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): November 30, 2022

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 Other Events.

On December 1, 2022, Ventyx Biosciences, Inc. ("Ventyx") will be attending meetings with investors, analysts and others in connection with the Piper Sandler 34th Annual Healthcare Conference. . During these meetings, Ventyx will present the slides attached as Exhibit 99.1 to this Current Report on Form 8-K, which are incorporated by reference herein.

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) 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 – December 2022.
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.

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

Date: November 30, 2022

Exhibit 99.1

Corporate Presentation

December 2022

Forward-Looking Statements

Ventyx Biosciences, Inc. ("we," "us," "our," "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: clinical development plans and related timing for Ventyx's product candidates; anticipated timing of data announcements; anticipated efficacy, safety, dosing and clinical differentiation of Ventyx's product candidates; potential indications for Ventyx's product candidates; market opportunities; the anticipated timing of IND submission for VTX3232; projected catalysts relating to Ventyx's product candidate pipeline; and anticipated cash runway. 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, including clinical trial delays; the Company's dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; the results of preclinical studies and early clinical trials are not necessarily predictive of future results; supply chain constraints; the success of Ventyx's clinical trials and preclinical studies for its product candidates; interim results do not necessarily predict final results and one or more of the outcomes may materially change as the 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 our 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; Ventyx may use its capital resources sooner than it expects; and other risks described in the Company's prior communications and the Company's filings with the Securities and Exchange Commission (SEC), including under the heading "Risk Factors" in the Company's Quarterly Report on Form 10-Q 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.

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

Our Mission: To Become a Leading Immunology Company

Underpinned by Strong Drug Discovery and Development Capabilities

With Three, Differentiated, Clinical-stage Candidates

and a deep pipeline of preclinical programs that target immune-mediated and inflammatory disease indications

Our Internally-discovered Small Molecule Drugs

allow us to own 100% commercial rights to our entire portfolio with long patent lives for all product candidates

Our Experienced Team And Our Internal R&D Engine

continue to generate candidates with potential to address diseases with high unmet need

Our Leadership Team

Management

Raju Mohan, PhD
CHIEF EXECUTIVE OFFICER, FOUNDER

Martin Auster, MD
CHIEF FINANCIAL OFFICER

Chris Krueger, JD
CHIEF BUSINESS OFFICER

John Nuss, PhD
CHIEF SCIENTIFIC OFFICER

William Sandborn, MD
PRESIDENT, CHIEF MEDICAL OFFICER

Board Of Directors

Sheila Gujrathi, MD
EXECUTIVE CHAIR, VENTYX

Jigar Choksey
PRINCIPAL, THIRD POINT

Richard Gaster, MD, PhD
MANAGING PARTNER, VENBIO

Raju Mohan, PhD
CHIEF EXECUTIVE OFFICER, VENTYX

Aaron Royston, MD
MANAGING PARTNER, VENBIO

Somu Subramaniam
MANAGING PARTNER, NEW SCIENCE VENTURES

William White
CHIEF FINANCIAL OFFICER, AKERO THERAPEUTICS

Broad Pipeline of Candidates With Multiple Near-Term Catalysts

Addressing Established Inflammatory and Immunology Markets with a Wholly Owned Product Portfolio

Target	Program	Preclinical	Phase 1	Phase 2	Phase 3	Next Anticipated Milestones
TYK2	VTX958	Psoriasis, psoriatic arthritis, Crohn's disease				Initiate Phase 2 trials Q4 2022
S1P1R	VTX002	Ulcerative Colitis				Report topline Phase 2 data 2023
NLRP3 *Peripheral*	VTX2735	CAPS, other potential indications include CV, dermatologic and rheumatologic diseases				Initiate Phase 2 trial in CAPS Q1 2023
NLRP3 *CNS-penetrant*	VTX3232	Neuroinflammatory diseases				File IND Q1 2023 Initiate Phase 1 trial Q1 2023

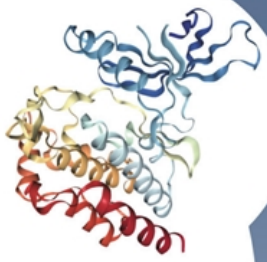
Cash, cash equivalents and marketable securities of $412.4M as of September 30, 2022 expected to fund operations into 2025

Pipeline Targeting Large Well-Established Markets

Indication*	Patients In The U.S.	Global Drug Revenue* (2020)	Target Population
Psoriasis Dermatology	~8M	~$20B	25-30% Moderate-to-severe
Crohn's disease IBD	~700K	~$13B	30-40% Moderate-to-severe
Ulcerative colitis IBD	~1M	~$7B	30-40% Moderate-to-severe
Psoriatic arthritis Rheumatology	~1M	~$4B	40-60% Moderate-to-severe
SLE Rheumatology	Up to 500K	~$1B	

Sources: Evaluate Pharma, Company Estimates, Wall Street Research
*Global drug revenue refers to the total market across all severity levels
Notes: SLE = systemic lupus erythematosus; *Group of indications based on current mid/late-stage trials for BMS's allosteric TYK2 inhibitor deucravacitinib; global commercial sales totaled $10.65B for biologics targeting IL-12/23 and IL-23 in 2020

ventyx BIOSCIENCES



ORALLY BIOAVAILABLE selective allosteric inhibitor of TYK2

VTX958: Orally Bioavailable, Selective Allosteric Inhibitor of TYK2

Clinically Validated Target

- Established clinical efficacy in IBD, psoriasis and psoriatic arthritis with biologics targeting IL-12 and IL-23*
- Allosteric TYK2 inhibitors target common pathways
- TYK2 inhibition is **clinically validated** in psoriasis, psoriatic arthritis and SLE
- First allosteric TYK2 inhibitor FDA-approved Sept. 9, 2022 -- **no boxed warning** differentiates TYK2i from JAKi therapeutics

