CT Application(s) Summary Report

- **Protocol title:** A Phase 3, Randomized, Placebo-controlled, Parallel-group, Multicenter Study to Evaluate the Efficacy and Safety of Guselkumab in Participants with Fistulizing, Perianal Crohn's Disease
- **Protocol code number:** CNTO1959CRD3005
- **Public Registry Number: EU TRIAL NUMBER**: 2023-504740-33
- **Version:** Amendment 4
- **Date:** 08 November 2024

- **Investigational Medicinal Product being tested:**
  Biological ■ **Pharmaceutical** ☐ **Innovative** ☐
  Herbal medicine ☐ **Medical device** ☐

- **Sponsor:** Janssen Scientific and Medical Affairs

- **Indication: :** Fistulizing, Perianal Crohn's Disease

- **Investigator's brochure (IB)**
  Version: 16
  Date: 29 August 2024

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- **EDA approval date:**
  1. Initial approval on Protocol version 1.0 dated 13/10/2021 and IB version 13 dated 14/12/2021 on 13/08/2023
  2. Amendment approval of Protocol Amendment 2 dated 11 January 2023 & IB version 14 dated 29 August 2022 on 25/03/2024
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  4. Amendment approval of Protocol Amendment 4 dated 08 November 2024 and IB Version 16 dated

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29 August 2024 on 21/12/2025

- **Summary of pre-clinical studies:**

❖ **Non-clinical Pharmacology**

1- Guselkumab Binds to Human IL-23

Guselkumab demonstrated specific binding to human IL-23, with no binding observed to related cytokines or subunits, confirming its selectivity for the IL-23 pathway.

2- Guselkumab Inhibits the Biological Activity of IL-23

Non-clinical studies showed that guselkumab effectively inhibited IL-23-mediated cellular signaling and downstream cytokine production in a concentration-dependent manner. These findings were consistently demonstrated across multiple in vitro models and confirmed the ability of guselkumab to suppress IL-23-driven immune responses.

3- Species Cross-reactivity of Guselkumab

Guselkumab exhibited pharmacological activity against IL-23 from selected non-human species, including non-human primates and guinea pigs, while no relevant activity was observed in mice or rats. These results supported the selection of appropriate species for subsequent non-clinical pharmacology, toxicology, and pharmacokinetic evaluations.

4- Safety Pharmacology Evaluations

Safety pharmacology studies in cynomolgus monkeys demonstrated that guselkumab was generally well tolerated following single and repeated intravenous and subcutaneous administration at doses up to 50 mg/kg. No adverse effects were observed on cardiovascular, neurological, behavioral, sensory/motor, or body temperature parameters.

A dedicated cardiovascular safety study identified only mild, non-adverse transient reductions in heart rate and body temperature at the highest dose tested, with no clinically relevant effects on ECG parameters and no treatment-related findings in cardiac or skeletal muscle tissues. The no-observed-adverse-effect level (NOAEL) was established at 50 mg/kg.

❖ **Nonclinical Pharmacokinetics and Immunogenicity**

The pharmacokinetic and immunogenicity profiles of Guselkumab were evaluated in nonclinical studies conducted in cynomolgus monkeys and guinea pigs following single and repeated-dose administration, including reproductive and developmental toxicity studies. These studies characterized systemic exposure, distribution, and immunogenic potential using validated bioanalytical methods for the measurement of Guselkumab concentrations and anti-drug antibodies (ADA).

❖ **The PK and toxicokinetic (TK) studies**

Nonclinical pharmacokinetic and toxicokinetic studies demonstrated that guselkumab exhibits a pharmacokinetic profile consistent with that of IgG-based monoclonal antibodies. Systemic exposure increased approximately proportionally with dose, moderate accumulation was observed following repeated administration, and pharmacokinetic characteristics were generally comparable across routes of administration and between sexes.

Studies in relevant animal species showed placental transfer of guselkumab following repeated administration during pregnancy, while transfer into breast milk was minimal or undetectable. Guselkumab

was immunogenic in animals, with anti-drug antibodies (ADA) detected in a small proportion of treated animals and offspring. In some ADA-positive animals, reduced systemic exposure to guselkumab was observed.

An in **vitro metabolism study** indicated that IL-23 does not affect the activity of major cytochrome P450 enzymes, suggesting a low potential for clinically relevant drug-drug interactions involving CYP450 substrates.

❖ **Non-clinical Toxicology**

The non-clinical toxicology program for Guselkumab included repeat-dose toxicity, reproductive and developmental toxicity, pharmacokinetic, tissue cross-reactivity, serum compatibility, hemolytic potential, and mechanistic toxicity studies conducted in relevant animal species, supported by in vitro assessments.

The available non-clinical safety data provided a comprehensive evaluation of the toxicological profile of Guselkumab. Pivotal safety studies were conducted in compliance with applicable Good Laboratory Practice (GLP) standards and internationally recognized regulatory requirements.

Study Description	Species/Strain or Tissue/Cell Line	Dose/Concentration/ Vehicle	Route/Duration of Dose Administration	Group: Number/Gender
In vitro tissue cross-reactivity	Human tissue and select cynomolgus monkey tissue	2, 50 µg/mL Control: 2, 50 µg/mL Biotin-Human Ig G1λ	in vitro	1 donor/tissue
In vitro tissue cross-reactivity	Human tissue and Cynomolgus monkey tissue	2, 50 µg/mL Control: 2, 50 µg/mL Biotin-Human Ig G1λ	in vitro	3 donors/tissue (human) 1 donor/tissue (monkey)
In vitro tissue cross-reactivity	Cynomolgus monkey (select) tissues	2, 10 and 50 µg/mL Control: Human Ig G1 antibody	in vitro	1 donor/tissue
Single-Dose PK	Cynomolgus monkey	50 mg/kg 1, 10 and 50 mg/kg Vehicle: 10 mM histidine	IV/single dose SC/single dose	50 mg/kg: 3M 1 mg/kg: 3M 10 mg/kg: 3M 50 mg/kg: 3M
5-week/24-week Repeat Dose Toxicity; + 3-month recovery (Phase 2)		Phase 1: 50 mg/kg 10 and 50 mg/kg Control: 0.9% NaCl	IV/weekly for 5 weeks SC/weekly for 5 weeks IV and SC/ once	50 mg/kg: 3M/3F 10 mg/kg: 3M/3F 50 mg/kg: 3M/3F 0 mg/kg: 3M/3F 0, 10, 50 mg/kg:

		injection, USP Phase 2: 10 and 50 mg/kg Control: 0.9% NaCl injection, USP	weekly for 5 weeks SC/once weekly for 24 weeks	3/sex per group plus 2/sex per group (recovery)
ePPND		0, 10, and 50 mg/kg 0.9% NaCl USP	SC/once weekly GD 20-22 to parturition, for approximately 21 weekly doses (ie, GD 160 ±10 days) (+6 months postnatal observations)	19-20F per group (total of 59 pregnant monkeys) + surviving infants
3-week Repeat Dose Toxicity	Dunkin Hartley guinea pig	10, 50 and 100 mg/kg Control: 0.9% NaCl injection, USP	SC/twice weekly for 3 weeks	10 mg/kg: 4M 50 mg/kg: 3M 100 mg/kg: M 0 mg/kg: 4M
Female Fertility		0 and 50 mg/kg Control: 0.9% NaCl, injection, USP	SC/twice weekly 3-weeks prior to estimated GD 0 and through G2D 7.	0 mg/kg: 8F and 8M (untreated) 50 mg/kg: 8F and 8M (untreated)
Female Fertility		0, 25, and 100 mg/kg Control: 0.9% NaCl injection, USP	SC/twice weekly approximately 3-weeks prior to estimated Gestation Day 0 and continued through G2D 7.	mg/kg: 30F and 15M (untreated) 25 and 100 mg/kg: 30F per group and 15M (untreated) per group
Male Fertility		0 and 50 mg/kg Control: 0.9% NaCl, injection, USP	SC/twice weekly approximately 6 weeks prior to the estimated day of mating and continued through the day prior to	0 mg/kg: 8M and 8F (untreated) 50 mg/kg: 8M and 8F (untreated)

			scheduled euthanasia (20 doses administered).	
Male Fertility		0, 25, and 100 mg/kg Control: 0.9% NaCl injection, USP	SC twice weekly approximately/7 weeks prior to the estimated day of mating and continuing until at least 20 doses were administered	0, 25, 100 mg/kg: 25/sex per group
Male Fertility		0, 0, and 100 mg/kg Control: 0.9% NaCl injection, USP	SC twice weekly/ approximately 7 weeks prior to the estimated day of mating through Day 71 (Main study: 21 doses; TK study 20 doses)	25M per group; 25F per group (untreated)
Mechanistic Toxicity		0 and 100 mg/kg (Prefilled syringes; Control: 0.9% NaCl injection, USP	SC twice weekly/ approximately 7 weeks prior to the estimated day of mating to termination on Days 2, 8, and 15 (Minimum 14 doses)	15M per group; 15F per group (untreated)
In vitro compatibility testing	Human serum	21 mg/mL Vehicle: 5% dextrose	in vitro	1 donor
In vitro compatibility testing		65 mg/mL Vehicle: 5% dextrose		
In vitro hemolytic potential	Human blood	21 mg/mL Vehicle: 5% dextrose	in vitro	1 donor
In vitro hemolytic potential		65 mg/mL Vehicle: 5% dextrose		

Guselkumab was generally well tolerated in non-clinical studies, including single-dose, repeat-dose, reproductive and developmental toxicity evaluations conducted in relevant animal species.
No treatment-related mortality or toxicologically significant adverse findings were observed, and no

clinically relevant effects were identified on cardiovascular, clinical pathology, immunological, reproductive, developmental, or local tolerance parameters.
Recovery assessments demonstrated no persistent treatment-related effects.
Reproductive and developmental studies showed no adverse effects on fertility, pregnancy, fetal development, or postnatal development. Although placental transfer was observed, no treatment-related developmental toxicity was identified. Transfer into breast milk was minimal or undetectable.
Guselkumab demonstrated acceptable local tolerance following repeated administration and showed compatibility with human serum without evidence of hemolytic potential. No evidence of immunotoxicity, carcinogenic risk signals, or pre-neoplastic changes was identified in the non-clinical program. Genotoxicity and conventional carcinogenicity studies were not conducted, consistent with current regulatory guidance for biotechnology-derived monoclonal antibodies.

➢ **Overall, the non-clinical data support the pharmacological activity and favorable safety profile of Guselkumab, with no findings that would preclude its clinical use at the investigated exposure levels.**

- **Summary of previous clinical studies:**

Completed and ongoing clinical studies (overview)

Study name	Study objectives
Protocol No. CNTO1959PSO1001 Therapeutic area: Psoriasis Study Start-End Dates: 16 June 2009-11 October 2010	**Primary objective:** Assess the safety and tolerability of guselkumab following: • Single IV and SC doses administered to healthy participants (Part1). • Single SC doses administered to participants with moderate-to-severe psoriasis (Part 2). **Secondary objectives:** • To assess the PK and immunogenicity (antibodies to guselkumab) following single IV and SC doses administered to healthy participants (Part1). • To assess the PK, PD, immunogenicity (antibodies to guselkumab), and clinical response to guselkumab following single SC doses administered to participants with moderate-to-severe psoriasis (Part 2)
Protocol No. CNTO1959PSO1002 Therapeutic area: Psoriasis Study Start-End Dates: 23August 2011-11 April 2013	**Primary objective:** • To assess the safety and tolerability of guselkumab following a single SC dose administered to Japanese participants with moderate-to-severe plaque psoriasis. Secondary objectives: • To assess the PK, immunogenicity (antibodies to guselkumab), and clinical response to guselkumab following single SC doses administered to Japanese participants with moderate-to-severe plaque psoriasis.
Protocol No. CNTO1959PSO1003 Therapeutic area: Psoriasis Study Start - End Dates: 16June2015-31August 2016	Primary objective: • To evaluate the potential effects of a single dose of 200mgguselkumab on the PK of a cocktail of representative probe substrates of CYP isozymes (CYP3A4, CYP2C9, CYP2C19,

	CYP2D6, and CYP1A2) in participants with moderate-to-severe psoriasis. **Secondary objective:** • To assess the safety and tolerability of a single SC dose of 200mg guselkumab and a cocktail of probe drug substrates for CYP isozymes when administered alone or in combination**.**
Protocol No. CNTO1959PSO2001 Therapeutic area: Psoriasis Study Start - End Dates: 25October 2011-5 August 2013	**Primary objectives:** • To evaluate the efficacy of guselkumab in the treatment of participants with moderate-to-severe plaque psoriasis. • To assess the safety and tolerability of guselkumab in participants with moderate-to-severe plaque psoriasis. **Secondary objectives:** • To evaluate the durability of clinical response to different dose levels and dose regimens of guselkumab in plaque psoriasis in order to guide the development of a maintenance regimen for the treatment of psoriasis. • To assess the relative difference of short-term and long-term responses between the adalimumab and guselkumab treatment groups. • To assess the PK and immunogenicity of guselkumab following SC administration in participants with moderate-to-severe plaque psoriasis. • To assess the impact of treatment with guselkumab on the HRQoLin participants with moderate-to-severe plaque psoriasis.
Protocol No. CNTO1959PSO3001 Therapeutic area: Psoriasis Study Start - End Dates: 3 December 2014-17June2020	**Primary objectives:** • To evaluate the efficacy of guselkumab for the treatment of participants with moderate-to-severe plaque-type psoriasis. • To assess the safety and tolerability of guselkumab in participants with moderate-to-severe plaque-type psoriasis. **Secondary objectives:** • To compare the efficacy of guselkumab to adalimumab in participants with moderate-to-severe plaque-type psoriasis. • To evaluate the effect of treatment with guselkumab on other measures of signs and symptoms of psoriasis. • To evaluate the effect of treatment with Guselkumab on HRQoL.
Protocol No. CNTO1959PSO3002 Therapeutic area: Psoriasis Study Start - End Dates: 3 November 2014-1July2020	**Primary objectives:** • To evaluate the efficacy of guselkumab for the treatment of participants with moderate-to-severe plaque-type psoriasis. • To assess the safety and tolerability of guselkumab in participants with moderate-to-severe plaque-type psoriasis. **Secondary objectives:** • To compare the efficacy of guselkumab to adalimumab in participants with moderate-to-severe plaque-type psoriasis.

