VTX958 Phase 2 Plaque Psoriasis Results

November 6, 2023

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Forward Looking Statements

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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.

Introduction

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

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Phase 2 Plaque Psoriasis Trial

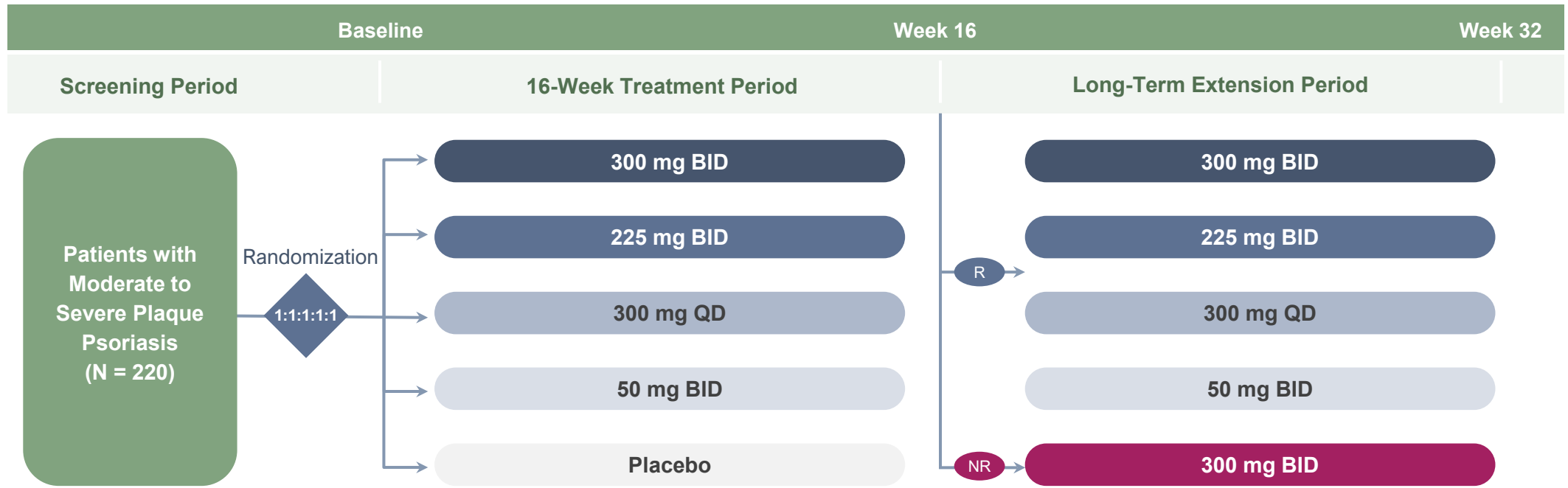
Trial Design Overview

Key eligibility criteria:

- Adult participants with moderate to severe plaque psoriasis as defined by PASI score ≥ 12, sPGA score ≥ 3 and BSA ≥ 10%.
- History of plaque psoriasis for ≥ 6 months and deemed eligible by investigator for phototherapy or systemic therapy.

Endpoints:

- **Primary Endpoint:** Proportion of participants achieving PASI 75 at Week 16.
- **Secondary Endpoints:** Proportion achieving PASI 90, PASI 100, sPGA 0/1. Change from baseline in PASI, DLQI, BSA.