Potential Best-in-Class Drug

- Selective allosteric TYK2 inhibitor
- TYK2 functional selectivity may differentiate clinical profile vs. less selective TYK2 inhibitors
- **Positive Phase 1 data:**
  - Broad therapeutic window
  - Excellent safety profile
  - **Class-leading target coverage** may position VTX958 for success across multiple indications

Large Addressable Markets

- Multiple autoimmune disorders in dermatology, IBD, renal and rheumatology total **~$48B**** in 2020 WW sales
- High unmet need for safe and **effective oral agents** in markets dominated by injectable biologics

*Includes approved drugs Stelara™ (JNJ), Tremfya® (JNJ), Skyrizi™(ABBV), Ilumya™ (Sun Pharma) and others in late-stage development (mirikizumab (LLY), brazikumab (AZN)
**Source: Positive Phase 3 efficacy results reported for deucravacitinib in psoriasis at AAD April 2021; positive Phase 2 efficacy results reported for psoriatic arthritis at ACR October 2020 and positive Phase 2 efficacy results reported for SLE at EULAR meeting June 2022
Source: EvaluatePharma 2020 indication sales estimates

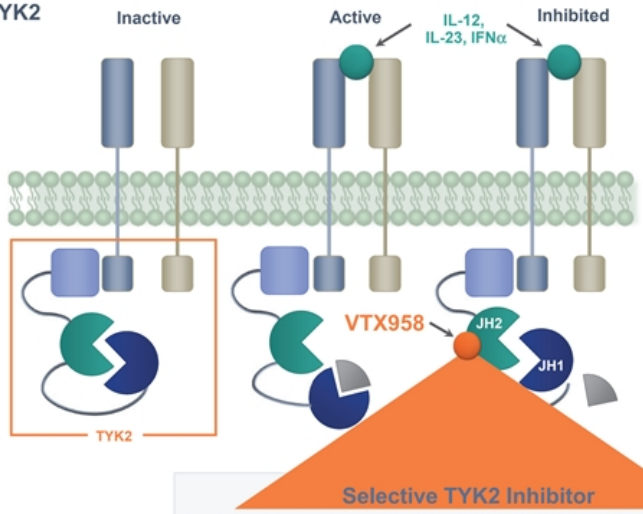
VTX958 Binds Selectively to the TYK2 Allosteric (JH2) Domain

Key Players in JAK/TYK2 Family Signaling

JH2 Allosteric Domain
Much less conserved amongst the JAK family with structurally distinct binding pockets

JH1 Kinase Domain
Highly conserved within JAK family; inhibitors targeting the kinase domain have poor selectivity

ATP Binding to JH1 allows phosphorylation of substrates



Features of VTX958 JH2 Allosteric Inhibition

Selectivity for TYK2 JH2 vs. JAK1 JH2 domain (>4,000 X)

No binding to JAK2/3 JH2 domains

No binding to TYK2 kinase JH1 **and**

No kinase enzyme inhibition of any JAK family member

Selective TYK2 Inhibitor

- Targeting the **allosteric domain** of TYK2 affords inhibitors with selectivity against other JAK isoforms
- May Avoid Potential Safety Risks of JAK1/2/3 Inhibition

VTX958 is Highly Selective for TYK2 JH2 Domain vs. Deucravacitinib

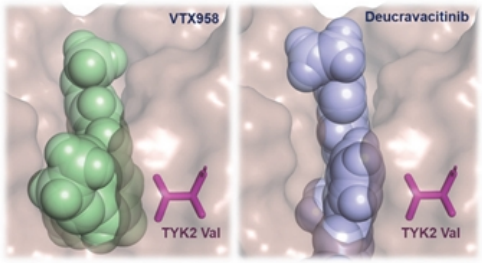
Inhibits TYK2 Pathways (IL-12, IL-23, IFNα) while Avoiding the JAK1/2/3 Pathways

Structural Rationale for VTX958 Selectivity:

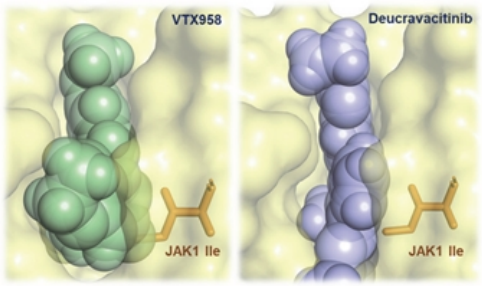
- Productive interaction for both VTX958 and deucravacitinib with valine residue in TYK2 JH2 domain
- VTX958 has a **steric clash** with the isoleucine residue (Ile) in the JAK1 JH2 domain – deucravacitinib does not
- Key determinant of the high TYK2 selectivity of VTX958

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



Source: Ventyx internal data

VTX958 Selectively Inhibits IL-12, IL-23 and IFNα Signaling

VTX958 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

VTX958 Has 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 psoriasis and other indications
- Broad therapeutic window with VTX958 may allow for higher exposures in Phase 2/Phase 3 studies

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

Summary of VTX958 Phase 1 Results

Safety, Exposure and Target Coverage

VTX958 **well tolerated** across all SAD and MAD cohorts

VTX958 exhibits **class-leading TYK2 IC_{90} coverage***

- Achieved TYK2 IC_{90} coverage for **up to 24 hours** with no dose-limiting toxicities

Robust, dose-dependent pharmacodynamic activity in *ex vivo* and *in vivo* assays

- Supports hypothesis that greater pathway inhibition may enable differentiated efficacy in clinic

*TYK2 IC_{90} coverage implies suppression of IL-12, IL-23 and IFNα pathways

VTX958 Phase 1 Day 10 (Steady State) MAD Results

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**

KEY TAKEAWAYS

- Safely achieved **class-leading** TYK2 IC_{90} coverage
- IC_{90} coverage up to **24 hours** for IL-12, IL-23 and IFNα
- Exposures achieved may approach biologic-like suppression of IL-12/23 pathways