	• To evaluate the maintenance of response to guselkumab in participants continuing on a 100mgq8w regimen compared with the maintenance of response in participants who have active treatment withdrawn. • To evaluate the effect of treatment with guselkumab on other measures of signs and symptoms of psoriasis. • To evaluate the effect of treatment with Guselkumab on HRQoLand health economic outcomes
Protocol No. CNTO1959PSO3003 Therapeutic area: Psoriasis Study Start - End Dates: 7 October 2014-24May 2016	**Primary objectives:** • To compare the efficacy of the following 2 treatment paradigms in participants who have achieved an inadequate (IGA≥2) response to ustekinumab at Week16: o Switching to guselkumab treatment. o Remaining on ustekinumab treatment. • To assess the safety and tolerability of guselkumab in participants with moderate-to-severe plaque-type psoriasis and an inadequate (IGA≥2) response to ustekinumab at Week16. **Secondary objectives:** • To evaluate the effect of switching to guselkumab on patient-reported signs and symptoms of psoriasis for participants with an inadequate (IGA≥2) response to ustekinumab at Week16. • To assess the PK and immunogenicity of guselkumab after SC administrations in participants with moderate-to-severe plaque-type psoriasis and an inadequate (IGA≥2) response to ustekinumab at Week16
Protocol No. CNTO1959PSO3004 Therapeutic area: Psoriasis Study Start - End Dates: 15 January 2015-8 February 2019	**Primary objective:** • To demonstrate the superiority of guselkumab to placebo in the treatment of participants with moderate-to-severe plaque-type psoriasis. **Secondary objectives:** • To evaluate the safety and tolerability of guselkumabin participants with moderate-to-severe plaque-type psoriasis. • To evaluate the impact of treatment with Guselkumab on HRQoL. • To evaluate the safety and efficacy of long-term exposure of guselkumab. • To evaluate the impact of treatment with guselkumabin the treatment of participants with PsA. • To evaluate the PK, immunogenicity and PK/PD analysis for safety and efficacy outcomes of guselkumab following SC administration in participants with moderate-to-severe plaque-type psoriasis. • To evaluate the recommended dose of guselkumab.
Protocol No. CNTO1959PSO3005 Therapeutic area: Psoriasis Study Start -	**Primary objective:** • To examine descriptively the efficacy of guselkumab in participants

End Dates: 28 January 2015-2 November 2018	with GPP or EP. **Secondary objectives:** • To evaluate the safety and tolerability of guselkumabin participants with GPP or EP. • To evaluate the safety and efficacy of long-term exposure of guselkumab. • To evaluate the PK and immunogenicity following SC administration in participants with GPP or EP.
Protocol No. CNTO1959PSO3006 Therapeutic area: Psoriasis Study Start - End Dates: 1 March 2017-6 February 2018	**Primary objectives:** • To evaluate the efficacy of guselkumab delivered using the PFS-S device in the treatment of participants with moderate-to-severe plaque psoriasis. • To assess the safety and tolerability of guselkumab delivered using the PFS-S device in participants with moderate-to-severe plaque psoriasis. **Secondary objectives:** • To assess the PK and immunogenicity of guselkumab following SC administration using the PFS-S device in participants with moderate-to-severe plaque psoriasis. • To assess usability and acceptability of thePFS-S device.
Protocol No. CNTO1959PSO3008 Therapeutic area: Psoriasis Study Start - End Dates: 13December2016 13December2019	**Primary objectives:** • To compare the efficacy of guselkumab to FAE in systemic treatment-naïve participants with moderate-to-severe plaque psoriasis. • To assess the safety and tolerability of guselkumab in systemic treatment-naïve participants with moderate-to-severe plaque psoriasis. **Secondary objectives:** • Study Parts I and II: to compare improvement of HRQoL and other patient-reported outcomes when systemic treatment-naïve participants with moderate-to-severe plaque psoriasis are treated with guselkumab compared to FAE. • Study Part II: to compare the sustainability of response to treatment when systemic treatment-naïve participants with moderate-to-severe plaque psoriasis are treated with Guselkumab compared to FAE.
Protocol No. CNTO1959PSO3009 Therapeutic area: Psoriasis Study Start - End Dates: 27 April 2017-20 September 2018	**Primary objective:** • To evaluate the efficacy of Guselkumab compared with Secukinumab for the treatment of participants with moderate-to-severe plaque psoriasis. **Secondary objectives:** • To evaluate the safety and tolerability of Guselkumab in participants with moderate-to-severe plaque psoriasis. • To evaluate the PK and immunogenicity of guselkumab after SC administration in participants with moderate-to-severe plaque

	psoriasis.
Protocol No. CNTO1959PSO3011(PROTOSTAR) Therapeutic area: Psoriasis Study Start - End Dates: 12 July 2018-ongoing	**Primary objective:** • To evaluate the efficacy and safety of guselkumab in pediatric participants aged ≥6 through <18 years with chronic plaque psoriasis. **Secondary objectives:** • To evaluate the PK and immunogenicity of guselkumab in pediatric participants aged ≥6 through <18 years with chronic plaque psoriasis. • To evaluate the effect of guselkumab on the dermatologic HRQoL in pediatric participants aged ≥6 through <18 years with chronic plaque psoriasis. • To evaluate maintenance of response in participants who have active treatment withdrawn. • To evaluate the efficacy and safety of retreatment with guselkumab. • To generate clinical usability data and use experience with the PFS-V in pediatric participants with chronic plaque psoriasis and a body weight <70kg.
Protocol No. CNTO1959PSO3012(GUIDE) Therapeutic area: Psoriasis Study Start - End Dates: 7February 2019–ongoing	**Primary objective:** • To demonstrate that super-responders (defined as psoriasis participants who receive on-label guselkumab treatment until Week 20 and response with a PASI score =0 at Weeks 20 and28) maintain control of disease until Week 68 with prolonged treatment intervals of 16 weeks (100 mg q16w). **Secondary objectives:** • To evaluate whether participants with short disease duration (≤2 years) show a more rapid and better guselkumab response compared to participants with longer disease duration and whether participants with shorter disease are more likely to maintain drug-free control of disease after guselkumab withdrawal. To be evaluated in Study Parts 1, 2 and 3. • To evaluate whether different treatment intervals (weeks 28 to 60: guselkumab 100 mg q8w versus guselkumab 100 mg q16w) affect the maintenance of drug-free control of disease after 68 weeks of guselkumab treatment. To be evaluated in Study Part 3. • to evaluate the safety and tolerability of guselkumab in participants with moderate-to-severe plaque-type psoriasis.
Protocol No. CNTO1959PSO3013 Therapeutic area: Psoriasis Study Start - End Dates: 3September2019 30November2021	**Primary objective:** • to evaluate the efficacy of guselkumab for the treatment of palmoplantar psoriasis. **Secondary objectives:** • to evaluate the efficacy of guselkumab in improving general plaque psoriasis in participants with palmoplantar psoriasis. • to evaluate the efficacy of guselkumab in improving clinician