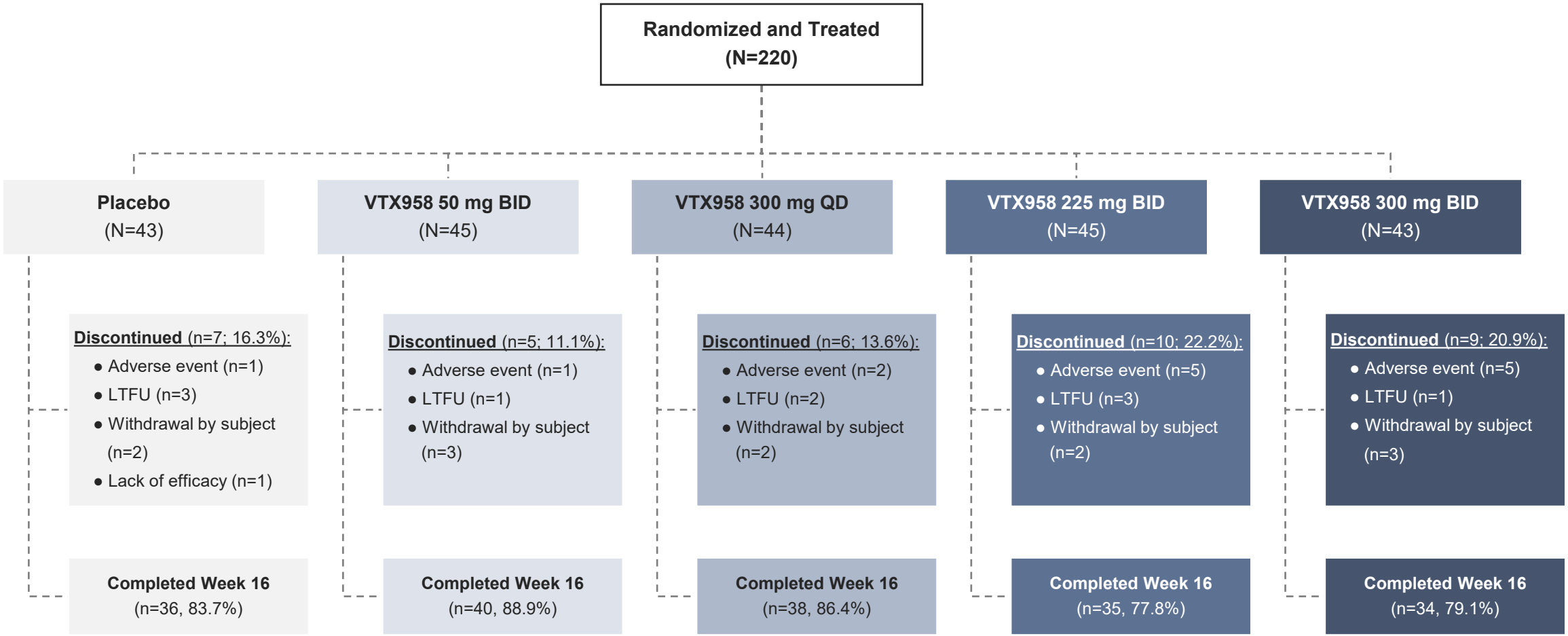
Note: NCT05655299. N = 220 represents number of participants randomized and treated. PASI: Psoriasis Area and Severity Index; sPGA: static Physician's Global Assessment; BSA: Body Surface Area; DLQI: Dermatology Life Quality Index; R: Responder (per PASI 75); NR: Non-responder (per PASI 75). BID: twice daily; QD: once daily.

Baseline Demographics and Disease Characteristics

	Placebo (N=43)	VTX958 50 mg BID (N=45)	VTX958 300 mg QD (N=44)	VTX958 225 mg BID (N=45)	VTX958 300 mg BID (N=43)
Age, years, mean (SD)	44.2 (13.1)	45.7 (13.1)	46.2 (12.7)	45.0 (14.5)	43.5 (13.8)
Male, n (%)	28 (65.1%)	28 (62.2%)	30 (68.2%)	32 (71.1%)	29 (67.4%)
Race, n (%)					
White	33 (76.7%)	40 (88.9%)	38 (86.4%)	41 (91.1%)	39 (90.7%)
Asian	2 (4.7%)	4 (8.9%)	3 (6.8%)	1 (2.2%)	2 (4.7%)
Black/African American	6 (14.0%)	1 (2.2%)	2 (4.5%)	3 (6.7%)	2 (4.7%)
Other	2 (4.7%)	0	1 (2.3%)	0	0
Weight, kg, mean (SD)	90.4 (20.6)	89.0 (17.7)	87.3 (18.8)	86.7 (13.9)	89.2 (17.8)
BMI, kg/m^2, mean (SD)	30.4 (5.7)	30.3 (5.0)	29.1 (5.8)	29.1 (4.6)	29.7 (5.5)
Duration of psoriasis, years, mean (SD)	17.2 (12.9)	17.4 (12.2)	16.1 (11.6)	17.2 (11.7)	18.4 (13.8)
PASI score, mean (SD)	17.6 (6.6)	18.6 (6.2)	17.9 (5.7)	17.7 (6.4)	18.0 (7.1)
BSA, mean (SD)	20.7 (13.3)	21.2 (11.8)	21.1 (10.8)	21.1 (13.9)	21.0 (10.8)
sPGA score, mean (SD)	3.3 (0.4)	3.2 (0.4)	3.2 (0.4)	3.2 (0.4)	3.2 (0.4)
3 (moderate), n (%)	32 (74.4)	34 (75.6)	37 (84.1)	35 (77.8)	33 (76.7)
4 (severe), n (%)	11 (25.6)	11 (24.4)	7 (15.9)	10 (22.2)	10 (23.3)
DLQI score, mean (SD)	13.3 (8.2)	12.8 (6.9)	12.3 (7.0)	11.9 (7.3)	10.9 (6.0)
Prior use of biologic therapy, n (%)	14 (32.6%)	15 (33.3%)	15 (34.1%)	15 (33.3%)	15 (34.9%)