*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

VTX958 Phase 1 MAD

Pre-IFNα Challenge Safety Assessment*

		VTX958					
TEAEs	Placebo (n=10)	50mg BID (n=6)	250mg QD (n=6)	175mg BID (n=6)	500mg QD (n=6)	350mg BID (n=6)	All cohorts (n=30)
Headache	1 (10.0%)	-	2 (33.3%)	2 (33.3%)	1 (16.7%)	1 (16.7%)	6 (20.0%)
Faeces soft	1 (10.0%)	1 (16.7%)	2 (16.7%)[@]	1 (16.7%)	-	1 (16.7%)	4 (13.3%)
Rash papular	-	-	1 (16.7%)[#]	-	-	2 (33.3%)[†]	3 (10.0%)
Dry mouth	-	-	-	-	1 (16.7%)	1 (16.7%)	2 (6.7%)
Abdominal pain	-	2 (33.3%)	-	1 (16.7%)	-	-	3 (10.0%)
ALT, AST, GGT increase	-	-	-	-	-	1 (16.7%)[‡]	1 (3.3%)

- All TEAEs (Treatment Emergent Adverse Events) reported in 2 or more subjects receiving VTX958 prior to IFNα Challenge on day 13 and single subject AEs of interest. IFNα challenge not performed in cohort 5 (350 mg BID), AEs for all 14 days of treatment are presented for Cohort 5.

[@] Both AEs in a single subject

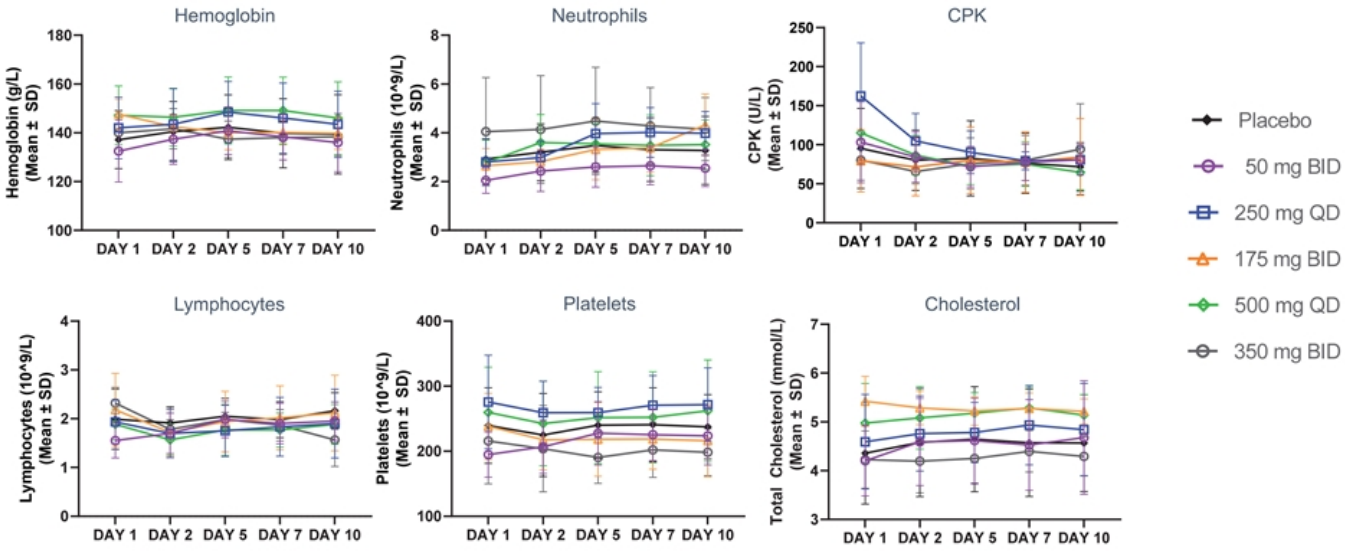
[#] Single skin papule on lower right cheek judged not drug related; mild; resolved with continued VTX958 dosing

[†] Two subjects in cohort 5 (350 mg BID) experienced mild skin papules judged not drug related
one subject with mild face papules that resolved with continued VTX958 dosing
one subject with mild face/trunk papules that improved with continued VTX958 dosing

[‡] One subject in cohort 5 (350 mg BID) experienced increase in ALT, AST, and GGT, classified as mild; overlapped with COVID diagnosis

VTX958 Phase 1 MAD Results: Selected Laboratory Data

No significant effects on hematological parameters, lipids, CPK laboratory values



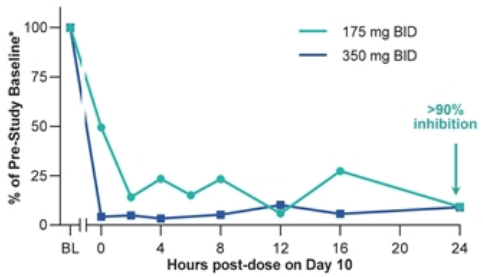
VTX958 Phase 1 MAD Results

Robust Dose-Dependent Pharmacodynamic Effects

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 (% Inhibition* 175 mg BID)**

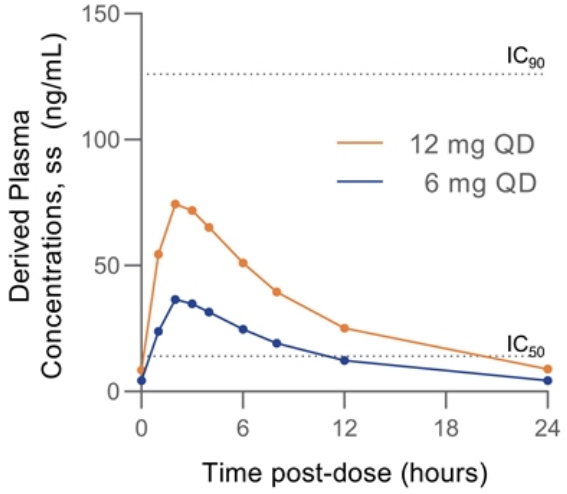
Time post-challenge	4h	6h	8h	12h	16h	24h
CXCL10	97	82	42	95	95	63
ISG20	80	69	54	79	101	39
IFI27	78	68	62	60	71	84