	assessments and disease-related patient-reported QoL measures in participants with palmoplantar psoriasis. • to evaluate the efficacy, patient-reported QoL assessments and other scores in the placebo-crossover group at different timepoints. • To evaluate the maintained efficacy of guselkumab for the treatment of palmoplantar psoriasis. • to evaluate the efficacy of guselkumab in improving work productivity and limitations in participants with palmoplantar psoriasis. • to evaluate safety of guselkumab in participants with palmoplantar psoriasis.
Protocol No. CNTO1959PSO3017 (SPECTREM) Therapeutic area: Psoriasis Study Start -End Dates: 24 Aug 2023 –ongoing	**Primary objective:** • To evaluate the clinical efficacy of guselkumab compared to placebo in participants with low BSA moderate plaque psoriasis with special site involvement. **Secondary objectives:** • To evaluate the efficacy of guselkumab compared with placebo in improving the signs and symptoms of psoriasis and PROs. • To evaluate the safety of guselkumab in participants with low BSA moderate plaque psoriasis with special site involvement.
Protocol No. CNTO1959PSO3018(VISIBLE) Therapeutic area: Psoriasis Study Start -End Dates: 11 July 2022–ongoing	**Primary objective:** • To evaluate the efficacy of Guselkumab treatment vs placebo in skin of color participants with predominant moderate-to-severe body psoriasis or predominant moderate-to-severe scalp psoriasis by assessing improvements in the signs and symptoms of psoriasis. **Secondary objectives:** • To evaluate the efficacy of guselkumab on additional measures of body and scalp psoriasis. • To evaluate the safety of guselkumab in participants with moderate to severe psoriasis. • To evaluate the effect of guselkumab on additional measures of scalp and body psoriasis, QoL, laboratory markers, and psoriasis induced post-inflammatory pigment alteration. • To evaluate PK and immunogenicity of guselkumab. • To evaluate PD effects of guselkumab in psoriasis patients. • To evaluate pharmacogenomic of guselkumab in psoriasis patients.
Protocol No. CNTO1959PSA1001 Therapeutic area: Psoriatic arthritis Study Start -End Dates: 3November 2021-1July2022	**Primary objective:** • To assess the tissue distribution of Guselkumab and risankizumab in healthy participants (Part 1). **Secondary objectives:** • To assess the PK of Guselkumab and risankizumab following SC administration in healthy participants (Part 1).

	• to evaluate the immunogenicity of guselkumab 100 mg SC and Risankizumab 150 mg SC in healthy participants (Part 1).
Protocol No. CNTO1959PSA2001 Therapeutic area: Psoriatic arthritis Study Start -End Dates: 27 March 2015-17January 2017	**Primary objectives:** • to evaluate the efficacy of guselkumab in participants with active PsA by assessing the reduction in signs and symptoms of PsA. • To assess the safety and tolerability of guselkumab in participants with active PsA. • To evaluate the efficacy of guselkumab in improving physical function. • To evaluate the impact of guselkumab on QoL. • To evaluate the efficacy of guselkumab on psoriatic skin lesions. • To evaluate the PK and immunogenicity of guselkumab in participants with active PsA. • To evaluate the PD characteristics of guselkumab with and without MTX in participants with active PsA. • To evaluate the efficacy and safety of guselkumab following 1year of exposure.
Protocol No. CNTO1959PSA2003 Therapeutic area: Psoriatic arthritis Study Start -End Dates: 25 October 2021 -ongoing	**Primary objective**: • To evaluate the efficacy of guselkumab +golimumab combination treatment in participants with active PsA and inadequate response to prior anti-TNFα therapy(ies)by assessing clinical response compared with guselkumab monotherapy. **Secondary objective**: • To evaluate the efficacy of guselkumab +golimumab combination treatment in participants with active PsA and inadequate response to prior anti-TNFα therapy(ies)by assessing the reduction in signs and symptoms of PsA compared with guselkumab monotherapy. • To evaluate the safety of guselkumab +golimumab combination treatment in participants with active PsA compared with guselkumab monotherapy. • To evaluate the PK and immunogenicity of guselkumab +golimumab combination treatment in participants with active PsA compared with guselkumab monotherapy.
Protocol No. CNTO1959PSA3001 Therapeutic area: Psoriatic arthritis Study Start -End Dates: 28 August 2017-14 November 2019	**Primary objective:** • To evaluate the efficacy of guselkumab treatment in participants with active PsA by assessing the reduction in signs and symptoms of PsA. **Secondary objective:** • To assess the following for guselkumab treatment: efficacy in improving psoriatic skin lesions; improvement in physical function; efficacy in improving general and disease-specific HRQoL and

	patient-reported health outcomes; safety; and PK, PD, and immunogenicity.
Protocol No. CNTO1959PSA3002 Therapeutic area: Psoriatic arthritis Study Start -End Dates: 13 July 2017-4December2020	**Primary objective:** • to evaluate the efficacy of guselkumab treatment in participants with active PsA by assessing the reduction in signs and symptoms of PsA. **Secondary objective:** • To assess the following for guselkumab treatment: efficacy in improving psoriatic skin lesions; improvement in physical function; efficacy in improving general and disease-specific HRQoL and patient-reported health outcomes; safety; and PK, PD, and immunogenicity
Protocol No. CNTO1959PSA3003 Therapeutic area: Psoriatic arthritis Study Start -End Dates: 27 March 2019 - 11 November 2020	**Primary objective:** • to evaluate guselkumab efficacy versus placebo in patients with active PsA and an inadequate response to anti-TNFα therapy by assessing the reduction in signs and symptoms of joint disease. **Secondary objectives:** • to assess efficacy in improving physical function. • to assess efficacy in improving general and disease-specific HRQoL and patient-reported health outcomes. • to assess efficacy in improving psoriatic skin lesions. • to assess safety.
Protocol No. CNTO1959PSA3004 Therapeutic area: Psoriatic arthritis Study Start -End Dates: 17 June 2021 - ongoing	**Primary objective:** • To evaluate the efficacy of guselkumab treatment in participants with active PsA by assessing the reduction in signs and symptoms of PsA. **Secondary objectives:** • To evaluate the inhibition of progression of structural damage in participants with active PsA. • to evaluate the safety in participants with active PsA. • to evaluate the PK and immunogenicity in participants with active PsA.
Protocol No. CNTO1959PSA3005 Therapeutic area: Psoriatic arthritis Study Start -End Dates: 10 October 2021-ongoing	**Primary objective:** • To evaluate the efficacy of guselkumab treatment in participants with active PsA and inadequate response and/or intolerance to a prior anti-TNF by assessing the reduction in signs and symptoms of PsA. **Secondary objectives:** • To evaluate the efficacy of guselkumab on additional measures of signs and symptoms of PsA, psoriasis, and patient well-being. • to evaluate the safety of guselkumab in participants with active PsA. • To evaluate the PK and immunogenicity of guselkumab in participants with active PsA
Protocol No. CNTO1275JPA3001 (PSUMMIT-Jr) Therapeutic area:	**Primary objectives:** • To evaluate PK of Ustekinumab and guselkumab in jPsA.