PASI: Psoriasis Area and Severity Index; sPGA: static Physician's Global Assessment; BSA: Body Surface Area; DLQI: Dermatology Life Quality Index; BID: twice daily; QD: once daily.
Source: Ventyx data on file

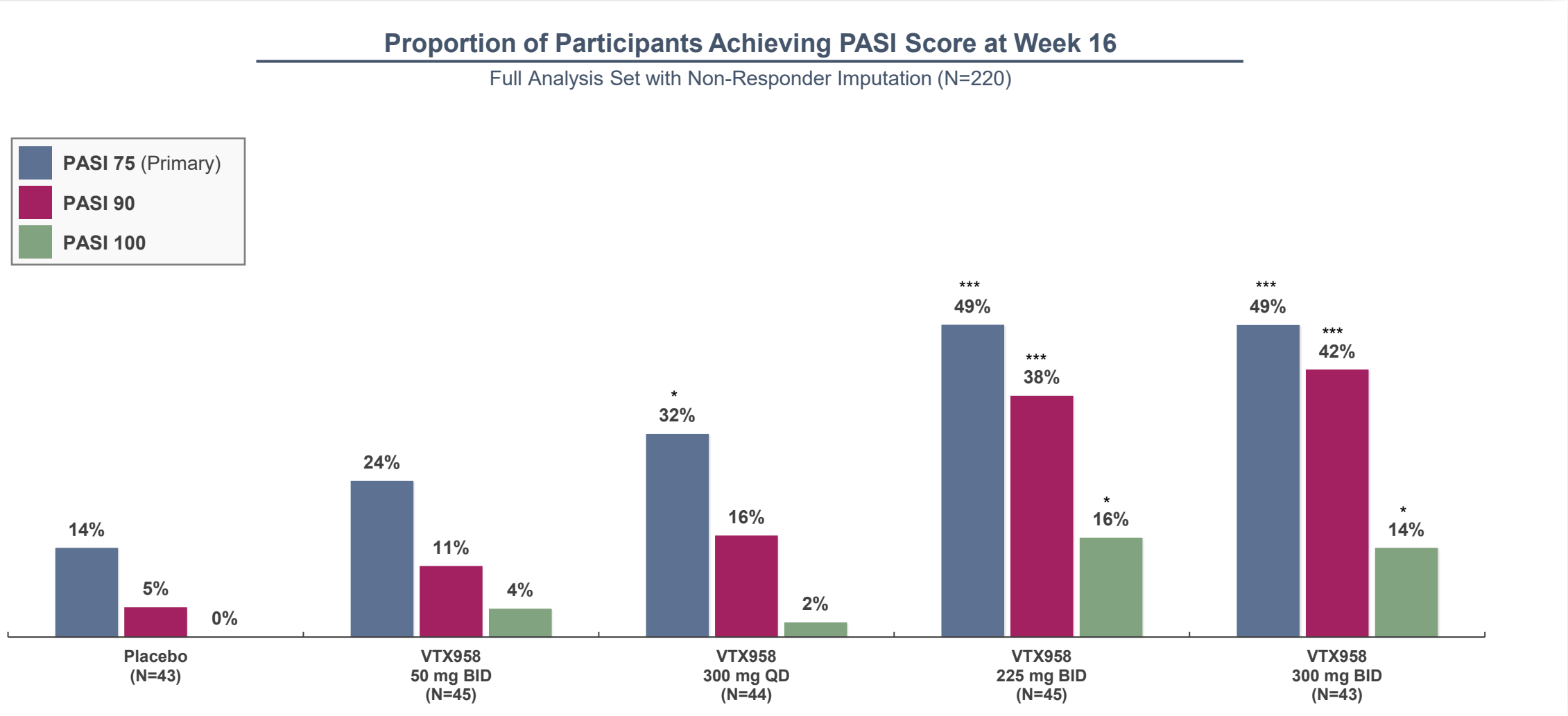
Participant Disposition



LTFU: Lost to follow up; BID: twice daily; QD: once daily. Source: Ventyx data on file.

Proportion of Participants Achieving PASI 75, 90, and 100

Primary and Secondary Endpoints at Week 16



*p<0.05; **p<0.005; ***p<0.001.
P values from Cochran-Mantel-Haenszel test, using prior biologic treatment as a stratification factor.
PASI: Psoriasis Area and Severity Index; BID: twice daily; QD: once daily. Full analysis set with non-responder imputation. Source: Ventyx data on file.

Safety Summary

Summary of Adverse Events through Week 16

Treatment Emergent Adverse Events (TEAE)	Placebo (N=43)	VTX958 50 mg BID (N=45)	VTX958 300 mg QD (N=44)	VTX958 225 mg BID (N=45)	VTX958 300 mg BID (N=43)
Subject with any adverse event, n (%)	**18 (42%)**	**17 (38%)**	**20 (46%)**	**28 (62%)**	**25 (58%)**
Adverse event related to study drug, n (%)	3 (7%)	5 (11%)	7 (16%)	10 (22%)	10 (23%)
AE leading to study discontinuation, n (%)	1 (2%)	1 (2%)	3 (7%)	5 (11%)	5 (12%)
Any Serious Adverse Event (SAE), n (%)*	1 (2%)	1 (2%)	1 (2%)	0	1 (2%)
SAE related to study drug, n (%)	0	0	0	0	0
Most frequent adverse events, n (%) †					