**% inhibition shown as placebo adjusted geometric mean*

Published TYK2 Target Coverage Data

Opportunity for VTX958 to Differentiate with Improved Therapeutic Window

Deucravacitinib (BMS) 6 mg & 12 mg QD Target Coverage



PK data modeled and graph adapted from Chimalakonda et al., Dermatol. Ther. 2021
Deucravacitinib TYK2 IC_{50} of 14 ng/mL from Catlatt et al. EULAR 2017
IC_{90} values generated assuming a Hill slope of 1. ss= steady state

First-generation allosteric TYK2 inhibitor exposures are limited by toxicities

- Deucravacitinib 6mg QD (PsO dose) achieves IC_{50} coverage for ~9 hours (does not reach IC_{90})
- Skin toxicities (acne, rash) emerge consistently at higher exposures

Fuller pathway inhibition (improved therapeutic window) expected to drive differentiation

- Greater coverage of TYK2 IC_{50}, IC_{90} may drive improved efficacy
- Achievement of durable IC_{90} coverage may be necessary to achieve efficacy in IBD

Deucravacitinib - Skin AEs and Target Coverage

VTX958 Phase 1 Data Establish Differentiation vs. Deucravacitinib

- Deucravacitinib elicits dose-dependent and potentially dose-limiting skin toxicities
- Skin findings observed with **high frequency** at exposures > 6 mg QD (~9h TYK2 IC_{50} coverage)
- VTX958 demonstrates potential **best-in-class** therapeutic window
  - Achieved high TYK2 IC_{90} coverage **without frequent skin AEs**

		Deucravacitinib					
Study	Skin AE	3 mg BID	6 mg QD	6 mg BID	12 mg QD	12 mg BID	Total
P1 MAD HV	Any skin related AEs			33%	56%	78%	42%
P2 PsO	Acne	2%		4%	9%		
	Pruritis	2%		7%	5%		
P3 PsO	Acne		2%				
	Folliculitis		2%				
P2 PsA	Acne		3%		2%		
	Acneiform dermatitis		3%		3%		
	Rash		4%		6%		
P2 Lupus	Acne	3%		9%	8%		
	Rash	2%		3%	8%		
	Any skin related AEs	17%		34%	34%		
P2 UC	Acne			9%			
	Rash			12%			

TYK2 IC_{50}: ~9 h
TYK2 IC_{90}: ~0 h

TYK2 IC_{50}: ~18 h
TYK2 IC_{90}: ~0 h

*Deucravacitinib AE data compiled from respective publications and/or company data releases
Deucravacitinib Phase 1 MAD dose ranged up to 12mg BID; trial had 7 discontinuations in deucravacitinib arms (8.4%) related to AEs (4 d/c associated with skin toxicities)
TYK2 target coverage sourced from Chimalakonda et al., 2021 represents IL-12-stimulated IFNγ production hWB assay

Acne, Folliculitis and Rash are not On-Target Effects of IFNα or IL12/23 Inhibition

Drug	Mechanism of inhibition	Acne	Folliculitis	Rash
Anifrolumab (Saphnelo)	IFNα	< 2%	< 2%	< 2%
Ustekinumab (Stelara)	IL12/23	< 1%	< 1%	< 1%
Guselkumab (Tremfya)	Anti-IL23	< 1%	< 1%	< 1%
Risankizumab (Skyrizi)	Anti-IL23	< 1%	< 1%	< 1%

ventyx BIOSCIENCES

Source: Prescribing information for each approved drug.

VTX958 vs. Competitor Allosteric TYK2 Inhibitors

Comparison of Phase 1 Safety and Exposures Data* in Healthy Volunteers

	VTX958 Phase 1 MAD 100 mg – 700 mg TDD	**NDI-034858** Phase 1 MAD 20 mg – 35 mg QD 50 mg – 100 mg QD	**Deucravacitinib** Phase 1 MAD 2 mg – 24 mg TDD

Adverse Events of Interest	• Skin and subcutaneous disorders, classified as unrelated (**10%**)
	  • Papular rash (**10%**)
	• 1 subject with mild ALT elevation overlapped with Covid (350 mg BID)
		• Acneiform dermatitis (**67%, 17%**)
		• Papular rash (**25%, 0%**)
		• Grade 3 CPK elevation (1 subject, 20 mg)
			• Skin and subcutaneous disorders (**42%**) including:
			  • Rash (**20%**)
			  • Acne (**13%**)

Relevant Dose	**175 mg BID** **350 mg BID**	**30 mg QD**	**6 mg QD**
TYK2 Coverage	IC_{50} 24 hours IC_{50} 24 hours IC_{90} 16 hours IC_{90} 24 hours	IC_{50} ~24 hours IC_{90} ~5 hours	IC_{50} ~9 hours IC_{90} ~0 hours

Ventyx: Internal data; Nimbus: JPM 2022 presentation; Deucravacitinib: Chimalakonda et al., Dermatol. Ther. 2021; TDD = total daily dose

