiated small molecule drug candidates following a year of tremendous progress," said Raju Mohan, Chief Executive Officer. "2023 is shaping up to be a transformational year for Ventyx with several key clinical readouts anticipated, including topline Phase 2 data for VTX002 in ulcerative colitis, which is expected in H2 2023, and topline Phase 2 data for VTX958 in psoriasis, which is expected in Q4 2023. Meanwhile, our peripheral NLRP3 inhibitor VTX2735 is Phase 2 ready and we expect to initiate a Phase 1 trial for our CNS-penetrant NLRP3 inhibitor VTX3232 in H1 2023. Finally, we are excited to announce a new discovery-stage program to develop small molecule IL-4Rα antagonists. The progress made in this program showcases the strength of our discovery capabilities and further strengthens our novel, small-molecule immunology pipeline. We look forward to providing additional details on these programs at this event."

Pipeline Updates and Anticipated Catalysts

VTX958 (TYK2 Inhibitor)

- Enrollment is ongoing in the Phase 2 SERENITY trial of VTX958 in moderate-to-severe plaque psoriasis and the Phase 2 HARMONY trial in Crohn's disease, while screening activities have initiated for the Phase 2 TRANQUILITY trial in psoriatic arthritis. Topline data from the Phase 2 SERENITY psoriasis trial are anticipated in Q4 2023. Topline readouts from the Phase 2 HARMONY and Phase 2 TRANQUILITY trials are expected in 2024.

- We are developing an extended release (ER) tablet formulation for VTX958 in collaboration with leading formulation development partners. We expect to provide an update on the ER tablet development in mid-2023 following completion of in-human testing.

VTX002 (S1P1R Modulator)

- We continue to make significant progress enrolling the Phase 2 trial of VTX002 in moderate-to-severe ulcerative colitis. We expect to complete enrollment by mid-2023, and topline results are anticipated in the second half of 2023.
- Preliminary pharmacodynamic data from the open-label extension of the ongoing Phase 2 trial in ulcerative colitis may support the potential best-in-class profile of VTX002. Among patients completing Week 26 (13 weeks of blinded therapy followed by 13 weeks of open-label treatment with VTX002 60mg) as of January 15, 2023, a mean reduction from baseline in absolute lymphocyte count of 74% was observed. Reduction in absolute lymphocyte count is an important pharmacodynamic (PD) marker for efficacy in ulcerative colitis and we believe these preliminary data suggest VTX002 may achieve a stronger PD response compared to other S1P receptor modulators approved or in development for the treatment of ulcerative colitis.

VTX2735 (Peripheral NLRP3 Inhibitor)

- We are presenting additional data from the completed Phase 1 trial of VTX2735 in healthy volunteers, in which VTX2735 demonstrated excellent safety and target coverage. VTX2735 was well tolerated across all doses tested, with anticipated Phase 2 dose regimens expected to achieve IC_{90} coverage of IL-1b for 20 hours or more. VTX2735 also exhibited dose- and concentration-dependent inhibition of IL-1b *ex vivo* and significant reductions from baseline in high sensitivity C-reactive protein.
- We have completed non-clinical toxicology studies and developed a solid oral dose (tablet) to position VTX2735 as a Phase 2-ready compound.
- A Phase 2 proof-of-mechanism trial of VTX2735 in cryopyrin-associated autoinflammatory syndromes is expected to initiate in Q1 2023.

VTX3232 (CNS-penetrant NLRP3 Inhibitor)

- We expect to file an IND and initiate a Phase 1 trial for VTX3232 during the first half of 2023. The Phase 1 trial is expected to characterize the safety, target engagement and bioavailability of VTX3232 in the central nervous system of healthy volunteers.

Discovery Programs

- We are introducing a new discovery-stage program focused on small molecule antagonists of IL-4Rα, a target validated by biologics in multiple large autoimmune indications, including atopic dermatitis, asthma and eosinophilic esophagitis. We are advancing multiple internally discovered novel chemical series through lead optimization with the goal of establishing *in vivo* proof-of-concept and nominating a lead candidate in 2023.

R&D Day and Webcast Information

Ventyx Biosciences' investor R&D Day will take place today, Thursday, January 26th, from 9:00AM to 11:30AM ET. A live webcast of the event will be available in the "Investors" section of the Ventyx website at www.ventyxbio.com. A webcast replay will also be available on this website shortly after conclusion of the event.

About Ventyx Biosciences

Ventyx is a clinical-stage biopharmaceutical company focused on developing innovative oral medicines for patients living with autoimmune and inflammatory disorders. We believe our ability to efficiently discover and develop differentiated drug candidates will allow us to address important unmet medical need with novel oral therapies that can shift immunology markets from injectable to oral drugs. Our current pipeline includes three internally discovered clinical programs targeting TYK2, S1P1R and NLRP3, positioning us to become a leader in the development of oral immunology therapies. Ventyx is headquartered in Encinitas, California. For more information about Ventyx, please visit www.ventyxbio.com.

Forward-Looking Statements

Ventyx cautions you that statements contained in this press release regarding matters that are not historical facts are forward-looking statements. These statements are based on Ventyx's current beliefs and expectations. Such forward-looking statements include, but are not limited to, statements regarding: the potential of Ventyx's product candidates and the anticipated continued progression of the development pipeline for such product candidates; and the anticipated timing of commencement, enrollment and completion of clinical trials for Ventyx's product candidates, including anticipated milestones for Ventyx's product candidates; and the expected timeframe for funding Ventyx's operating plan with current cash, cash equivalents and marketable securities. 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 press release 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; disruption to our operations from the ongoing global outbreak of the COVID-19 pandemic, or from the ongoing military conflict in Ukraine, including clinical trial delays; 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; and other risks described in Ventyx's prior 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 quarterly period ended September 30, 2022 filed on November 4, 2022, 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.

Investor Relations Contact
Patti Bank
Managing Director
ICR Westwicke
(415) 513-1284
IR@ventyxbio.com