Upper respiratory tract infection	1 (2%)	1 (2%)	3 (7%)	3 (7%)	5 (12%)
Nausea	0	3 (7%)	0	1 (2%)	2 (5%)
Acne	0	0	0	3 (7%)	1 (2%)

*Subjects with SAEs: Myocardial infarction (placebo, unrelated to study drug); vomiting (50 mg BID, unrelated); malignant neoplasm of the ascending colon (300 mg QD, unrelated); acute appendicitis (300 mg BID, unrelated).

† Includes treatment emergent adverse events reported by ≥ 3 participants in any treatment arm, excluding events elicited by laboratory testing.

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Source: Ventyx data on file

Safety Summary

Treatment Emergent Laboratory Shifts with CTCAE Grade ≥3

Treatment Emergent Laboratory Shifts with CTCAE Grade ≥3	Placebo (N=43)	VTX958 50 mg BID (N=45)	VTX958 300 mg QD (N=44)	VTX958 225 mg BID (N=45)	VTX958 300 mg BID (N=43)
Anemia	0	0	0	0	0
Lymphopenia	0	0	0	0	0
Neutropenia	0	0	0	0	0
Thrombocytopenia	0	0	0	0	0
INR increased	0	0	0	0	0
Alanine aminotransferase elevation	0	0	1 (2%)	1 (2%)	2 (5%)
Alkaline phosphatase elevation	0	0	0	0	0
Aspartate aminotransferase elevation	0	0	1 (2%)	0	1 (2%)
Bilirubin elevation	0	0	0	0	0
Gamma-glutamyltransferase elevation	0	0	0	1 (2%)	2 (5%)
Creatine phosphokinase elevation	3 (7%)	1 (2%)	1 (2%)	2 (5%)	1 (2%)
Creatinine elevation	0	0	0	0	0
Cholesterol elevation	0	0	0	0	0
Triglyceride elevation	3 (7%)	1 (2%)	0	3 (7%)	1 (2%)