VTX958 vs. Competitor Allosteric TYK2 Inhibitors

Demonstrates Potential Best-in-Class Therapeutic Window

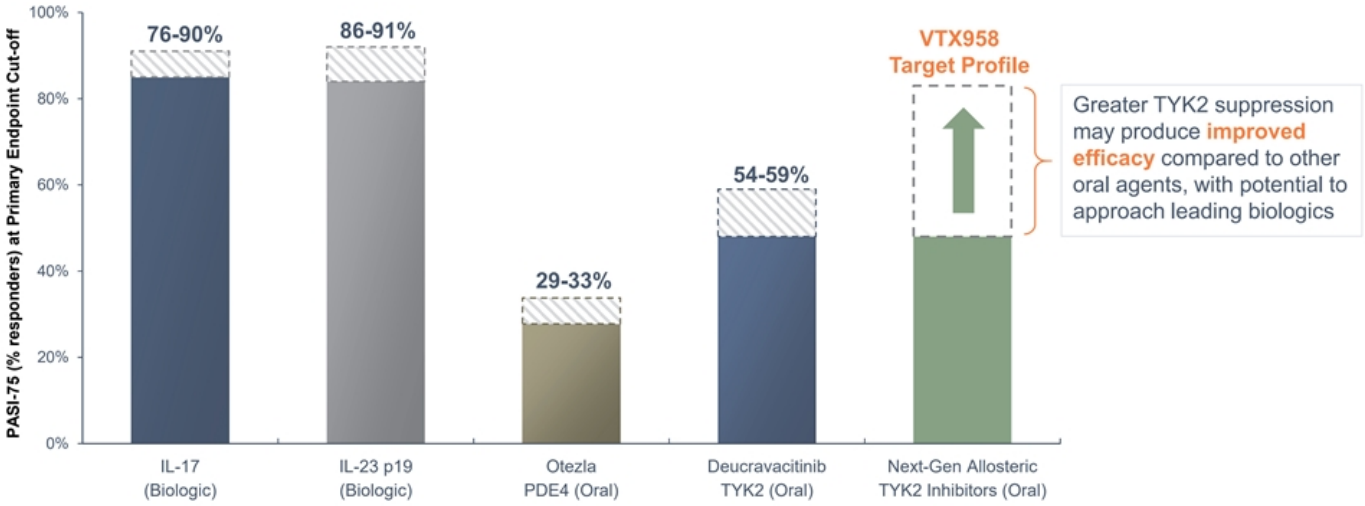
Differentiating Parameter	VTX958	Deucravacitinib	NDI-034858
Relevant Dose / Exposure Comparisons	175 mg BID	6 mg QD	30 mg QD
Target Coverage:*			
TYK2 IC_{50}	**24 hours**	9 hours	24 hours
TYK2 IC_{90}	**16 hours**	None	5 hours
Adverse Events of Interest:			
Skin Findings	**None**	Acne, acneiform dermatitis, folliculitis, rash	Acne, rash
Laboratory Findings	**None**	Rare CPK and triglyceride elevations in PsO Phase 3	Neutropenia, CPK elevation, triglyceride elevations
Opportunity in IBD	**Best-in-class therapeutic window**	Ph2 UC failed – limited therapeutic window	No currently active program– limited therapeutic window

Source: Papp et al., 2018 (NEJM); McElwee et al., 2022 (AAD); Gangolli et al., 2022 (SID); internal data
*TYK2 target coverage measured with IL-12 assay for VTX958 and deucravacitinib; assay not disclosed for NDI-034858

VTX958 Profile Expected to Drive Clinical Differentiation

Best-in-Disease Oral Potential in the ~$20B WW Annual Psoriasis Market

Psoriasis Competitive Landscape



Note: Solid area represents pbo-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

Unlocking the Opportunity in IBD

Higher Doses 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 **substantially higher exposures** are required for efficacy in Crohn's vs. PsO
- Deucravacitinib Phase 2 in UC failed (6 mg BID dose 0 hours IC_{90} coverage)
- Higher doses of VTX958 may approach biologic IL-12/23 pathway suppression
- Profile of VTX958 may unlock a major market opportunity in Crohn's, a **>$13B global market**

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

VTX958: Broad Development Opportunities and Commercial Potential

- **Phase 2 trials will explore a broad dose range, enabling optimal Phase 3 dose selection based on safety and maximizing target coverage**
  - We plan to initiate three Phase 2 trials in Q4 2022 (PsO, Crohn's and PsA) with additional Phase 2 indications (including SLE) being considered given the unique profile of VTX958
  - Phase 2 trials will be dosed with an immediate release (IR) tablet; a modified-release (MR) formulation is in development to approximate BID exposures with a QD oral dose
    - Bridging study before Phase 3 (Precedent for approved compounds: Rinvoq, Xeljanz, etc.)

VTX958 Development Landscape

Robust Market Opportunity for a Potential Best-in-Class TYK2 Inhibitor

	Biologics		Oral Agents		
INDICATION	ANTI-IL-23	ANTI-IL-17	APREMILAST	DEUCRAVACITINIB	VTX958*
Psoriasis	+++	+++	+	++	+++
Psoriatic arthritis	+++	+++	+	++	+++
Crohn's disease	+++	—	N/A	?	+++
Ulcerative colitis	++	—	N/A	—	++
Lupus	—	N/A	N/A	++	+++

VTX958

- Excellent safety profile
- Class-leading TYK2 coverage
- Potentially superior therapeutic window
- Unique opportunity in IBD

Well positioned to capitalize on several large, biologic-dominated autoimmune markets

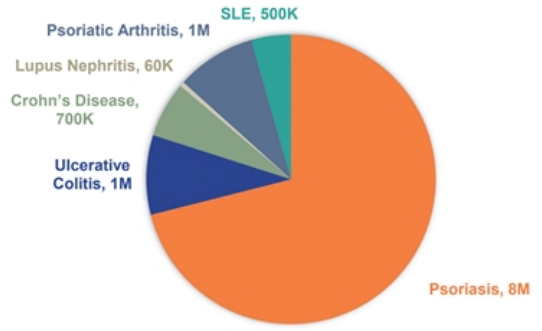
Therapeutic Efficacy — — Ineffective + Weaker ++ Moderate +++ Stronger +++ VTX958 target efficacy

Sources: Internal assessment of published efficacy data.
*Aspirational target efficacy profile based on VTX958 TYK2 target coverage achieved in Phase 1 healthy volunteer study