Juvenile psoriatic arthritis Study start date: 30 August 2022 -ongoing	• To evaluate efficacy of ustekinumab and guselkumab in jPsA. **Secondary objectives:** • To evaluate PK of ustekinumab and Guselkumab in jPsA. • To evaluate efficacy of ustekinumab and Guselkumab in jPsA. • To evaluate safety of ustekinumab and Guselkumab in jPsA. • To evaluate immunogenicity of ustekinumab and Guselkumab in jPsA
Protocol No. CNTO1959PPP2001 Therapeutic area: Palmoplantar pustulosis Study Start -End Dates: 14 May 2013-27 September 2014	**Primary objectives:** • To evaluate the efficacy of guselkumab, in the treatment of participants with PPP at Week16. • To assess the safety and tolerability of guselkumab in participants with PPP. **Secondary objectives:** • To assess the PK and immunogenicity of guselkumab following SC administration in participants with PPP. • To assess the impact of treatment with Guselkumab on the HRQoL measurements in participants with PPP at Week16. • To assess the possible time point with maximum clinical response of guselkumab after 2dose injections.
Protocol No. CNTO1959PPP3001 Therapeutic area: Palmoplantar pustulosis Study Start -End Dates: 15 December 2015 -17 July 2018	**Primary objectives:** • To evaluate the efficacy of guselkumab for the treatment of participants with PPP. • To assess the safety and tolerability of guselkumabin participants with PPP. **Secondary objectives:** • To evaluate the effect of treatment with guselkumab on patient-reported signs and symptoms of PPP. • To evaluate the durability of clinical response to different dose levels and dose regimens of guselkumabin PPP. • To evaluate the PK and immunogenicity following SC administration of guselkumab. • To evaluate the effect of treatment with Guselkumab on HRQoL.
Protocol No. CNTO1275ARA2001 Therapeutic area: Rheumatoid arthritis Study Start -End Dates: 13 June 2012-5 May 2014	**Primary objectives:** • To evaluate the efficacy of ustekinumab and guselkumab in reducing the signs and symptoms of disease in participants with active RA despite concomitant MTX therapy. • To evaluate the safety of ustekinumab and guselkumab in this population. **Secondary objectives:** • To evaluate the PK, immunogenicity, and PD of ustekinumab and guselkumab in participants with active RA despite concomitant MTX therapy.

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Protocol No. CNTO1959CRD3001 Therapeutic area: Crohn's disease Study Start -End Dates: 10 May 2018-ongoing	**study objectives (GALAXI-1):** **Primary objectives:** • To evaluate the clinical efficacy of guselkumab in participants with Crohn's disease. • To evaluate the safety of guselkumab. **Secondary objectives:** • To evaluate the dose-response of guselkumab to inform dose selection for the Phase 3 portion of this protocol. • To evaluate the efficacy of guselkumab on endoscopic improvement. • To evaluate the PK, immunogenicity, and PD of guselkumab therapy, including changes in CRP and fecal calprotectin. **Study objectives (GALAXI-2 and GALAXI-3):** **Primary objectives:** • To evaluate the clinical efficacy of guselkumab in participants with Crohn's disease. • To evaluate the safety of guselkumab. **Secondary objectives:** • To evaluate the efficacy of guselkumab on endoscopic improvement. • To evaluate the impact of Guselkumab on HRQoL. • To evaluate the PK, immunogenicity, and PD of guselkumab therapy, including changes in CRP and fecal calprotectin
Protocol No. CNTO1959CRD3003 Therapeutic area: Crohn's disease Study Start -End Dates: 14 August 2020 - ongoing	**Primary objective:** • to evaluate the safety of guselkumab in participants with Crohn's disease. **Secondary objectives:** • To evaluate the efficacy of guselkumab in participants with Crohn's disease. • to evaluate the PK, immunogenicity, and PD of guselkumab, including changes in CRP and fecal calprotectin.
Protocol No. CNTO1959CRD3004(GRAVITI) Therapeutic area: Crohn's disease Study Start -End Dates: 19 January 2022-ongoing	**Primary objective:** • To evaluate the efficacy, including clinical remission and endoscopic response, of guselkumab SC induction. **Secondary objectives:** • to evaluate the efficacy of guselkumab SC across a range of outcome measures. • to evaluate the safety of guselkumab SC.
Protocol No. CNTO1959CRD3005 (FUZION CD) Therapeutic area: Crohn's disease Study Start -End Dates: 26 September 2022-ongoing	**Study objectives:** • To evaluate the clinical efficacy of guselkumab in fistulizing, perianal Crohn's disease. • To assess the overall safety of guselkumab.
Protocol No.	**Primary objective:**

CNTO1959CRD3007(PROGRESS) Therapeutic area: Crohn's disease Study Start -End Dates: 21 February 2023-10 October 2023 (early termination)	• To evaluate the efficacy of guselkumab treatment versus placebo in preventing endoscopic recurrence of Crohn's disease in participants after surgery. **Secondary objectives:** • To evaluate clinical remission without disease recurrence in participants treated with guselkumab versus placebo after surgery. • To evaluate disease recurrence in participants treated with guselkumab versus placebo after surgery. • To evaluate symptoms such as stool frequency and abdominal pain scores in guselkumab versus placebo after surgery. • To evaluate the safety and PK of guselkumab in participants with Crohn's disease in the postoperative period. • The evaluate the efficacy of guselkumab in limiting steroid use and maintaining remission in the postoperative period.
Protocol No. CNTO1959CRD3008(REASON) Therapeutic area: Crohn's disease Study Start -End Dates: 17 April 2024 - ongoing	**Primary objective:** • To evaluate the efficacy of guselkumab in achieving transmural healing based on MaRIA at Week 48. **Secondary objectives**: • Based on MaRIA, to evaluate the efficacy of guselkumab: o in achieving transmural healing at Week 16 and Week 96. o in achieving transmural healing of severe inflammatory lesions. o in achieving transmural healing based on: - MaRIA and endoscopy. - MaRIA and clinical data. - MaRIA and biomarker. - MaRIA and endoscopy and clinical data. o in achieving transmural remission based on MaRIA. o in achieving transmural remission based on MaRIA and endoscopic remission based on SES-CD. o based on global Simple MaRIA score over time. o in eliminating the need for corticosteroids while maintaining disease control based on MRE assessed transmural remission. • Based on IUS, to evaluate the efficacy of guselkumab o in achieving transmural (segmental and total) response. o in achieving transmural remission. o based on IBUS-SAS over time o in eliminating the need for corticosteroids while maintaining disease control based on IUS-assessed transmural remission. o based on BWT as assessed by IUS over time. o based on IUS score for Crohn's disease (SUS-CD) over time. o based on BWT as assessed by IUS over time. • Based on endoscopy, to evaluate the efficacy of guselkumab: o in achieving endoscopic response throughout the study.

