STUDY RESULTS SYNOPSIS

Study Title:	A Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of VTX958 in Participants with Moderately to Severely Active Crohn's Disease
Study Number:	VTX958-202
Study Drug:	VTX958 (cenacitinib)
Study Phase:	Phase 2
EudraCT Number:	2022-003365-38
Indication:	Moderately to severely active Crohn's disease
Sponsor:	Ventyx Biosciences, Inc.
First Participant Enrolled:	28 December 2022
Last Participant Last Visit:	20 December 2024

Study Center(s): Total of 105 study sites in 15 countries: Australia, Brazil, Bulgaria, Canada, Czech Republic, Georgia, Germany, Hungary, Israel, Italy, Lithuania, Moldova, Poland, Slovakia, and USA

Number of Participants: *Planned*: 93 participants; *Enrolled*: 109 participants

Test Product, Dose, and Mode of Administration:

Placebo-Controlled 12-Week Induction Treatment Period and 40-Week Maintenance Treatment Period:

VTX958 at 300 mg twice daily (BID) or 225 mg BID administered orally.

Open-Label Extension (OLE) Period:

VTX958 at 300 mg BID administered orally for up to 144 weeks.

Reference Therapy, Dose, and Mode of Administration: For the placebo treatment group in the Induction and Maintenance Treatment Periods, matching placebo was administered orally BID.

No placebo was administered in the OLE Period.

Duration of Study: The maximum study duration for each participant was up to 164 weeks, including a 4-week Screening Period, a 12-week placebo-controlled Induction Treatment Period, 144 weeks total in the Maintenance Treatment and OLE Periods, and 4 weeks of follow-up.

Compliance Statement: This clinical study was conducted in accordance with the International Council for Harmonisation Guideline for Good Clinical Practice (E6), the protocol and with other applicable regulatory requirements.

Publications

Danese S, Jairath V, Sands BE, et al. P1001 Efficacy and safety of an oral tyrosine kinase 2 inhibitor VTX958 in moderately to severely active Crohn's disease: a randomised, double-blind, placebo-controlled, phase 2 trial. Journal of Crohn's and Colitis. 2025;19(Supplement_1):i1853-i1854

Early Termination of the Study

On 29 July 2024, the Sponsor announced the results of the Induction Treatment Period. Following a review of the results from the Induction Treatment Period Analysis, the Sponsor determined that the data were adequate for planning the next phase of clinical development and announced the decision to terminate the study conduct for the Maintenance and Open-Label Extension (OLE) Treatment Periods. The decision to terminate the study was not due to safety concerns.

Study Design/Methodology

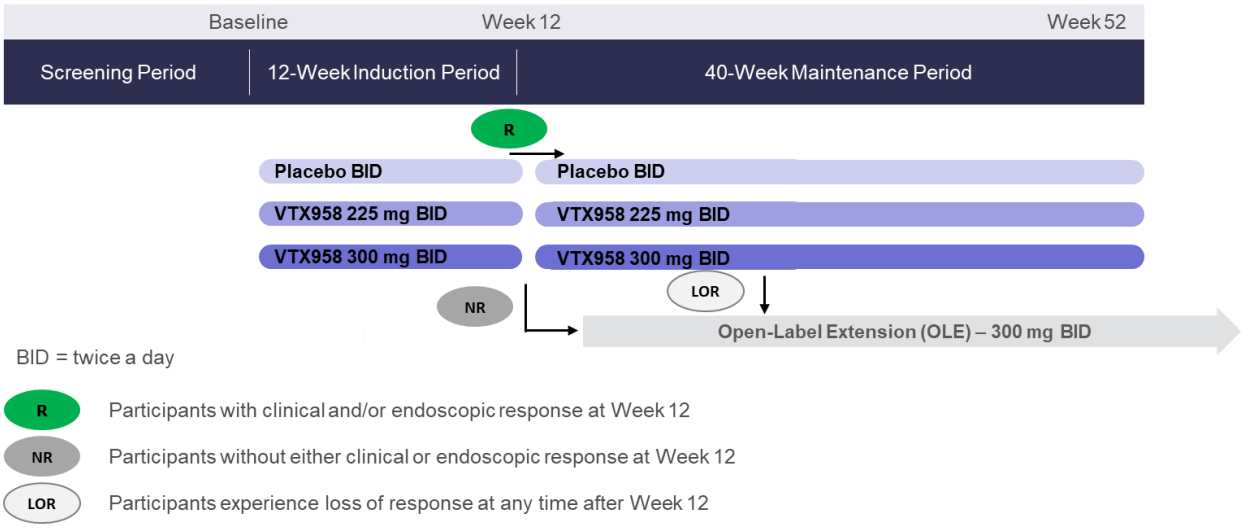
This was a multicenter, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy and safety of VTX958 (225 mg twice daily [BID], 300 mg BID, or placebo) in participants with moderately to severely active Crohn's disease (CD). Approximately 93 eligible patients were planned to be randomized, and randomization was stratified by prior use of biologics for the treatment of CD (yes/no). The study design is presented in Figure 1.

The target population included:

- Participants who have had an inadequate response, loss of response, or intolerance to conventional therapy and are naïve to biologic agents (conventional treatment failed)
- Participants who have had an inadequate response, loss of response, or intolerance to a biologic agent (biologic failed). Participants in this category may have received prior conventional therapy. It was expected that approximately 70% of participants in the study may have had an inadequate response to biologics. The number of patients with prior exposure to biologic therapy targeting interleukin (IL)-12/IL-23 (eg, ustekinumab) to be randomized into this study was capped at 20% of the total number of participants.

Participants who completed the Induction Treatment Period were assessed for response at Week 12 and could continue at their assigned dose in the Maintenance Treatment Period if they had a clinical and/or endoscopic response. Non-responders at Week 12, participants who demonstrated a loss of response any time during the Maintenance Treatment Period, or participants who completed the 40-week Maintenance Treatment Period could receive open-label VTX958 300 mg BID in the OLE Period.

Figure 1: Study Design



Objectives and Endpoints

Objectives	Endpoints
Primary	
• Evaluate the efficacy of VTX958 in achieving reduction in CDAI score at the end of the Induction Treatment Period	• Change from baseline in mean CDAI score at Week 12
Key Secondary	
• Evaluate the efficacy of VTX958 in inducing clinical and symptomatic response and remission at the end of the Induction Treatment Period• • Evaluate the efficacy of VTX958 in inducing endoscopic response and clinical remission at the end of the Induction Treatment Period	• Proportion of participants achieving endoscopic response at Week 12 • Change from baseline in mean SES-CD at Week 12 • Proportion of participants achieving clinical remission at Week 12 • Proportion of participants achieving PRO2 remission at Week 12 • Proportion of participants achieving clinical response at Week 12 • Proportion of participants achieving endoscopic response and clinical remission (in the same participant) at Week 12
Safety	
• Evaluate the safety and tolerability of VTX958	• Incidence and severity of AEs, laboratory abnormalities, and change from baseline in laboratory values

Objectives	Endpoints
	• Incidence of clinically significant vital sign abnormalities and change from baseline

Abbreviations: AE, adverse event; CDAI, Crohn's disease activity index; PRO2, Patient-reported outcome 2; SES-CD, simple endoscopic score in Crohn's disease.

Endpoint Definitions

- Endoscopic response: ≥ 50% reduction in simple endoscopic score in Crohn's disease (SES-CD) score from baseline
- Clinical Remission: Crohn's disease activity index (CDAI) score < 150
- Patient-reported outcome 2 (PRO2) remission: Unweighted CDAI component of daily abdominal pain score ≤ 1 and unweighted CDAI component of daily average stool frequency score ≤ 3
- Clinical response: ≥ 100 points reduction from baseline in CDAI score or CDAI score < 150
- Endoscopic response and clinical remission: ≥ 50% reduction in SES-CD score from baseline and CDAI score < 150

Diagnosis and Main Inclusion Criteria

This study consisted of male or female participants 18 to 75 years of age diagnosed with moderately to severely active CD . defined as CDAI ≥ 220 and ≤ 450 at baseline, and centrally read SES-CD ≥ 6 for patients with ileocolonic or colonic disease, or SES-CD ≥ 4 for patients with isolated ileal disease. Participants were required to have demonstrated inadequate response to, loss of response to, or intolerance to at least 1 of the following: intravenous (IV) or oral systemic corticosteroids; oral locally acting corticosteroids, immunosuppressants, or biologic therapy (e.g., anti-tumor necrosis factor alpha [TNFα] or anti-integrin antibodies). Stable doses of 5-ASA or oral corticosteroid therapy was permitted during study treatment.