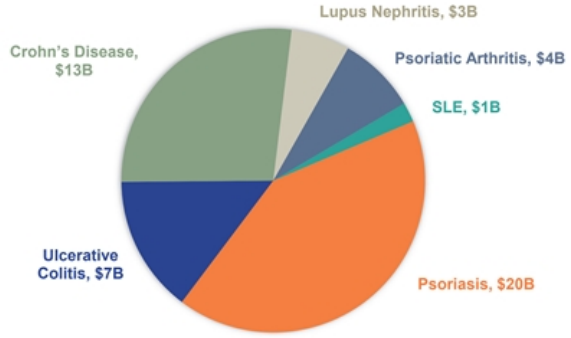
Robust Market Opportunity for VTX958

- **Best-in-class profile of VTX958 may enable clinical differentiation across multiple indications**
  - VTX958 has potential to offer a differentiated clinical profile in PsO, PsA and SLE by dosing to levels that achieve greater TYK2 inhibition relative to competitors
  - VTX958 may be uniquely positioned among TYK2 inhibitors to address Crohn's/IBD indications where anti-IL-12/23 and anti-IL-23 antibodies have proven effective at higher dose levels than in psoriasis

~10.75M Patients in the US



~$48B Global Drug Revenue



Sources: CCFA, Evaluate Pharma (2020 indication sales estimates)

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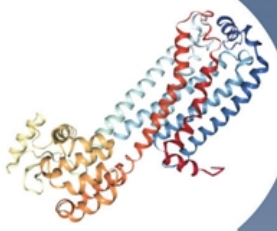


PERIPHERALLY RESTRICTED S1P1R MODULATOR

with potential for treatment of ulcerative colitis

VTX002 Program Summary

Phase 2 S1P1R Modulator for Ulcerative Colitis

Potentially Differentiated S1P1R Modulator

- Selective S1P1R modulator
- Differentiated on key parameters
- Demonstrated pharmacodynamic activity in Phase 1 trial
- Pursuing clinical development plan in both treatment-naïve and biologic-experienced patients

Clinically Validated Target

- S1P1R modulators approved for MS and UC with clinical trials ongoing in other indications
- BMS' ozanimod approved for UC in May 2021

Large Addressable Markets

- Ulcerative colitis is lead indication totaling up to $7B in worldwide revenue

VTX002 Differentiates on Multiple Key Parameters vs. Competitors

Potential for Differentiated Clinical Profile in UC Patients	**Safety Profile**	**No Drug-Drug Interactions**
Sustained lymphocyte reduction up to 65% across multiple doses in MAD trial	No SAEs, elevated LFTs, abnormal PFTs or macular edema	No CYP inhibition; no food effect; favorable profile for patients with co-morbidities

Fast Onset of Action Faster Lymphocyte Recovery	**Ability to Dose Titrate**	**Peripherally Restricted**
No long-acting circulating metabolites Optimal half life ($t_{1/2}$~20h)	Potential to avoid first-dose cardiac monitoring in label	Very low CNS penetration; not a repurposed MS drug; potential to avoid macular edema

Notes: SAE=serious adverse event

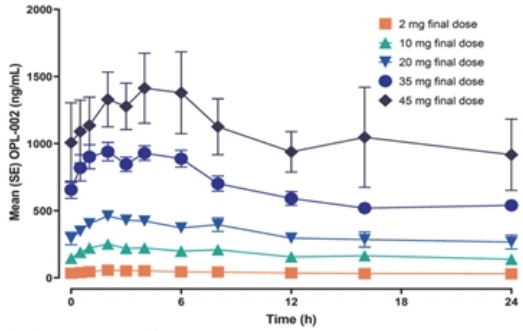
VTX002 Differentiates on Multiple Key Parameters vs. Competitors

Differentiating Parameter	Ozanimod	Etrasimod	VTX002
Receptor Selectivity	S1P 1,5	S1P 1,4,5	S1P 1,5
CYP450 Interactions	Yes	No	No
Liver Enzyme Elevations	Yes	No	No
Active Metabolites	Yes	No	No
Half-life	19 h, Met 10-13 d	**33 h**	**~20 h**
Fast Lymphocyte Recovery Time	No	Yes	Yes
First Dose Heart Rate Reduction	Yes	Yes	Yes
Dose Titration	Yes	**No**	**Yes**
First Dose Monitoring	No	TBD	TBD

Phase 1 MAD Results: Dose-Dependent Exposure and Lymphocyte Reduction

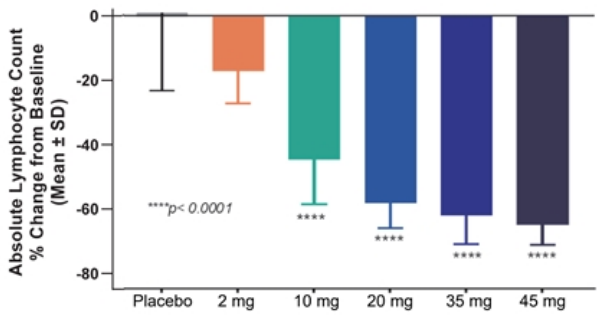
Absolute Lymphocyte Count (ALC) Reductions of 40-50% Correlated with Clinical Efficacy Observed in UC*

Pharmacokinetics



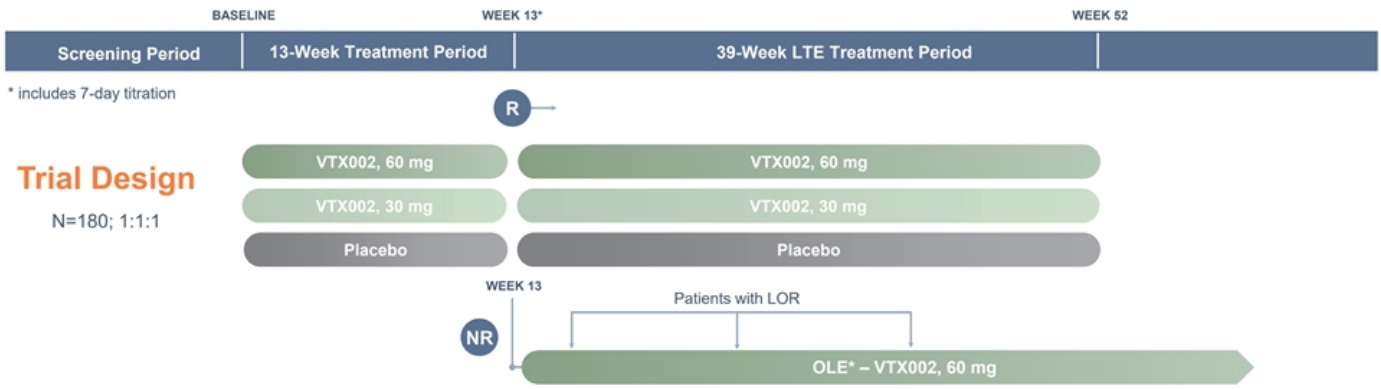
- $T_{1/2}$ of ~20 hours
- Dose-proportionate exposure after single and multiple doses of VTX002 with steady-state reached after 4 to 7 days of target-dose exposure