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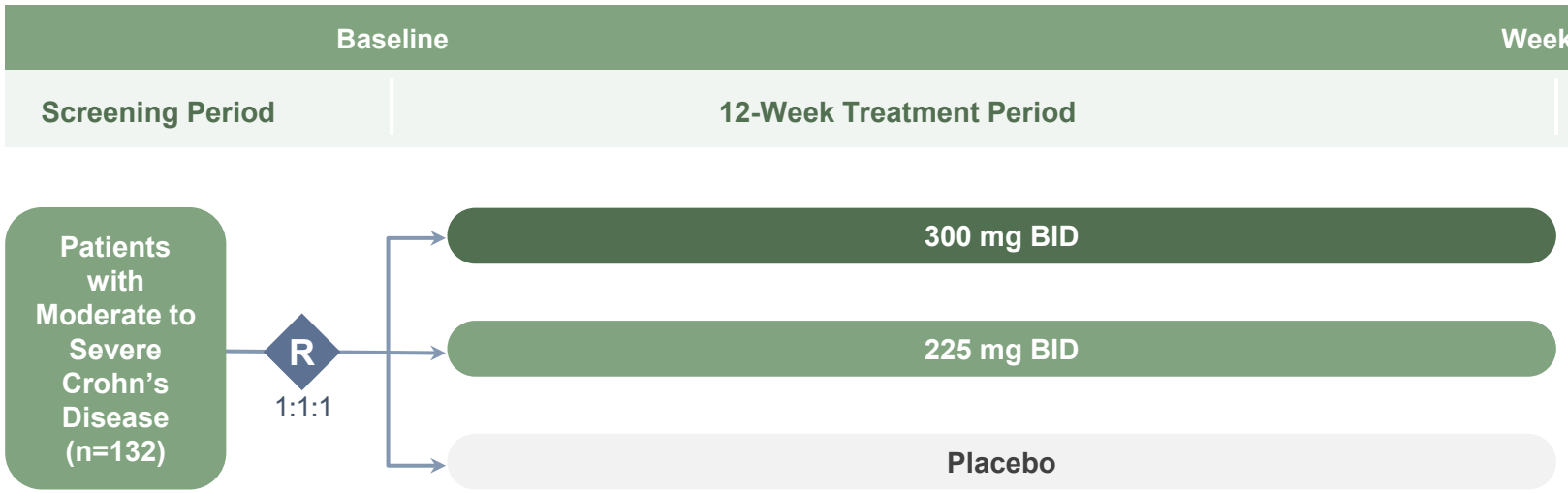
CTCAE: Common Terminology Criteria for Adverse Event (version 5.0); INR: International Normalized Ratio. Source: Ventyx data on file.

VTX958 Program Status and Next Steps

Crohn's Trial to Proceed to Interim Analysis in Q1 2024

- **Phase 2 plaque psoriasis and psoriatic arthritis trials to be terminated**
  - Trial results in PsO do not meet threshold for advancement into Phase 3
- **Phase 2 trial in Crohn's disease to continue with interim efficacy analysis in Q1 2024**
  - Addition of interim analysis to efficiently identify efficacy signal and support go-forward decision



Co-Primary Endpoints (Week 12)