Key Statistical Methods:

Analysis Sets

- Full Analysis Set (FAS): The FAS consists of all randomized participants who received at least one dose of study treatment. Participants were analyzed according to the treatment to which they were randomized.
- Safety (SAF) Set: The SAF Set consists of all randomized participants who received at least 1 dose of study treatment. For this set, participants were analyzed according to the treatment received, regardless of the randomization. The SAF Set was used for all safety analyses in the Induction Treatment Period and in combination of study periods.

- Safety-Maintenance Treatment (SAF-MNT) set: The SAF-MNT set includes all participants who received at least 1 dose of study treatment in the Maintenance Treatment Period. The SAF-MNT Set will be used for safety analyses in Maintenance Treatment Period. Participants will be analyzed according to treatment received in the Maintenance Treatment Period.
- Safety-OLE Treatment (SAF-OLE) Set: The SAF-OLE Set includes all participants who received at least 1 dose of study treatment in the OLE Treatment Period. The SAF-OLE Set was used for safety analyses in OLE Treatment Period. Participants were analyzed according to treatment received in the Induction Treatment Period and the OLE Treatment Period.

Primary Endpoint Analysis

The study was designed to show the superiority of VTX958 300 mg to placebo for the primary efficacy endpoint of change from baseline in mean CDAI score at Week 12 of the Induction Treatment Period. The primary efficacy analysis was completed based on the FAS. The hypothesis was to be tested at a 5% level of significance. Testing was done using Mixed Model for Repeated Measures (MMRM) with change from baseline as the dependent variable; prior biologics use for CD as per randomization, disease location per SES-CD at baseline, treatment group, post-baseline visit, treatment group by post baseline visit interaction as fixed effects; the baseline score as a covariate; and participant as a random effect. The differences in the least square means between the treatment groups at Week 12 estimated by the model with 95% confidence interval (CI) was provided.

Key Secondary Endpoint Analyses

The primary analysis of the key secondary endpoints was completed based on the FAS. The null hypothesis was tested at a two-sided 5% level of significance. Testing was done using an adjusted Cochran-Mantel-Haenszel (CMH) test with prior biologics use for CD (yes/no) as per randomization and disease location per SES-CD at baseline as the stratification factors. The CMH chi-square p-value, stratified risk difference ("common" risk difference) with 95% CI using the Newcombe method, Mantel-Haenszel odds ratio, 95% CI for the Mantel-Haenszel odds ratio and Clopper-Pearson exact 95% confidence intervals were reported, along with number and percentage of participants with endoscopic response in each as-randomized treatment group.

Safety Analysis

Safety was assessed through summaries of AEs, clinical laboratory tests, physical exams, other safety parameters. All safety analyses were based on the Safety Set (SAF-OLE for the OLE Period). No statistical inferences were performed on the safety endpoints. All AEs were coded according to the Medical Dictionary for Regulatory Activities (MedDRA) Version 27.0.

Study Results

Participant Disposition

A total of 109 participants were randomized in a 1:1:1 ratio to receive VTX958 225 mg BID, VTX958 300 mg BID, or placebo BID, with 37 participants in each VTX958 treatment group

and 35 participants in the placebo group. Participant disposition for the full study (i.e., all study periods) is presented in Table 1.

Table 1: Participant Disposition (All Randomized Participants)

	Placebo (N=35) n (%)	**VTX958 225 mg (N=37) n (%)**	**VTX958 300 mg (N=37) n (%)**	**All VTX958 (N=74) n (%)**	**Total (N=109) n (%)**
Participants randomized and treated [a]	35 (100)	37 (100)	37 (100)	74 (100)	109 (100)
Participants who completed Induction Treatment Period [a]	30 (85.7)	29 (78.4)	32 (86.5)	61 (82.4)	91 (83.5)
Entered Maintenance Treatment Period from Induction [a, b]	16 (45.7)	20 (54.1)	22 (59.5)	42 (56.8)	58 (53.2)
Entered OLE from Induction [a, b]	11 (31.4)	6 (16.2)	10 (27.0)	16 (21.6)	27 (24.8)
Did not enter Maintenance/OLE from Induction [a, b]	3 (8.6)	3 (8.1)	0	3 (4.1)	6 (5.5)
Participants who discontinued Induction Treatment Period [a, b]	5 (14.3)	8 (21.6)	5 (13.5)	13 (17.6)	18 (16.5)
Reasons for Induction Treatment Period discontinuation [a]					
Lack of Clinical Response	0	1 (2.7)	0	1 (1.4)	1 (0.9)
Disease worsening	3 (8.6)	0	3 (8.1)	3 (4.1)	6 (5.5)
Non-compliance with study schedule	0	1 (2.7)	0	1 (1.4)	1 (0.9)
Protocol Deviation	0	1 (2.7)	0	1 (1.4)	1 (0.9)
Withdrawal of consent	0	2 (5.4)	1 (2.7)	3 (4.1)	3 (2.8)
Adverse Event	2 (5.7)	3 (8.1)	1 (2.7)	4 (5.4)	6 (5.5)
Participants enrolled to Maintenance Treatment Period [a]	16 (45.7)	20 (54.1)	22 (59.5)	42 (56.8)	58 (53.2)
Participants who completed Maintenance Treatment Period [a]	6 (17.1)	8 (21.6)	5 (13.5)	13 (17.6)	19 (17.4)
Participants who completed Maintenance Treatment Period [c]	6 (37.5)	8 (40.0)	5 (22.7)	13 (31.0)	19 (32.8)
Entered OLE from Maintenance [c,d]	5 (31.3)	8 (40.0)	6 (27.3)	14 (33.3)	19 (32.8)
Did not enter OLE from Maintenance [c,d]	11 (68.8)	12 (60.0)	16 (72.7)	28 (66.7)	39 (67.2)
Participants who discontinued Maintenance Treatment Period [c,d]	10 (62.5)	12 (60.0)	17 (77.3)	29 (69.0)	39 (67.2)
Reasons for Maintenance Treatment Period discontinuation [c]					
Loss of response	0	0	2 (9.1)	2 (4.8)	2 (3.4)
Disease worsening	1 (6.3)	0	0	0	1 (1.7)

	Placebo (N=35) n (%)	VTX958 225 mg (N=37) n (%)	VTX958 300 mg (N=37) n (%)	All VTX958 (N=74) n (%)	Total (N=109) n (%)
Lost to Follow-up	1 (6.3)	0	0	0	1 (1.7)
Withdrawal of consent	0	1 (5.0)	1 (4.5)	2 (4.8)	2 (3.4)
Adverse Event	0	1 (5.0)	1 (4.5)	2 (4.8)	2 (3.4)
Study Terminated by Sponsor	8 (50.0)	10 (50.0)	13 (59.1)	23 (54.8)	31 (53.4)
Participants enrolled to OLE Treatment Period [a]	16 (45.7)	14 (37.8)	16 (43.2)	30 (40.5)	46 (42.2)
Entered OLE from Induction [e]	11 (68.8)	6 (42.9)	10 (62.5)	16 (53.3)	27 (58.7)
Entered OLE from Maintenance [e]	5 (31.3)	8 (57.1)	6 (37.5)	14 (46.7)	19 (41.3)
Participants who discontinued OLE Treatment Period [e,f]	16 (100)	14 (100)	16 (100)	30 (100)	46 (100)
Reasons for OLE Treatment Period discontinuation [e]					
Disease worsening	6 (37.5)	2 (14.3)	3 (18.8)	5 (16.7)	11 (23.9)
Investigator decision	0	1 (7.1)	2 (12.5)	3 (10.0)	3 (6.5)
Withdrawal of consent	1 (6.3)	1 (7.1)	1 (6.3)	2 (6.7)	3 (6.5)
Adverse Event	1 (6.3)	0	0	0	1 (2.2)
Study Terminated by Sponsor	8 (50.0)	10 (71.4)	10 (62.5)	20 (66.7)	28 (60.9)

Source: Study VTX958-202 CSR Final Analysis Table 14.1.2.1.ALL
Abbreviations: EDC, electronic data capture; OLE, Open-Label Extension.
[a] Percentages are based on the number of participants randomized and treated in Induction Treatment Period (Full Analysis Set) assigned to the relevant table column.
[b] Information as collected on 'End of Induction Treatment Period' EDC page.
[c] Percentages are based on the number of participants enrolled in the Maintenance Treatment Period (Full Analysis Set) assigned to the relevant table column.
[d] Information as collected on 'End of Maintenance Period' EDC page.
[e] Percentages are based on the number of participants enrolled in the OLE Treatment Period (Full Analysis Set) assigned to the relevant table column.
[f] Information as collected on 'End of Open Label Extension Period' EDC page.