Pharmacodynamics



- Demonstrated consistent, sustained reduction of lymphocytes up to 65% across multiple dose groups

Phase 2 Induction Trial in Moderate-to-Severe Ulcerative Colitis



Trial Design

N=180; 1:1:1

KEY TAKEAWAYS

- Powered for primary endpoint of clinical remission
- Trial may serve as the first of two pivotal trials required for registration

Note: Phase 2 tablet doses of 30mg and 60mg provide comparable VTX002 exposure as Phase 1 suspension doses of 20mg and 40mg, respectively
*Induction and OLE non-responder dosing includes 7-day titration period followed by 12 weeks of placebo or VTX002 dose

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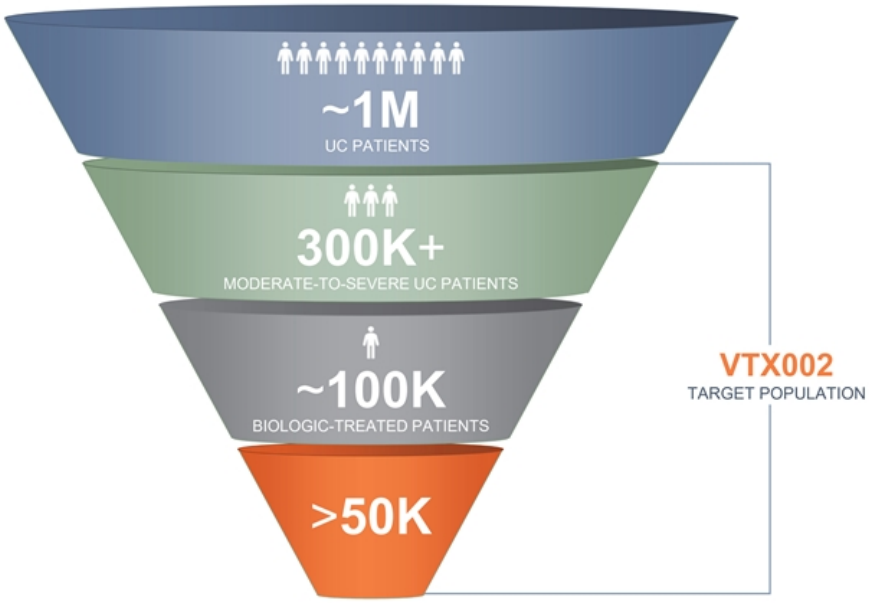
Underpenetrated Market for Biologic Refractory Patients

Addressable UC Patient Population in US



- Existing agents leave room for new treatments
- Novel oral agents may expand penetrance of treated moderate-to-severe UC population beyond current ~25-30%
- S1P well positioned to emerge as leading oral therapeutic class based on its attractive class efficacy/safety profile

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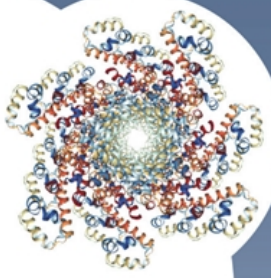

SELECTIVE NLRP3 INFLAMMASOME INHIBITORS for systemic and CNS indications

Rationale for Targeting the NLRP3 Inflammasome

NLRP3 Inflammasome Inhibitors Target IL-1β, a Key Driver of Inflammatory Disease

In vivo Evidence

- The NLRP3 inflammasome can become overactive in the presence of persistent tissue damage or crystal deposits
- Inflammasome activation results in release of IL-1β & IL-18 recruiting neutrophils and driving Th17 response
- This leads to pyroptosis and further tissue damage

Genetic Evidence

- Gain-of-function mutations in the NLRP3 gene, associated with certain severe orphan inflammatory diseases, are classified as cyropyrin-associated periodic syndromes (CAPS)

Clinical Validation of Downstream Target

- IL-1β signaling, downstream of inflammasome activation, is a clinically-validated, anti-inflammatory target with biologics
- Ilaris® ($873M sales in 2020) approved for CAPS and other orphan periodic fever syndromes

NLRP3 = NOD-like receptor family, pyrin domain-containing protein 3; IL-1β = interleukin-1β
Sources: Novartis annual report; Ilaris prescribing information

NLRP3 Inhibitor Program Summary

Peripheral NLRP3 Inhibitor: VTX2735

- Selective NLRP3 inhibitor
- Well tolerated in GLP safety and tox assessment
- Phase 1 completed with attractive safety/tolerability profile and evidence of pharmacodynamic activity
- Phase 2 trial in CAPS planned Q1 2023; additional indications are being evaluated

CNS NLRP3 Inhibitor: VTX3232

- Selective compounds generated with high CNS bioavailability
- Novel and proprietary lead series
- Plan to file IND in Q1 2023
- Potential to be first, truly CNS-directed NLRP3 inhibitor to enter clinic

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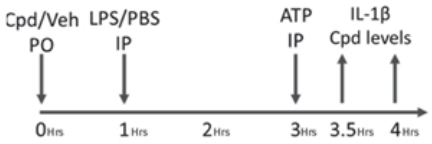
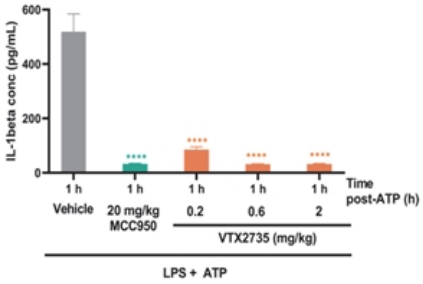
Source: Ventyx internal data