	o in achieving endoscopic remission throughout the study. o based on SES-CD over time. o in eliminating the need for corticosteroids while maintaining disease control based on endoscopic remission. o in achieving endoscopic healing of the intestinal mucosa. • Based on clinical data, to evaluate the efficacy of guselkumab o in achieving clinical remission during the study. o in achieving clinical response during the study. o in eliminating the need for corticosteroids while maintaining disease control based on clinical remission. o based on CDAI over time. • to evaluate the efficacy of Guselkumab based on HRQoL and PROs. • To evaluate the efficacy of guselkumab based on biomarker outcomes.
Protocol No. CNTO1959PBCRD3007 (MACARONI-23) Therapeutic area: Crohn's disease Study Start -End Dates: 13 March 2024 -ongoing	**Primary objective:** • To evaluate the clinical and endoscopic efficacy of guselkumab in pediatric participants with Crohn's disease at the end of maintenance therapy among participants who were in clinical response to guselkumab at Week 12. **Secondary objectives:** • To evaluate the clinical efficacy of guselkumab in pediatric participants with Crohn's disease. • To evaluate the efficacy with guselkumab in clinical remission by PRO at Week 12 and/or Week 52. • To evaluate the PK and immunogenicity of guselkumab in pediatric participants with Crohn's disease. • To assess the impact of guselkumab therapy on growth. • To evaluate the safety of guselkumab in pediatric participants with Crohn's disease. • To evaluate the efficacy of treatment with guselkumab in participants who are assigned at Week 12 to receive a guselkumab SC does regimen based on their body weight for maintenance therapy and do not receive non-investigational product rescue therapy.
Protocol No. 78934804CRD2001 (DUET-CD) Therapeutic area: Crohn's disease Study Start -End Dates: 22 July 2022 -ongoing	**Primary objective:** • to evaluate the efficacy of JNJ-78934804 at Week 48 compared with each monotherapy (guselkumab alone and golimumab alone). **Secondary objectives:** • To evaluate the efficacy of JNJ-78934804 compared with each monotherapy across a range of outcomes. • To evaluate the efficacy of JNJ-78934804 at Week 24 compared with placebo. • To evaluate the safety based on AEs of JNJ-78934804 compared

	with each monotherapy and placebo. • To evaluate the PK and immunogenicity of JNJ-78934804 compared with each monotherapy.
Protocol No. CNTO1959UCO2002 (VEGA) Therapeutic area: Ulcerative colitis Study Start -End Dates: 20November2018 15November2021	**Primary objectives:** Combination Comparison Phase • To evaluate the clinical efficacy of combination therapy with guselkumab and golimumab in participants with moderately-to-severely active UC. • to evaluate the safety of combination therapy with guselkumab and golimumab in participants with moderately-to-severely active UC. **Secondary objectives:** Combination Comparison Phase • To evaluate the effect of combination therapy with guselkumab and golimumab on endoscopic improvement. • To evaluate the impact of combination therapy with guselkumab and golimumab on disease-specific HRQoL, including fatigue. • To evaluate the efficacy of combination therapy with guselkumab and golimumab by negative response signature status at baseline. • To evaluate the PK, immunogenicity, and PD of combination therapy with guselkumab and golimumab, including changes in CRP, fecal calprotectin, and other PD biomarkers. Monotherapy Phase • To evaluate the clinical efficacy of combination therapy followed by guselkumab monotherapy. • To evaluate the safety of combination therapy followed by guselkumab monotherapy. • To evaluate the effect of combination therapy followed by guselkumab monotherapy on endoscopic improvement. • To evaluate the impact of combination therapy followed by guselkumab monotherapy on disease-specific HRQoL, including fatigue. • To evaluate the efficacy of combination therapy followed by guselkumab monotherapy by negative response signature status at baseline. • To evaluate the PK, immunogenicity, and PD of combination therapy followed by guselkumab monotherapy, including changes in CRP, fecal calprotectin, and other PD biomarkers.
Protocol No. CNTO1959UCO3001 (QUASAR) Therapeutic area: Ulcerative colitis Study Start -End Dates: 26 September 2019 -ongoing	**Study objectives (Induction Study 1):** **Primary objectives:** The primary objectives of this study are, in participants with moderately-to-severely active UC: • To evaluate the efficacy of guselkumab as induction therapy. • To evaluate the safety of guselkumab as induction therapy. • To evaluate the dose-response of guselkumab to inform induction

	dose selection for the Phase 3 induction study. **Secondary objectives:** The secondary objectives of this study are, in participants with moderately-to-severely active UC: • To evaluate the impact of guselkumab on HRQoL and health economics outcome measures. • To evaluate the PK, immunogenicity, and PD of guselkumab therapy, including changes in CRP and fecal calprotectin. **Study objectives (Induction Study 2):** Primary objectives: The primary objectives of this study are, in participants with moderately-to-severely active UC: • to evaluate the efficacy of guselkumab as induction therapy. • to evaluate the safety of guselkumab as induction therapy Secondary objectives: The secondary objectives of this study are, in participants with moderately-to-severely active UC: • To evaluate the impact of guselkumab on HRQoL and health economics outcome measures. • To evaluate the PK, immunogenicity, and PD of guselkumab therapy, including changes in CRP and fecal calprotectin. **Study objectives (Phase 3 Maintenance Study):** **Primary objectives:** The primary objectives of this study are, in participants with moderately-to-severely active UC who were induced into clinical response with guselkumabin either Induction Study 1 or 2: • to evaluate the efficacy of maintenance regimens of guselkumab. • To evaluate the safety of maintenance regimens of guselkumab. **Secondary objectives:** The secondary objectives of this study are, in participants with moderately-to-severely active UC who were induced into clinical response with guselkumabin either Induction Study 1 or 2: • To evaluate the impact of guselkumab on HRQoL and health economic outcome measures. • To evaluate the PK, immunogenicity, and PD of guselkumab therapy, including changes in CRP and fecal calprotectin.
Protocol No. CNTO1959UCO3004 (ASTRO) Therapeutic area: Ulcerative colitis Study Start -End Dates: 8 September 2022 -ongoing	**Primary objective:** • To evaluate the efficacy, including clinical remission, of guselkumab SC induction compared toplacebo in participants with moderately to severely active UC. **Secondary objectives:** • To further evaluate the efficacy of guselkumab SC induction