Demographics

Overall, the demographics and baseline characteristics were generally balanced between treatment groups. Demographic and baseline characteristics are summarized in Table 2.

Table 2: Demographics and Baseline Characteristics – Induction Treatment Period (Full Analysis Set)

	Statistic	Placebo (N=35)	VTX958 225 mg (N=37)	VTX958 300 mg (N=37)	All VTX958 (N=74)	Total (N=109)
Age at screening (years)	n	35	37	37	74	109

	Statistic	Placebo (N=35)	VTX958 225 mg (N=37)	VTX958 300 mg (N=37)	All VTX958 (N=74)	Total (N=109)
	Mean (SD)	38.7 (12.80)	41.8 (14.40)	39.3 (13.20)	40.5 (13.78)	39.9 (13.44)
	Q1	28.0	29.0	29.0	29.0	28.0
	Median	39.0	44.0	38.0	42.0	41.0
	Q3	46.0	52.0	50.0	51.0	50.0
	Min - Max	18 - 70	20 - 71	18 - 63	18 - 71	18 - 71
Sex at birth						
Male	n (%)	18 (51.4)	19 (51.4)	20 (54.1)	39 (52.7)	57 (52.3)
Female	n (%)	17 (48.6)	18 (48.6)	17 (45.9)	35 (47.3)	52 (47.7)
Region, Country						
North America	n (%)	7 (20.0)	11 (29.7)	11 (29.7)	22 (29.7)	29 (26.6)
Canada	n (%)	1 (2.9)	1 (2.7)	1 (2.7)	2 (2.7)	3 (2.8)
United States of America	n (%)	6 (17.1)	10 (27.0)	10 (27.0)	20 (27.0)	26 (23.9)
Western Europe	n (%)	6 (17.1)	3 (8.1)	3 (8.1)	6 (8.1)	12 (11.0)
Germany	n (%)	4 (11.4)	2 (5.4)	2 (5.4)	4 (5.4)	8 (7.3)
Italy	n (%)	2 (5.7)	1 (2.7)	1 (2.7)	2 (2.7)	4 (3.7)
Eastern Europe	n (%)	17 (48.6)	14 (37.8)	21 (56.8)	35 (47.3)	52 (47.7)
Bulgaria	n (%)	0	2 (5.4)	2 (5.4)	4 (5.4)	4 (3.7)
Czech Republic	n (%)	4 (11.4)	3 (8.1)	5 (13.5)	8 (10.8)	12 (11.0)
Georgia	n (%)	0	1 (2.7)	0	1 (1.4)	1 (0.9)
Hungary	n (%)	2 (5.7)	1 (2.7)	2 (5.4)	3 (4.1)	5 (4.6)
Moldova	n (%)	0	0	2 (5.4)	2 (2.7)	2 (1.8)
Poland	n (%)	8 (22.9)	6 (16.2)	10 (27.0)	16 (21.6)	24 (22.0)
Slovakia	n (%)	3 (8.6)	1 (2.7)	0	1 (1.4)	4 (3.7)
South America	n (%)	4 (11.4)	5 (13.5)	1 (2.7)	6 (8.1)	10 (9.2)
Brazil	n (%)	4 (11.4)	5 (13.5)	1 (2.7)	6 (8.1)	10 (9.2)
Other	n (%)	1 (2.9)	4 (10.8)	1 (2.7)	5 (6.8)	6 (5.5)
Australia	n (%)	0	2 (5.4)	0	2 (2.7)	2 (1.8)
Israel	n (%)	1 (2.9)	2 (5.4)	1 (2.7)	3 (4.1)	4 (3.7)
Race						
Black or African American	n (%)	3 (8.6)	1 (2.7)	1 (2.7)	2 (2.7)	5 (4.6)
White	n (%)	32 (91.4)	35 (94.6)	35 (94.6)	70 (94.6)	102 (93.6)

	Statistic	Placebo (N=35)	VTX958 225 mg (N=37)	VTX958 300 mg (N=37)	All VTX958 (N=74)	Total (N=109)
Not Reported	n (%)	0	0	1 (2.7)	1 (1.4)	1 (0.9)
Other	n (%)	0	1 (2.7)	0	1 (1.4)	1 (0.9)
Ethnicity						
Hispanic or Latino	n (%)	1 (2.9)	4 (10.8)	1 (2.7)	5 (6.8)	6 (5.5)
Not Hispanic or Latino	n (%)	33 (94.3)	33 (89.2)	35 (94.6)	68 (91.9)	101 (92.7)
Not Reported	n (%)	1 (2.9)	0	1 (2.7)	1 (1.4)	2 (1.8)

Source: Study VTX958-202 CSR Interim Analysis Table 14.1.5.1
Abbreviations: Max, maximum; Min, minimum; Q1, first quartile; Q3, third quartile; SD, standard deviation.

Primary Efficacy Endpoint Results

The primary endpoint of this study was not met. Though changes from baseline to Week 12 in CDAI score were observed in all treatment groups at Week 12 with mean (SD) change from baseline of -123.2 (108.97), -153.6 (109.49), and -119.7 (122.99) for VTX958 300 mg, 225 mg, and placebo, respectively, decreases for VTX958 300 mg and 225 mg doses were not statistically significant ($p > 0.05$) different from placebo (Table 3).

Table 3: Change from Baseline in CDAI Score at Week 12 – Induction Treatment Period (Full Analysis Set)

Timepoints Summary	Placebo (N=35)	VTX958 225 mg (N=37)	VTX958 300 mg (N=37)	All VTX958 (N=74)
Baseline				
Actual values				
n	35	37	37	74
Mean (SD)	319.1 (50.68)	328.2 (56.73)	302.3 (54.96)	315.3 (56.97)
Q1	286.0	291.0	261.0	269.0
Median	314.0	317.0	292.0	305.5
Q3	349.0	383.0	339.0	353.0
Min - Max	220 - 435	207 - 446	228 - 438	207 - 446
Week 12				
Actual values				
n	30	29	32	61
Mean (SD)	198.2 (116.77)	170.7 (91.53)	178.0 (93.98)	174.5 (92.12)
Q1	120.0	106.0	93.0	104.0
Median	205.5	162.0	185.5	171.0

Timepoints Summary	Placebo (N=35)	VTX958 225 mg (N=37)	VTX958 300 mg (N=37)	All VTX958 (N=74)
Q3	310.0	245.0	237.0	245.0
Min - Max	4 - 466	23 - 331	36 - 432	23 - 432
Change from baseline				
N	30	29	32	61
Mean (SD)	-119.7 (122.99)	-153.6 (109.49)	-123.2 (108.97)	-137.6 (109.38)
Q1	-197.0	-250.0	-210.0	-220.0
Median	-127.0	-165.0	-132.0	-147.0
Q3	-49.0	-59.0	-45.0	-57.0
Min - Max	-340 - 171	-382 - 16	-294 - 179	-382 - 179
Difference from Placebo [a]				
LS mean (SE) [b]	-104.3 (18.14)	-134.1 (18.34)	-113.6 (18.03)	-124.5 (12.96)
95% CI	-140.3, -68.3	-170.4, -97.7	-149.4, -77.8	-150.2, -98.8
LS mean difference (SE)		-29.7 (25.46)	-9.3 (24.98)	-19.5 (21.70)
95% CI		-80.2, 20.8	-58.8, 40.3	-62.6, 23.5
p-value		0.2457	0.7112	0.3700