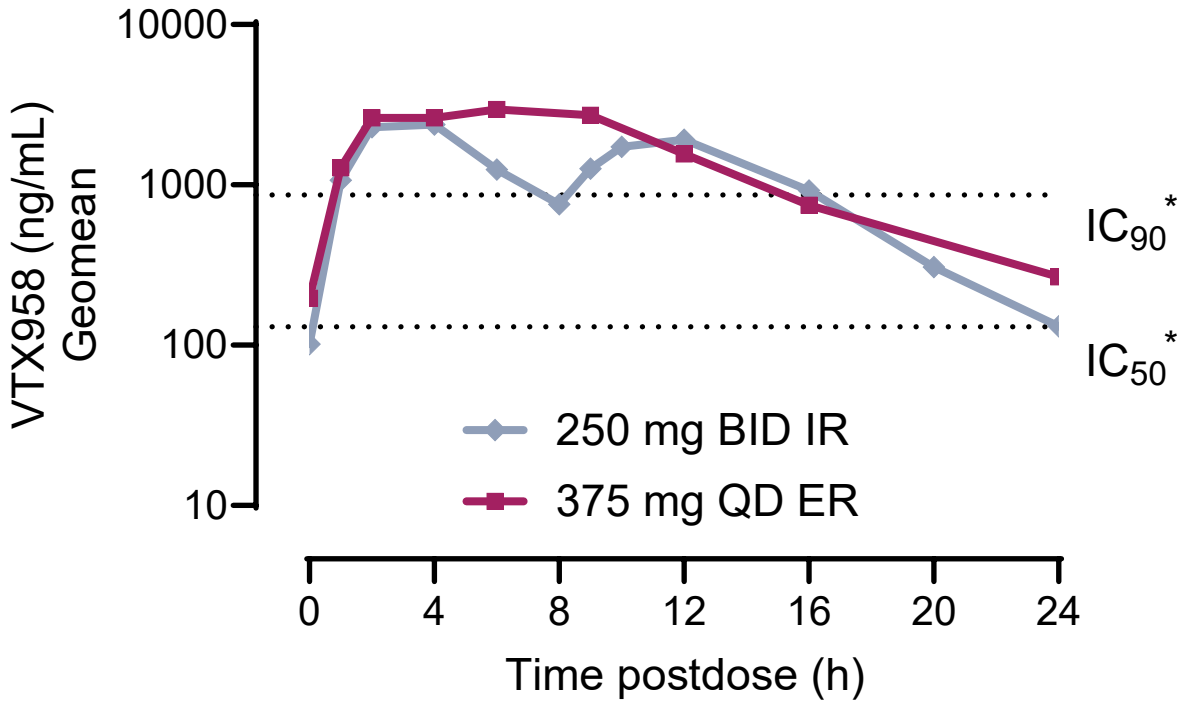
- Change from baseline in mean CDAI score
- Proportion of patients achieving endoscopic response per SES-CD (≥50% reduction from baseline)

SES-CD: Simple Endoscopic Score for Crohn's Disease; CDAI: Crohn's Disease Activity Index

Extended-Release Formulation Update

Once-Daily Formulation Achieved with Target Release Profile

- **Target profile achieved with extended-release (ER) formulation:**
  - QD dose with ER formulation approximates BID exposures observed with immediate release (IR) tablets
  - IC_{90} coverage achieved with 375 mg QD dose for the majority of the day
  - ER formulation allows for lower total dose than IR tablets, with reduction in C_{max} and variability (as %CV)



*IC_{50}/IC_{90} measured by IL-12. CV: Coefficient of variance.

Broad Pipeline of Small Molecule Candidates

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			Crohn's disease (CD)		Phase 2 CD interim analysis **Q1 2024**
S1P1R	VTX002			Ulcerative Colitis		Phase 2 UC OLE update **Q1 2024** Initiate Phase 3 trial **2024**
NLRP3 *Peripheral*	VTX2735			CAPS, other potential indications include CV, dermatologic and rheumatologic diseases		Phase 2 CAPS data update **Q1 2024**
NLRP3 *CNS-penetrant*	VTX3232		Neuroinflammatory diseases			Phase 1 data update **Q1 2024**

Cash, cash equivalents and marketable securities of $300.8M as of September 30, 2023

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Conclusions

Ventyx to Provide Portfolio Updates in Q1 2024

- **Phase 2 plaque psoriasis trial achieved primary and all secondary endpoints**
  - Trial results in PsO fall short of threshold for advancement into Phase 3
  - Phase 2 trials in plaque psoriasis and psoriatic arthritis to be discontinued
- **Ongoing Phase 2 trial of VTX958 in Crohn's disease to proceed**
  - Working with our regulatory advisors, we intend to conduct an interim efficacy analysis in Q1 2024
- **Comprehensive pipeline updates to be provided in the first quarter of 2024:**
  - **VTX002** Phase 2 UC OLE update
  - **VTX958** Crohn's disease interim analysis
  - **VTX2735** Phase 2 CAPS update
  - **VTX3232** Phase 1 data update
- **Cash, cash equivalents, and marketable securities balance of $300.8M as of Sep 30, 2023**

Q&A Session

Ventyx Management Team