	compared to placebo across a range of outcome measures. • To evaluate the safety of guselkumab SC induction compared to placebo
Protocol No. 78934804UCO2001 (DUET-UC) Therapeutic area: Ulcerative colitis Study Start -End Dates: 9 September 2022 -ongoing	**Primary objectives:** • To evaluate the efficacy of JNJ-78934804 at Week 48 compared with each monotherapy (guselkumab alone and golimumab alone). **Secondary objectives:** • To evaluate the efficacy of JNJ-78934804 compared with each monotherapy across a range of outcome measures. • To evaluate the efficacy of JNJ-78934804 at Week 24 compared with placebo. • To evaluate the safety of JNJ-78934804 compared with each monotherapy and placebo. • to evaluate the PK and immunogenicity of JNJ-78934804 compared to each monotherapy
Protocol No. CNTO1959PUC3001 (QUASAR Jr) Therapeutic area: Ulcerative colitis Study Start -End Dates: 19January 2024 -ongoing	**Primary objective:** • To evaluate the efficacy of guselkumab at the end of maintenance therapy among participants who were induction responders. **Secondary objectives:** • To evaluate the efficacy of guselkumab as induction therapy. • To evaluate the efficacy of guselkumab maintenance regiments among participants who were induction responders. • To evaluate the PK and immunogenicity of guselkumab. • To evaluate the safety of guselkumab.
Protocol No. CNTO1959HDS2001 Therapeutic area: Hidradenitis suppurativa Study Start -End Dates: 5 September 2018 -22May2020	**Primary objective:** • To evaluate the initial efficacy, safety, and tolerability of guselkumab in adult participants with moderate-to-severe HS. **Secondary objectives:** • To evaluate the efficacy of guselkumab in adult participants with moderate-to-severe HS during the maintenance phase. • To evaluate the effect of guselkumab on the dermatologic HRQoL in adult participants with moderate-to-severe HS. • to evaluate the PK, immunogenicity, and PD of guselkumab therapy in adult participants with moderate-to-severe HS.
Protocol No. CNTO1959COR1001 Therapeutic area: Familial adenomatous polyposis Study Start -End Dates: 22 February 2019 -23 March 2022	**Primary objective:** • To determine the effect of treatment with guselkumab in participants with FAP on rectal/pouch polyp burden (the sum of the polyp diameters). **Secondary objectives:** • To determine the effect of treatment with guselkumab on the following additional measurements:

	o Number of colorectal polyps. o Number of J-pouch polyps. o J-pouch polyp burden (sum of polyp diameters). o Number of duodenal polyps. o Duodenal polyp burden (sum of polyp diameters). o International Society for Gastrointestinal Hereditary Tumors (InSiGHT) polyposis stage. o Spigelman staging. • to evaluate the PK, and immunogenicity of guselkumab in participants with FAP. • to evaluate the safety of guselkumab in participants with FAP. • to assess PD/MOA biomarkers of guselkumab activity in FAP biopsies.
Protocol No. CNTO1959GCA2001 Therapeutic area: Giant cell arteritis Study Start -End Dates: 11 January 2021 -ongoing	**Primary objective:** • to evaluate the efficacy of guselkumab compared to placebo, in combination with a 26-week GC taper regimen, in adult participants with new-onset or relapsing GCA. **Secondary objectives:** • To evaluate the efficacy of guselkumab compared to placebo, in combination with a 26-week GC taper regimen, in adult participants with new-onset or relapsing GCA as measured by alternative definitions of GC free remission, GC-sparing effects, and prevention of disease flares. • To evaluate the safety of guselkumab, in combination with a 26-week GC taper regimen, in adult participants with new-onset or relapsing GCA. • to evaluate the PK and immunogenicity of guselkumab, in combination with a 26-week GC taper regimen, in adult participants with new-onset or relapsing GCA. • to evaluate the changes in immune-markers to guselkumab compared to placebo, in combination with a 26-week GC taper regimen, in adult participants with new-onset or relapsing GCA.
Protocol No. CNTO1959LUN2001 Therapeutic area: Lupus nephritis Study Start -End Dates: 18 November 2020 1 February 2023 (early termination)	**Primary objective:** • to evaluate the efficacy of guselkumab in participants with active LN. **Secondary objectives:** • to evaluate the safety and tolerability of guselkumab in participants with active LN. • to evaluate the PK and immunogenicity in participants with active LN.
Protocol No. CNTO1959SSC2001 Therapeutic area: Systemic sclerosis Study Start -End Dates: 24 February 2021 -ongoing	**Primary objective:** • To evaluate the efficacy of guselkumab in participants with SSc based on modified Rodnan skin score at 24 weeks. **Secondary objectives:**

	• to evaluate the efficacy of guselkumab in participants with SSc based on additional efficacy measures. • to evaluate the safety and tolerability of guselkumab in participants with SSc. • to evaluate the PK and immunogenicity of guselkumab.
protocol No. 64304500CLD1001 Therapeutic area: Celiac disease Study Start -End Dates: 17 June 2021 -13 September 2021 (enrollment discontinued)	**Primary objective:** • to evaluate the safety and tolerability of guselkumab compared to placebo in participants with celiac disease. **Secondary objectives:** • to evaluate the efficacy of guselkumab compared to placebo as measured by change in a histological assessment of disease activity. • to evaluate the change in participant well-being after treatment with guselkumab using ePROs and HRQoL tools. • To evaluate the PK, immunogenicity, and PD of guselkumab, including changes in clinical biomarkers CRP and fecal calprotectin.
Protocol No. CNTO1959NAP1001 Therapeutic area: Healthy participants Study Start -End Dates: 15 May 2013 -9 October 2013	**Primary objectives:** • To evaluate the PK comparability of lyophilized and liquid formulations following a single SC administration of 100mg guselkumab in healthy participants. • To evaluate the PK comparability of a single SC administration of 100mg guselkumab delivered by a PFS-U or PFS-FID in healthy participants. **Secondary Objectives:** • To assess the absolute bioavailability of guselkumab following SC administration in healthy participants. • To evaluate the safety, tolerability, and immunogenicity of single SC or IV administrations of 100mg guselkumab in healthy participants.
Protocol No. CNTO1959NAP1002 Therapeutic area: Healthy participants Study Start -End Dates: 5 October 2015 -12 January 2016	**Primary objective:** • To characterize the elimination of Guselkumab glycoform variants following a single IV administration of guselkumab at a 10mg/kg dose in healthy participants. **Secondary objective:** • To obtain additional safety and tolerability data following a single IV administration of guselkumab at a 10mg/kg dose in healthy participants
Protocol No. CNTO1959CRD1001 Therapeutic area: Healthy participants Study Start -End Dates: 9 December 2019- 31December2020	**Primary objectives:** • to evaluate the PK of guselkumab following a single IV or SC administration in healthy Chinese participants. • To evaluate the PK of ustekinumab following a single IV administration in healthy Chinese participants. **Secondary objectives:**