Source: Study VTX958-202 CSR Interim Analysis Table 14.2.1.1
Abbreviations: CD, Crohn's disease; CDAI, Crohn's disease activity index; CI, confidence interval; LS, least squares; Max, maximum; Min, minimum; MMRM, Mixed Model for Repeated Measures; Q1, first quartile; Q3, third quartile; SD, standard deviation; SE, standard error; SES-CD, simple endoscopic score in Crohn's disease.
Baseline is the last measurement prior to the first dose of study treatment.
Participants missing an assessment at the specified analysis visit are not included in the analysis for this visit. Data collected on/after rescue therapy start date will not be included in the analysis for later visits.
[a] LS mean estimates, difference in LS mean estimates (each VTX958 225 mg and VTX958 300 mg groups versus placebo, and all VTX958 versus placebo in 2 separate models) and their 95% CI, and p-values are from a MMRM model including the change from baseline, the prior biologics use for CD per randomization, disease location per SES-CD at baseline, treatment group, post-baseline visit, treatment group-by-post-baseline visit interaction as fixed effects, the baseline score as a covariate, and participants as a random effect.
[b] Results for placebo group are estimated from the model comparing VTX958 225 mg and VTX958 300 mg groups versus placebo.

Key Secondary Efficacy Endpoint Results

In endoscopic key secondary endpoints, nominally significantly greater reductions from baseline in SES-CD were observed at Week 12 for VTX958 300 mg (-2.7) and 225 mg (-3.5) compared to placebo (2.1; $p = 0.0005$ and $p < 0.0001$, respectively), and nominally significantly greater proportions of participants achieved endoscopic response with VTX958 300 mg (32.4%) and 225 mg (24.3%) treatment compared to placebo (5.7%; $p = 0.0066$ and $p = 0.0263$, respectively). The same trend was observed with the proportions of participants achieving the combined endpoint of endoscopic response and clinical remission (18.9% with VTX958 300 mg; 16.2% with VTX958 225 mg; compared with 2.9% with placebo). Overall, higher rates for most

objective outcomes were observed with VTX958 300 mg, including a nominally statistically significant improvement in combined clinical remission and endoscopic response. Results for all key secondary endpoints are summarized in Table 4.

Table 4: Key Secondary Efficacy Endpoints at Week 12 – Induction Treatment Period (Full Analysis Set)

Timepoints Summary	Placebo (N=35)	VTX958 225 mg (N=37)	VTX958 300 mg (N=37)	All VTX958 (N=74)
Proportion of participants achieving endoscopic response				
Participants meeting endpoint [a], n (%)	2 (5.7)	9 (24.3)	12 (32.4)	21 (28.4)
95% CI [b]	0.7, 19.2	11.8, 41.2	18.0, 49.8	18.5, 40.1
Numeric % Difference from Placebo [c]		18.6	26.7	22.7
Odds ratio (95% CI) [d]		5.1 (0.99, 55.18)	7.4 (1.40, 71.60)	6.3 (1.46, 62.56)
Risk differences				
Common (stratified) difference (95% CI) [e]		19.4 (0.38, 35.97)	27.1 (6.67, 43.93)	23.3 (5.55, 35.38)
2-sided p-value [f]		0.0263	0.0066	0.0064
Change from baseline in mean simple endoscopic score in Crohn's disease (SES-CD) [g]				
Change from baseline based on paired segments [h]				
N	30	29	32	61
Mean (SD)	1.1 (6.57)	-3.7 (7.01)	-4.1 (6.11)	-3.9 (6.50)
Q1	-2.0	-6.0	-7.5	-7.0
Median	0.0	-3.0	-3.0	-3.0
Q3	3.0	0.0	0.0	0.0
Min - Max	-11 - 17	-28 - 6	-17 - 7	-28 – 7
Difference from Placebo [i]				
LS mean (SE) [j]	2.1 (0.99)	-3.5 (0.98)	-2.7 (1.00)	-3.1 (0.72)
95% CI	0.1, 4.1	-5.5, -1.5	-4.7, -0.7	-4.5, -1.7
LS mean difference (SE)		-5.6 (1.36)	-4.8 (1.33)	-5.2 (1.16)
95% CI		-8.3, -2.9	-7.5, -2.2	-7.5, -2.9
p-value		<0.0001	0.0005	<0.0001
Proportion of participants achieving clinical remission [k]				
Participants meeting endpoint [l], n (%)	13 (37.1)	14 (37.8)	13 (35.1)	27 (36.5)
95% CI [b]	21.5, 55.1	22.5, 55.2	20.2, 52.5	25.6, 48.5
Numeric % Difference from Placebo [c]		0.7	-2.0	-0.7

Timepoints Summary	**Placebo (N=35)**	**VTX958 225 mg (N=37)**	**VTX958 300 mg (N=37)**	**All VTX958 (N=74)**
Odds ratio (95% CI) [d]		1.1 (0.37, 3.07)	1.0 (0.31, 2.97)	1.0 (0.40, 2.53)
Risk differences				
Common (stratified) difference (95% CI) [e]		1.5 (-20.33, 23.06)	-0.9 (-23.08, 21.03)	-0.1 (-19.68, 18.19)
2-sided p-value [f]		0.8955	0.9347	0.9881
Proportion of participants achieving patient-reported outcome 2 (PRO2) remission				
Participants meeting endpoint [m], n (%)	9 (25.7)	12 (32.4)	8 (21.6)	20 (27.0)
95% CI [b]	12.5, 43.3	18.0, 49.8	9.8, 38.2	17.4, 38.6
Numeric % Difference from Placebo [c]		6.7	-4.1	1.3
Odds ratio (95% CI) [d]		1.5 (0.47, 4.95)	0.9 (0.23, 3.21)	1.1 (0.41, 3.30)
Risk differences				
Common (stratified) difference (95% CI) [e]		8.2 (-12.98, 28.15)	-2.5 (-22.44, 17.40)	2.2 (-16.51, 18.37)
2-sided p-value [f]		0.4461	0.8084	0.8046
Proportion of participants achieving clinical response				
Participants meeting endpoint [n], n (%)	18 (51.4)	19 (51.4)	21 (56.8)	40 (54.1)
95% CI [b]	34.0, 68.6	34.4, 68.1	39.5, 72.9	42.1, 65.7
Numeric % Difference from Placebo [c]		-0.1	5.3	2.6
Odds ratio (95% CI) [d]		1.0 (0.35, 2.75)	1.3 (0.45, 3.72)	1.1 (0.44, 2.61)
Risk differences				
Common (stratified) difference (95% CI) [e]		-0.6 (-22.71, 21.67)	6.3 (-16.55, 28.45)	1.9 (-17.51, 21.28)
2-sided p-value [f]		0.9628	0.6062	0.8572
Proportion of participants achieving endoscopic response and clinical remission (in the same participant)				
Participants meeting endpoint [o], n (%)	1 (2.9)	6 (16.2)	7 (18.9)	13 (17.6)
95% CI [b]	0.1, 14.9	6.2, 32.0	8.0, 35.2	9.7, 28.2
Numeric % Difference from Placebo [c]		13.4	16.1	14.7
Odds ratio (95% CI) [d]		5.2 (0.72, 305.92)	6.4 (0.83, 342.85)	6.2 (0.98, 310.70)
Risk differences				
Common (stratified) difference (95% CI) [e]		13.6 (-5.05, 29.19)	15.8 (-3.63, 31.77)	14.8 (-2.92, 25.68)

Timepoints Summary	Placebo (N=35)	VTX958 225 mg (N=37)	VTX958 300 mg (N=37)	All VTX958 (N=74)
2-sided p-value [f]		0.0590	0.0408	0.0342

Source: VTX958-202 CSR Interim Analysis Tables 14.2.2.1.1.1, 14.2.2.1.2.1, 14.2.2.1.3.1, 14.2.2.1.4.1, 14.2.2.1.5.1, 14.2.2.1.6.1

Abbreviations: ANCOVA, Analysis of Covariance; CD, Crohn's disease; CDAI, Crohn's disease activity index; CI, confidence interval; CMH, Cochran-Mantel-Haenszel; LS, least squares; Max, maximum; Min, minimum; PRO2, Patient-reported outcome 2; Q1, first quartile; Q3, third quartile; SD, standard deviation; SE, Standard error; SES-CD, simple endoscopic score in Crohn's disease.