VTX2735 Is a Selective & Orally Bioavailable NLRP3 Inhibitor

Mouse Pharmacodynamic Assay



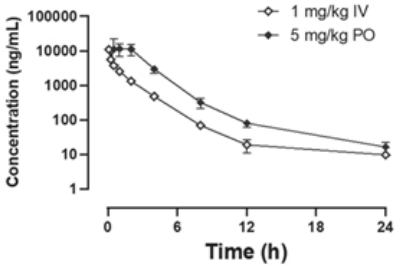


In Vitro Potency & Selectivity

		IL-1β IC_{50} (nM)
On Target	human monocytes	2
	human whole blood	75
Off Target	AIM2	>10000
	NLRC4	>10000
	NF-κB	>10000

Non-Human Primate PK

IV Clearance: 1.6 mL/min/kg;
Oral Bioavailability: 80%



KEY TAKEAWAYS

- Well-tolerated preclinically in IND-enabling GLP studies
- Oral bioavailability (80%) in NHP and dose-proportional exposure that predicts potential for wide safety margins based on PK/PD modeling

Source: Ventyx internal data; MCC950 is an NLRP3 inhibitor and a control compound used in in vitro and in vivo studies

Summary of VTX2735 Phase 1 Results

Excellent Safety and Pharmacodynamic Activity

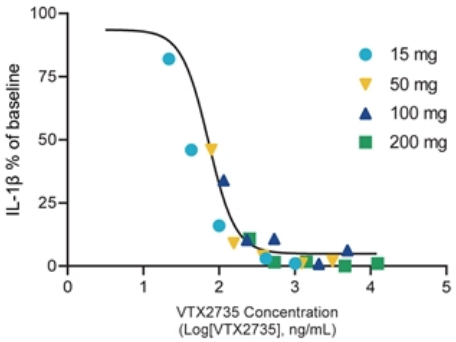
Safety
- All AEs considered mild
- No LFT abnormalities
- No dose-related increase in frequency of AEs observed

PK
- Dose-proportionate increases in exposure (C_{max} and AUC)

PD
- Robust dose and concentration-dependent suppression of IL-1β *ex vivo*

Target Coverage
- Ability to cover IL-1β IC_{50}, IC_{90}
- Potential wide therapeutic window (safe across wide exposure range)

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



Data from Day 10 of Phase 1 MAD, 1 to 8h post-dose
Ex vivo LPS plus ATP-mediated IL-1β release assay

*PK: Pharmacokinetics; PD: Pharmacodynamics

VTX2735 Has 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); CAPS=Cryopyrin-Associated Periodic Syndromes

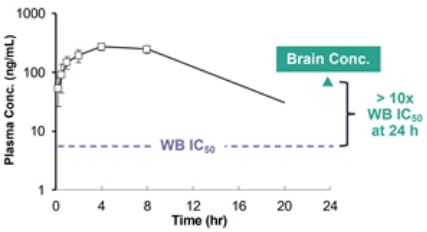
CNS-Penetrant NLRP3 Inhibitor VTX3232

In Vitro Potency & Selectivity

		IL-1β IC_{50} (nM)
NLRP3	huWB	13
AIM2	BMDM	>10000
NLRC4		>10000
NF-kb		>10000

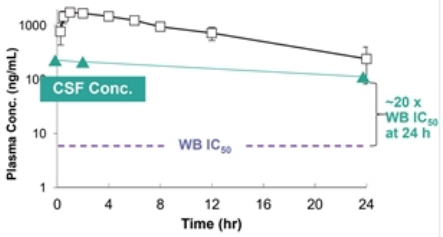
Rat PK (PO, 5mg/kg)

T½ = 4.4 h; Oral Bioavailability = 75%



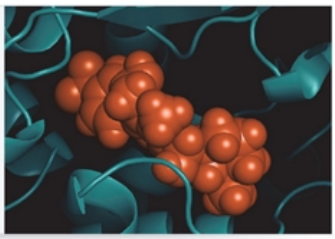
Dog PK (PO, 5mg/kg)

T½ = 8 h; Oral Bioavailability = 100%



KEY TAKEAWAYS

- Novel, potent, brain-penetrant inhibitor of NLRP3
- **13 nM IC_{50} in human whole blood IL-1β release assay**
- Unique structural chemotype vs. peripheral NLRP3 inhibitors
- Provisional application filed June 2021
- Phase 1 start in Q1 2023



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Source: Ventyx internal data

NLRP3 Program Clinical Development Plan

Our Comprehensive NLRP3 Portfolio Targets 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

Investment Highlights

EFFICIENT & PRODUCTIVE IMMUNOLOGY PLATFORM

- **Internal R&D engine** designed to generate candidates to address autoimmune and inflammatory diseases with high unmet need
- **100% commercial rights** to entire portfolio; long patent life for all product candidates

POTENTIALLY DIFFERENTIATED MEDICINES

- **Multiple selective, oral, small molecule product candidate portfolio**:
  - **VTX958:** allosteric TYK2 inhibitor for multiple autoimmune indications
  - **VTX002:** peripherally-restricted S1P1R modulator for ulcerative colitis
  - **VTX2735:** peripheral NLRP3 inhibitor for multiple autoimmune indications
  - **VTX3232:** CNS-targeted NLRP3 inhibitor for multiple neurodegenerative indications

TARGET MAJOR INFLAMMATORY & IMMUNOLOGY DISEASE MARKETS

- **Our portfolio can address I&I markets**, such as psoriasis, IBD, and other indications
- Opportunity to disrupt existing markets dominated by biologics with varying degrees of efficacy and safety in order to:
  - ✓ Capture refractory patients
  - ✓ Expand market share of moderate-to-severe patient populations with patient-friendly oral therapy

CAPITAL-EFFICIENT BUSINESS MODEL

- **Cash, cash equivalents and marketable securities balance** of $412.4M expected to provide cash runway into 2025


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