Note: Baseline is the last measurement prior to the first dose of study treatment.

[a] Endoscopic response: ≥ 50% reduction in SES-CD from baseline; missing assessments and assessments after start of rescue therapy are assumed to be non-responders.

[b] 95% CI for the proportion of participants are calculated using the Clopper-Pearson method.

[c] Numeric difference between VTX958 and Placebo responder rates.

[d] Estimated exact Mantel-Haenszel odds ratio and 95% confidence interval.

[e] Estimated common (stratified) risk difference and 95% confidence interval are from a CMH test, stratified by randomization stratification factor and disease location per SES-CD at baseline, and calculated with Newcombe method.

[f] The two-sided CMH 'general association' p-value (based on table scores) is used to decide if the null hypothesis of no difference in proportion of participants meeting endpoint is rejected.

[g] Participants missing an assessment at the specified analysis visit are not included in the analysis for this visit. Data collected on/after rescue therapy start date will not be included in the analysis for later visits.

[h] SES-CD score with paired segments applied, only participants with an assessment at both baseline and Visit 6 (Week 12) for at least some segment (and without rescue therapy started before the assessment) are included. These values are used for the change from baseline evaluation and in the model.

[i] LS mean estimates, difference in LS mean estimates (each VTX958 225 mg and VTX958 300 mg arms versus placebo, and all VTX958 versus placebo in 2 separate models) and their 95% CI, and p-values are from a ANCOVA model including the change from baseline as the dependent variable, the prior biologics use for CD per randomization, disease location per SES-CD at baseline, treatment group, the baseline score as a covariate.

[j] Results for placebo arm are estimated from the model comparing VTX958 225 mg and VTX958 300 mg arms versus placebo.

[k] All the estimates and analyses are done for each visit separately.

[l] Clinical remission: CDAI score < 150; missing assessments and assessments after start of rescue therapy are assumed to be non-responders.

[m] PRO2 remission: Unweighted CDAI component of daily abdominal pain score ≤ 1 and unweighted CDAI component of daily average stool frequency score ≤ 3; missing assessments and assessments after start of rescue therapy are assumed to be non-responders.

[n] Clinical response: ≥ 100 points reduction from baseline in CDAI score or CDAI score < 150; missing assessments and assessments after start of rescue therapy are assumed to be non-responders.

[o] Endoscopic response and clinical remission: ≥ 50% reduction in SES-CD from baseline (missing assessments and assessments after start of rescue therapy are assumed to be non-responders) and CDAI score < 150 (missing assessments and assessments after start of rescue therapy are assumed to be non-responders).

Safety Results

VTX958 was generally well-tolerated at all tested doses following oral administration in participants with moderate to severe psoriasis in Study VTX958-201. The majority of treatment-emergent adverse events (TEAEs) were of Grade 1 (mild) or Grade 2 (moderate) in severity and considered not related to the study treatment. No TEAEs led to death in any study period.

Induction Treatment Period

During the Induction Treatment Period, TEAEs were reported in a similar proportion of participants in the VTX958 225 mg (24 participants, 64.9%) and placebo (22 participants, 62.9%) groups and fewer participants in the VTX958 300 mg group reported TEAEs (18 participants, 48.6%) (Table 5). Overall, 30 participants (27.5%) experienced TEAEs considered related to CD, which ranged from 24.3 to 31.4% across treatment groups.

The incidence of treatment-emergent serious adverse events (SAEs) was similar across treatment groups with SAEs reported in 4 participants (10.8%) in the VTX958 300 mg group, 5 participants (13.5%) in the VTX958 225 mg group, and 3 participants (8.6%) in the placebo group. An SAE of Guillain-Barre syndrome in 1 participant (2.7%) in the VTX958 225 mg group was considered related to study treatment (ie, assessed as related by the Investigator and possibly related by the Sponsor); this event was also submitted as a suspected unexpected serious adverse reaction (SUSAR) as per regulatory requirements. Incidence of treatment-emergent SAEs is presented in Table 6.

The proportion of participants who experienced at least 1 TEAE leading to study treatment discontinuation was lowest in the VTX958 300 mg group (1 participant [2.7%]), followed by 3 participants (8.1%) in the VTX958 225 mg group, and 4 participants (11.4%) in the placebo group.

Incidence of non-serious TEAEs reported in ≥ 5% of participants in any group is presented in Table 7.

Table 5: Overall Summary of TEAEs – Induction Treatment Period (Safety Set)

Category	Placebo (N=35) n (%)	VTX958 225 mg (N=37) n (%)	VTX958 300 mg (N=37) n (%)	All VTX958 (N=74) n (%)	Total (N=109) n (%)
TEAEs	22 (62.9)	24 (64.9)	18 (48.6)	42 (56.8)	64 (58.7)
Treatment-Emergent SAEs [a]	3 (8.6)	5 (13.5)	4 (10.8)	9 (12.2)	12 (11.0)
Non-serious TEAEs	20 (57.1)	22 (59.5)	18 (48.6)	40 (54.1)	60 (55.0)
TEAEs related to study treatment [b]	11 (31.4)	9 (24.3)	6 (16.2)	15 (20.3)	26 (23.9)
Treatment-Emergent SAEs related to study treatment [a, b]	0	1 (2.7)	0	1 (1.4)	1 (0.9)
TEAEs related to Crohn's disease	11 (31.4)	9 (24.3)	10 (27.0)	19 (25.7)	30 (27.5)
TEAEs by maximum CTCAE grade [c]					
Grade 1: Mild	9 (25.7)	10 (27.0)	10 (27.0)	20 (27.0)	29 (26.6)
Grade 2: Moderate	8 (22.9)	10 (27.0)	4 (10.8)	14 (18.9)	22 (20.2)
Grade 3: Severe	4 (11.4)	4 (10.8)	4 (10.8)	8 (10.8)	12 (11.0)
Grade 4: Life-Threatening	1 (2.9)	0	0	0	1 (0.9)
Grade 5: Death	0	0	0	0	0
Grade 3, 4 or 5	5 (14.3)	4 (10.8)	4 (10.8)	8 (10.8)	13 (11.9)

Category	Placebo (N=35) n (%)	VTX958 225 mg (N=37) n (%)	VTX958 300 mg (N=37) n (%)	All VTX958 (N=74) n (%)	Total (N=109) n (%)
TEAEs leading to study treatment discontinuation	4 (11.4)	3 (8.1)	1 (2.7)	4 (5.4)	8 (7.3)
TEAEs leading to study treatment discontinuation related to study treatment	2 (5.7)	2 (5.4)	1 (2.7)	3 (4.1)	5 (4.6)
TEAEs leading to study treatment interruption	4 (11.4)	2 (5.4)	4 (10.8)	6 (8.1)	10 (9.2)
TEAEs leading to study treatment interruption related to study treatment	2 (5.7)	1 (2.7)	2 (5.4)	3 (4.1)	5 (4.6)
TEAEs leading to discontinuation from study	3 (8.6)	3 (8.1)	1 (2.7)	4 (5.4)	7 (6.4)
TEAEs leading to discontinuation from study related to study treatment	2 (5.7)	2 (5.4)	1 (2.7)	3 (4.1)	5 (4.6)

Source: VTX958-202 CSR Interim Analysis Table 14.3.2.1
Abbreviations: AE, adverse event; CTCAE, common terminology criteria for adverse events; OLE, Open-Label Extension; SAE, serious adverse event; TEAE, treatment-emergent adverse event.
TEAEs are defined as any AE that started or worsened in severity on or after the first dose of study treatment. TEAEs with an onset or worsening on or after the date and time of first study treatment intake during the Induction Treatment Period but prior to last participation in the Induction Treatment Period will be associated with Induction, including AEs which occur between Visit 6 (Week 12) and the Follow-up visit for participants who do not continue to the Maintenance/OLE Treatment Periods. Percentages are based on the number of participants in the analysis set assigned to the relevant table column.
[a] Missing seriousness is counted as serious.
[b] Missing relatedness is counted as related.
[c] Severity is classified using CTCAE, version 5.0. Participants are counted only once at the highest severity. Missing severity is counted as CTCAE Grade 3.

Table 6: Treatment-Emergent SAEs by MedDRA SOC and PT – Induction Treatment Period (Safety Set)

System Organ Class Preferred Term	Placebo (N=35) n (%)	VTX958 225 mg (N=37) n (%)	VTX958 300 mg (N=37) n (%)	All VTX958 (N=74) n (%)	Total (N=109) n (%)
Participants with at least 1 treatment-emergent SAE	3 (8.6)	5 (13.5)	4 (10.8)	9 (12.2)	12 (11.0)
Gastrointestinal disorders	1 (2.9)	4 (10.8)	3 (8.1)	7 (9.5)	8 (7.3)
Crohn's disease	1 (2.9)	3 (8.1)	1 (2.7)	4 (5.4)	5 (4.6)
Abdominal pain	0	1 (2.7)	1 (2.7)	2 (2.7)	2 (1.8)
Diarrhoea haemorrhagic	0	1 (2.7)	0	1 (1.4)	1 (0.9)
Small intestinal obstruction	0	0	1 (2.7)	1 (1.4)	1 (0.9)
Large intestine perforation	1 (2.9)	0	0	0	1 (0.9)

System Organ Class Preferred Term	Placebo (N=35) n (%)	VTX958 225 mg (N=37) n (%)	VTX958 300 mg (N=37) n (%)	All VTX958 (N=74) n (%)	Total (N=109) n (%)
Nervous system disorders	0	1 (2.7)	0	1 (1.4)	1 (0.9)
Guillain-Barre syndrome	0	1 (2.7)	0	1 (1.4)	1 (0.9)
Psychiatric disorders	0	0	1 (2.7)	1 (1.4)	1 (0.9)
Bipolar disorder	0	0	1 (2.7)	1 (1.4)	1 (0.9)
Renal and urinary disorders	0	1 (2.7)	0	1 (1.4)	1 (0.9)
Nephrolithiasis	0	1 (2.7)	0	1 (1.4)	1 (0.9)
Respiratory, thoracic and mediastinal disorders	0	0	1 (2.7)	1 (1.4)	1 (0.9)
Asthma	0	0	1 (2.7)	1 (1.4)	1 (0.9)
Hepatobiliary disorders	1 (2.9)	0	0	0	1 (0.9)
Hepatic function abnormal	1 (2.9)	0	0	0	1 (0.9)
Infections and infestations	3 (8.6)	0	0	0	3 (2.8)
Escherichia sepsis	1 (2.9)	0	0	0	1 (0.9)
Influenza	1 (2.9)	0	0	0	1 (0.9)
Rectal abscess	1 (2.9)	0	0	0	1 (0.9)
Septic shock	1 (2.9)	0	0	0	1 (0.9)
Investigations	1 (2.9)	0	0	0	1 (0.9)
Aspartate aminotransferase increased	1 (2.9)	0	0	0	1 (0.9)

Source: Study VTX958-202 CSR Interim Analysis Table 14.3.2.3.1
Abbreviations: MedDRA, Medical Dictionary for Regulatory Activities; PT, preferred term; SAE, serious adverse event; SOC, system organ class; TEAE, treatment-emergent adverse event.
TEAEs are defined as any adverse event that started or worsened in severity on or after the first dose of study treatment. Terms are coded using MedDRA version 27.0.
Percentages are based on the number of participants in the analysis set assigned to the relevant table column.
Participants are counted only once per summarization level.
Adverse events are first sorted by decreasing frequency of SOC in the All VTX958 column, and then within each SOC, by decreasing frequency of PT counts in the All VTX958 column.

Table 7: Non-Serious TEAEs in ≥ 5% of Participants in Any Treatment Group by SOC and PT – Induction Treatment Period (Safety Set)

System Organ Class Preferred Term	Placebo (N=35) n (%)	VTX958 225 mg (N=37) n (%)	VTX958 300 mg (N=37) n (%)	All VTX958 (N=74) n (%)	Total (N=109) n (%)
Participants with at least 1 TEAE	20 (57.1)	22 (59.5)	18 (48.6)	40 (54.1)	60 (55.0)
Gastrointestinal disorders	7 (20.0)	9 (24.3)	7 (18.9)	16 (21.6)	23 (21.1)
Nausea	1 (2.9)	4 (10.8)	2 (5.4)	6 (8.1)	7 (6.4)

System Organ Class Preferred Term	Placebo (N=35) n (%)	VTX958 225 mg (N=37) n (%)	VTX958 300 mg (N=37) n (%)	All VTX958 (N=74) n (%)	Total (N=109) n (%)
Abdominal pain	2 (5.7)	5 (13.5)	0	5 (6.8)	7 (6.4)
Vomiting	0	1 (2.7)	3 (8.1)	4 (5.4)	4 (3.7)
Crohn's disease	2 (5.7)	0	3 (8.1)	3 (4.1)	5 (4.6)
Infections and infestations	6 (17.1)	9 (24.3)	6 (16.2)	15 (20.3)	21 (19.3)
COVID-19	0	3 (8.1)	0	3 (4.1)	3 (2.8)
Influenza	0	1 (2.7)	2 (5.4)	3 (4.1)	3 (2.8)
Upper respiratory tract infection	2 (5.7)	1 (2.7)	2 (5.4)	3 (4.1)	5 (4.6)
Nasopharyngitis	1 (2.9)	2 (5.4)	0	2 (2.7)	3 (2.8)
Skin and subcutaneous tissue disorders	5 (14.3)	5 (13.5)	6 (16.2)	11 (14.9)	16 (14.7)
Rash	0	2 (5.4)	3 (8.1)	5 (6.8)	5 (4.6)
Acne	1 (2.9)	1 (2.7)	3 (8.1)	4 (5.4)	5 (4.6)
General disorders and administration site conditions	0	2 (5.4)	2 (5.4)	4 (5.4)	4 (3.7)
Pyrexia	0	2 (5.4)	0	2 (2.7)	2 (1.8)
Nervous system disorders	4 (11.4)	1 (2.7)	2 (5.4)	3 (4.1)	7 (6.4)
Headache	4 (11.4)	1 (2.7)	1 (2.7)	2 (2.7)	6 (5.5)
Vascular disorders	2 (5.7)	1 (2.7)	0	1 (1.4)	3 (2.8)
Hypertension	2 (5.7)	1 (2.7)	0	1 (1.4)	3 (2.8)

Source: Study VTX958-202 CSR Interim Analysis Table 14.3.2.4.1
Abbreviations: PT, preferred term; SOC, system organ class; TEAE, treatment-emergent adverse event.
TEAEs are defined as any adverse event that started or worsened in severity on or after the first dose of study treatment.
Percentages are based on the number of participants in the analysis set assigned to the relevant table column.
Adverse events are first sorted by decreasing frequency of SOC in the All VTX958 column, and then within each SOC, by decreasing frequency of PT counts in the All VTX958 column.
Participants are counted only once per summarization level.

Maintenance Treatment Period

TEAEs occurred in 29 total participants (50.0%) in the Maintenance Treatment Period, which included 11 participants (50.0%) in the VTX958 300 mg group, 8 participants (40.0%) in the VTX958 225 mg group, and 10 participants (62.5%) in the placebo group (Table 8). Overall, 8 participants (13.8%) experienced TEAEs considered related to CD, which ranged from 9.1 to 31.3% of participants across treatment groups.

Treatment-emergent SAEs occurred in 2 total participants (3.4%), with 1 participant each in the VTX958 225 mg group (5.0%) and placebo group (6.3%) (Table 9). None of the SAEs were reported as related to study treatment.

TEAEs leading to study treatment discontinuation were reported in 2 total participants (3.4%) with 1 participant each in the VTX958 treatment groups.

Incidence of non-serious TEAEs reported in ≥ 2 participants in any group is presented in Table 10.

Table 8: Overall Summary of TEAEs – Maintenance Treatment Period (Safety Set-MNT)

Category	Placebo (N=16) n (%)	VTX958 225 mg (N=20) n (%)	VTX958 300 mg (N=22) n (%)	All VTX958 (N=42) n (%)	Total (N=58) n (%)
TEAEs	10 (62.5)	8 (40.0)	11 (50.0)	19 (45.2)	29 (50.0)
Treatment-Emergent SAEs [a]	1 (6.3)	1 (5.0)	0	1 (2.4)	2 (3.4)
Non-serious TEAEs	10 (62.5)	8 (40.0)	11 (50.0)	19 (45.2)	29 (50.0)
TEAEs related to study treatment [b]	3 (18.8)	1 (5.0)	4 (18.2)	5 (11.9)	8 (13.8)
Treatment-Emergent SAEs related to study treatment [a, b]	0	0	0	0	0
TEAEs related to Crohn's disease	5 (31.3)	1 (5.0)	2 (9.1)	3 (7.1)	8 (13.8)
TEAEs by maximum CTCAE grade [c]					
Grade 1: Mild	5 (31.3)	4 (20.0)	7 (31.8)	11 (26.2)	16 (27.6)
Grade 2: Moderate	4 (25.0)	3 (15.0)	3 (13.6)	6 (14.3)	10 (17.2)
Grade 3: Severe	1 (6.3)	1 (5.0)	1 (4.5)	2 (4.8)	3 (5.2)
Grade 4: Life-Threatening	0	0	0	0	0
Grade 5: Death	0	0	0	0	0
Grade 3, 4 or 5	1 (6.3)	1 (5.0)	1 (4.5)	2 (4.8)	3 (5.2)
TEAEs leading to study treatment discontinuation	0	1 (5.0)	1 (4.5)	2 (4.8)	2 (3.4)
TEAEs leading to study treatment discontinuation related to study treatment	0	0	0	0	0
TEAEs leading to study treatment interruption	2 (12.5)	1 (5.0)	2 (9.1)	3 (7.1)	5 (8.6)
TEAEs leading to study treatment interruption related to study treatment	1 (6.3)	0	0	0	1 (1.7)
TEAEs leading to discontinuation from study	0	1 (5.0)	1 (4.5)	2 (4.8)	2 (3.4)
TEAEs leading to discontinuation from study related to study treatment	0	0	0	0	0

Source: Study VTX958-202 CSR Final Analysis Table 14.3.2.1.MNT
Abbreviations: AE, adverse event; CTCAE, common terminology criteria for adverse events; MNT, Maintenance; OLE, Open-Label Extension; SAE, serious adverse event; TEAE, treatment-emergent adverse event.
TEAEs related to the Maintenance Treatment Period are defined as any AE that started or worsened in severity after the end of the Induction Treatment Period through to last participation in the Maintenance Treatment Period, including AEs which occurred between the last visit in the Maintenance and Follow-up visit for participants who do not continue to the OLE Treatment Period.

[a] Missing seriousness is counted as serious.
[b] Missing relatedness is counted as related.
[c] Severity is classified using CTCAE, version 5.0. Participants are counted only once at the highest severity. Missing severity is counted as CTCAE Grade 3.

Table 9: Treatment-Emergent SAEs by MedDRA SOC and PT – Maintenance Treatment Period (Safety Set-MNT)

System Organ Class Preferred Term	Placebo (N=16) n (%)	VTX958 225 mg (N=20) n (%)	VTX958 300 mg (N=22) n (%)	All VTX958 (N=42) n (%)	Total (N=58) n (%)
Participants with at least 1 treatment-emergent SAE	1 (6.3)	1 (5.0)	0	1 (2.4)	2 (3.4)
Gastrointestinal disorders	0	1 (5.0)	0	1 (2.4)	1 (1.7)
Crohn's disease	0	1 (5.0)	0	1 (2.4)	1 (1.7)
Infections and infestations	1 (6.3)	0	0	0	1 (1.7)
Gastroenteritis	1 (6.3)	0	0	0	1 (1.7)

Source: Study VTX958-202 CSR Final Analysis Table 14.3.2.3.1.MNT
Abbreviations: AE, adverse event; MNT, Maintenance; OLE, Open- Label Extension; PT, preferred term; SAE, serious adverse event; SOC, system organ class; TEAE, treatment-emergent adverse event.
TEAEs related to the Maintenance Treatment Period are defined as any AE that started or worsened in severity after the end of the Induction Treatment Period through to the last participation in the Maintenance Treatment Period, including AEs which occurred between the last visit in the Maintenance Treatment Period and the Follow-up visit for participants who do not continue to the OLE Treatment Period.
Percentages are based on the number of participants in the analysis set assigned to the relevant table column.
Adverse events are first sorted by decreasing frequency of SOC in the All VTX958 column, and then within each SOC, by decreasing frequency of PT counts in the All VTX958 column.
Participants are counted only once per summarization level.

Table 10: Non-Serious TEAEs in ≥ 2 Participants in Any Treatment Group by SOC and PT – Maintenance Treatment Period (Safety Set – MNT)

System Organ Class Preferred Term	Placebo (N=16) n (%)	VTX958 225 mg (N=20) n (%)	VTX958 300 mg (N=22) n (%)	All VTX958 (N=42) n (%)	Total (N=58) n (%)
Participants with at least 1 TEAE	10 (62.5)	8 (40.0)	11 (50.0)	19 (45.2)	29 (50.0)
Infections and infestations	6 (37.5)	4 (20.0)	10 (45.5)	14 (33.3)	20 (34.5)
Nasopharyngitis	1 (6.3)	2 (10.0)	2 (9.1)	4 (9.5)	5 (8.6)
Upper respiratory tract infection	0	1 (5.0)	3 (13.6)	4 (9.5)	4 (6.9)
COVID-19	3 (18.8)	1 (5.0)	1 (4.5)	2 (4.8)	5 (8.6)
Gastrointestinal disorders	5 (31.3)	2 (10.0)	2 (9.1)	4 (9.5)	9 (15.5)
Crohn's disease	1 (6.3)	0	2 (9.1)	2 (4.8)	3 (5.2)

Source: Study VTX958-202 CSR Final Analysis Table 14.3.2.4.1.MNT
Abbreviations: AE, adverse event; MNT, maintenance; OLE, open-label extension; PT, preferred term; SOC, system organ class; TEAE, treatment-emergent adverse event.

TEAEs related to Maintenance Treatment Period are defined as any AE that started or worsened in severity after the end of Induction Treatment Period through to last participation in the Maintenance Treatment Period, including AEs which occurred between last visit in Maintenance and Follow-up visit for participants who do not continue to the OLE Treatment Period.
Percentages are based on the number of participants in the analysis set assigned to the relevant table column.
Adverse events are first sorted by decreasing frequency of SOC in the All VTX958 column, and then within each SOC, by decreasing frequency of PT counts in the All VTX958 column.
Participants are counted only once per summarization level.

Open-Label Extension Treatment Period

TEAEs occurred in 20 total participants (43.5%) in the OLE Treatment Period (Table 11). Overall, 11 participants (23.9%) experienced TEAEs considered related to CD.

Treatment-emergent SAEs occurred in 3 total participants (6.5%), none of which were considered to be related to study treatment. (Table 12) TEAEs leading to study treatment discontinuation were reported in 3 total participants (6.5%).

Incidence of non-serious TEAEs reported in ≥ 2 participants overall is presented in Table 13.

Table 11: Overall Summary of TEAEs by Induction Treatment Group – OLE Treatment Period (Safety Set-OLE)

Category	OLE Period Treatment VTX958 300 mg (N=46)				
	Induction Period Treatment				
	Placebo (N=16) n (%)	VTX958 225 mg (N=14) n (%)	VTX958 300 mg (N=16) n (%)	All VTX958 (N=30) n (%)	Total (N=46) n (%)
TEAEs	9 (56.3)	4 (28.6)	7 (43.8)	11 (36.7)	20 (43.5)
Treatment-Emergent SAEs [a]	0	1 (7.1)	2 (12.5)	3 (10.0)	3 (6.5)
Non-serious TEAEs	9 (56.3)	3 (21.4)	7 (43.8)	10 (33.3)	19 (41.3)
TEAEs related to study treatment [b]	2 (12.5)	1 (7.1)	0	1 (3.3)	3 (6.5)
Treatment-Emergent SAEs related to study treatment [a, b]	0	0	0	0	0
TEAEs related to Crohn's disease	3 (18.8)	3 (21.4)	5 (31.3)	8 (26.7)	11 (23.9)
TEAEs by maximum CTCAE grade [c]					
Grade 1: Mild	5 (31.3)	1 (7.1)	1 (6.3)	2 (6.7)	7 (15.2)
Grade 2: Moderate	4 (25.0)	2 (14.3)	4 (25.0)	6 (20.0)	10 (21.7)
Grade 3: Severe	0	1 (7.1)	2 (12.5)	3 (10.0)	3 (6.5)
Grade 4: Life-Threatening	0	0	0	0	0
Grade 5: Death	0	0	0	0	0
Grade 3, 4 or 5	0	1 (7.1)	2 (12.5)	3 (10.0)	3 (6.5)
TEAEs leading to study treatment discontinuation	1 (6.3)	0	2 (12.5)	2 (6.7)	3 (6.5)

Category	OLE Period Treatment VTX958 300 mg (N=46)				
	Induction Period Treatment				
	Placebo (N=16) n (%)	VTX958 225 mg (N=14) n (%)	VTX958 300 mg (N=16) n (%)	All VTX958 (N=30) n (%)	Total (N=46) n (%)
TEAEs leading to study treatment discontinuation related to study treatment	0	0	0	0	0
TEAEs leading to study treatment interruption	0	0	0	0	0
TEAEs leading to study treatment interruption related to study treatment	0	0	0	0	0
TEAEs leading to discontinuation from study	1 (6.3)	0	0	0	1 (2.2)
TEAEs leading to discontinuation from study related to study treatment	0	0	0	0	0

Source: Study VTX958-202 CSR Final Analysis Table 14.3.2.1.OLE
Abbreviations: CTCAE, common terminology criteria for adverse events; OLE, Open-Label Extension; SAE, serious adverse event; TEAE, treatment-emergent adverse event.
TEAEs related to the OLE Treatment Period are defined as any adverse event that started or worsened in severity after the end of the Induction Treatment Period (for participants not enrolled in the Maintenance Treatment Period) or after the end of the Maintenance Treatment Period (for participants enrolled in the Maintenance Treatment Period).
[a] Missing seriousness is counted as serious.
[b] Missing relatedness is counted as related.
[c] Severity is classified using CTCAE, version 5.0. Participants are counted only once at the highest severity. Missing severity is counted as CTCAE Grade 3.

Table 12: Treatment-Emergent SAEs by MedDRA SOC and PT – OLE Treatment Period (Safety Set-OLE)

System Organ Class Preferred Term	OLE Period Treatment VTX958 300 mg (N=46)				
	Induction Period Treatment				
	Placebo (N=16) n (%)	VTX958 225 mg (N=14) n (%)	VTX958 300 mg (N=16) n (%)	All VTX958 (N=30) n (%)	Total (N=46) n (%)
Participants with at least 1 treatment-emergent SAE	0	1 (7.1)	2 (12.5)	3 (10.0)	3 (6.5)
Gastrointestinal disorders	0	1 (7.1)	2 (12.5)	3 (10.0)	3 (6.5)
Crohn's disease	0	0	1 (6.3)	1 (3.3)	1 (2.2)
Small intestinal obstruction	0	0	1 (6.3)	1 (3.3)	1 (2.2)
Subileus	0	1 (7.1)	0	1 (3.3)	1 (2.2)
Cardiac disorders	0	0	1 (6.3)	1 (3.3)	1 (2.2)

System Organ Class Preferred Term	OLE Period Treatment VTX958 300 mg (N=46)				
	Induction Period Treatment				
	Placebo (N=16) n (%)	VTX958 225 mg (N=14) n (%)	VTX958 300 mg (N=16) n (%)	All VTX958 (N=30) n (%)	Total (N=46) n (%)
Palpitations	0	0	1 (6.3)	1 (3.3)	1 (2.2)

Source: Study VTX958-202 CSR Final Analysis Table 14.3.2.3.1.OLE
Abbreviations: MedDRA, Medical Dictionary for Regulatory Activities; OLE, Open-Label Extension; PT, preferred term; SAE, serious adverse event; SOC, system organ class; TEAE, treatment-emergent adverse event.
TEAEs related to the OLE Treatment Period are defined as any adverse event that started or worsened in severity after the end of the Induction Treatment Period (for participants not enrolled in the Maintenance Treatment Period) or after the end of the Maintenance Treatment Period (for participants enrolled in the Maintenance Treatment Period).
Percentages are based on the number of participants in the analysis set assigned to the relevant table column.
Adverse events are first sorted by decreasing frequency of SOC in the All VTX958 column, and then within each SOC, by decreasing frequency of PT counts in the All VTX958 column.
Participants are counted only once per summarization level.

Table 13: Non-Serious TEAEs in ≥ 2 Participants Overall by SOC and PT – OLE Treatment Period (Safety Set - OLE)

System Organ Class Preferred Term	OLE Treatment Period Treatment VTX958 300 mg (N=46)				
	Induction Treatment Period Treatment				
	Placebo (N=16) n (%)	VTX958 225 mg (N=14) n (%)	VTX958 300 mg (N=16) n (%)	All VTX958 (N=30) n (%)	Total (N=46) n (%)
Participants with at least 1 TEAE	9 (56.3)	3 (21.4)	7 (43.8)	10 (33.3)	19 (41.3)
Gastrointestinal disorders	3 (18.8)	2 (14.3)	4 (25.0)	6 (20.0)	9 (19.6)
Abdominal pain	0	1 (7.1)	2 (12.5)	3 (10.0)	3 (6.5)
Crohn's disease	2 (12.5)	0	0	0	2 (4.3)
Infections and infestations	8 (50.0)	0	3 (18.8)	3 (10.0)	11 (23.9)
Bronchitis	1 (6.3)	0	1 (6.3)	1 (3.3)	2 (4.3)
COVID-19	2 (12.5)	0	1 (6.3)	1 (3.3)	3 (6.5)
Gastroenteritis viral	2 (12.5)	0	0	0	2 (4.3)
Nasopharyngitis	2 (12.5)	0	0	0	2 (4.3)
Upper respiratory tract infection	2 (12.5)	0	0	0	2 (4.3)

Source: Study VTX958-202 CSR Final Analysis Table 14.3.2.4.1.OLE
Abbreviations: AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities; OLE, open-label extension; PT, preferred term; SOC, system organ class; TEAE, treatment-emergent adverse event.

TEAEs related to OLE Treatment Period are defined as any adverse event that started or worsened in severity after end of Induction Treatment Period (for participant not enrolled to Maintenance) or after the end of Maintenance Treatment Period (for participants enrolled to the MaintenanceTreatment Period).
Percentages are based on the number of participants in the analysis set assigned to the relevant table column.
Adverse events are first sorted by decreasing frequency of SOC in the All VTX958 column, and then within each SOC, by decreasing frequency of PT counts in the All VTX958 column.
Participants are counted only once per summarization level.

Conclusions

The efficacy and safety data from this study suggest that VTX958 is generally well tolerated in participants with moderately to severely active CD. The overall safety profile was consistent with previously conducted trials of VTX958 and there were no unexpected safety findings from this study. Although the primary endpoint of CDAI change from baseline was not met, higher response rates for most objective outcomes were observed at Week 12 with VTX958 300 mg compared with placebo, including combined endoscopic response and clinical remission, as well as endoscopic response.