	• To evaluate the safety, tolerability, and immunogenicity of guselkumab following a single IV or SC administration in healthy Chinese participants. • to evaluate the safety, tolerability, and immunogenicity of ustekinumab following a single IV administration in healthy Chinese participants.
Protocol No. CNTO1959CRD1002 Therapeutic area: Healthy participants Study Start -End Dates: 1 June 2018 -25 October 2018	**Primary objective:** • to assess the safety and tolerability of guselkumab following single-dose IV infusion in Japanese healthy male participants. **Secondary objective:** • to assess the PK and immunogenicity of guselkumab following single-dose IV infusion in Japanese healthy male participants.
Protocol No. CNTO1959CRD1003 Therapeutic area: Healthy participants Study Start -End Dates: 4 November 2019 -7 December 2021	**Primary objective:** • To evaluate the PK bioequivalence of 200mg guselkumab administered by a single SC injection with 2mL PFS-U or 2mL PFS-Y with 200mg guselkumab administered by 2SC injections with standard 1mL PFS-U in healthy participants. **Secondary objective:** • to evaluate the safety, tolerability, and immunogenicity of a single SC administration of 200 mg guselkumab delivered by 2 different 2 mL injection devices in healthy participants.
Protocol No. CNTO1959EDI1001 Therapeutic area: Healthy participants Study Start -End Dates: 30 November 2020 -20 July 2021	**Primary objective:** • to evaluate the bioequivalence of a single 200 mg IV administration of the guselkumab formulation using, 100 mg PFS-U to create the IV solution versus the guselkumab formulation using 10 mg/mL FVP(IV) to create the IV solution. **Secondary objectives**: • to evaluate the safety, tolerability, and immunogenicity of a single 200mg IV administration of 2 different formulations of guselkumab.
Protocol No. CNTO1959PSO1008 Therapeutic area: Healthy participants Study Start -End Dates: 4October2023 – ongoing	**Primary objective:** • To evaluate the relative bioavailability of 100 mg guselkumab administered by a single SC injection with 1.0 mL PFS-Y with the approved 1.0 mL PFS-U in healthy participants. **Secondary objective:** • To evaluate the safety, tolerability of a single SC administration of 100mg guselkumab delivered by 2 different 1.0mL injection devices in healthy participants.

❖ Safety and Efficacy (Efficacy/Pharmacodynamics – Safety and tolerability)

1. Psoriasis

Psoriasis is a chronic, immunologically mediated, inflammatory skin disease of unknown etiology affecting 2% to 3% of the general population (Plaque Psoriasis, Erythrodermic Psoriasis, Generalized Pustular

Psoriasis)

1.1.Phase 1 Study CNTO1959PSO1001

Study CNTO1959PSO1001 was a randomized, double-blind, placebo-controlled, ascending-dose study of guselkumab following a single IV or SC administration. The primary objective of the study was to assess the safety and tolerability of guselkumab. The study was conducted in 2 parts.

This first-in-human Phase 1 study with guselkumab, established the proof-of-concept and provided information on the magnitude and duration of efficacy following single doses of guselkumab.

- **Efficacy:** Clinical efficacy results in Japanese participants were consistent with those observed in the first Phase 1 study, demonstrating substantial improvements in psoriasis severity assessments.
- **Safety and Tolerability:** Guselkumab was generally well tolerated with no deaths, serious treatment-related safety concerns, malignancies, MACE, or treatment discontinuations due to adverse events.

1.2.Phase 1 Study CNTO1959PSO1002

Study CNTO1959PSO1002 was a randomized, double-blind, placebo-controlled, ascending single-dose study of guselkumab in Japanese participants with moderate-to-severe plaque psoriasis.

- **Clinical efficacy**: Clinical efficacy results in Japanese participants were consistent with those observed in the first Phase 1 study, demonstrating substantial improvements in psoriasis severity assessments.
- **Safety and Tolerability:** Guselkumab was generally well tolerated with no deaths, serious treatment-related safety concerns, malignancies, MACE, or treatment discontinuations due to adverse events.

1.3.Phase 1 Study CNTO1959PSO1003

Study CNTO1959PSO1003 was an open-label, multicenter, drug interaction study designed to evaluate the effect of a single SC dose of 200 mg guselkumab on the PK of a cocktail of representative probe substrates of CYP isozymes (midazolam [CYP3A4], warfarin [CYP2C9], omeprazole [CYP2C19], dextromethorphan [CYP2D6], and caffeine [CYP1A2]) in moderate-to-severe plaque psoriasis.

- **The clinical efficacy:** Clinically meaningful improvements in psoriasis severity were observed following treatment with Guselkumab.
- **Safety and Tolerability:** Guselkumab was generally well tolerated, with no new safety findings identified. The study did not suggest clinically meaningful drug-drug interactions.

1.4.Phase 2 Study CNTO1959PSO2001

Study CNTO1959PSO2001 was a randomized, placebo- and active comparator-controlled, parallel-group, multicenter dose-ranging 7-arm study, which included the following treatment groups: placebo, guselkumab (Week 0, Week 4, and q12w for 5, 50, and 200 mg and q8w for 15 and 100 mg), and adalimumab in participants with moderate-to-severe plaque psoriasis. A total of 293 participants were randomized into the study.

- **Clinical Efficacy:** Guselkumab demonstrated significantly greater efficacy than placebo and showed favorable efficacy compared with the active comparator. Clinical responses were maintained throughout the treatment period.
- **Safety and Tolerability:** Guselkumab was generally well tolerated, with a safety profile comparable to

the active comparator and no unexpected safety findings.

1.5.Phase 3 Study CNTO1959PSO3001

Study CNTO1959PSO3001 was a Phase 3, randomized, double-blind, multicenter placebo- and active comparator-controlled study in participants with moderate-to-severe plaque psoriasis

The target population included adult men or women with a diagnosis of plaque-type psoriasis (with or without PsA) for at least 6 months before the first administration of study drug. Participants were required to have moderate-to-severe plaque-type psoriasis defined by IGA ≥3, PASI ≥12, and involved BSA ≥10%, and were required to be candidates for either systemic therapy or phototherapy for psoriasis (previously treated or naïve).

- **Clinical Efficacy:** Guselkumab achieved all primary and major secondary endpoints, demonstrating superior efficacy versus placebo and sustained efficacy compared with the active comparator. Clinical responses and quality-of-life improvements were maintained during long-term follow-up.
- **Safety and Tolerability:** Guselkumab demonstrated a favorable long-term safety profile with no new safety signals identified during extended treatment.

1.6.Phase 3 Study CNTO1959PSO3002

Study CNTO1959PSO3002 was a Phase 3, randomized, double-blind, multicenter, placebo- and active comparator-controlled study of guselkumab in participants with moderate-to-severe plaque psoriasis with randomized withdrawal and retreatment. The target population was the same as for study CNTO1959PSO3001

- **Clinical Efficacy:** Guselkumab demonstrated significant efficacy compared with placebo and maintained disease control with continued treatment. Participants who discontinued treatment generally regained response after retreatment.
- **Safety and Tolerability** The safety profile was consistent with previous studies, with low rates of serious adverse events and no new safety concerns during long-term follow-up.

1.7.Phase 3 Study CNTO1959PSO3003

Study CNTO1959PSO3003 was a Phase 3, randomized, double-blind, multicenter study that evaluated the efficacy and safety of guselkumab for the treatment of participants with moderate-to-severe plaque-type psoriasis and an inadequate (IGA≥2) response to ustekinumab at Week 16. The target population was the same as for study CNTO1959PSO3001.

- **Clinical Efficacy:** Guselkumab provided improved clinical outcomes in participants with an inadequate response to prior biologic therapy and demonstrated sustained efficacy through the study period.
- **Safety and Tolerability:** The safety profile was consistent with previous studies and no new safety signals were identified.

1.8.Phase 3 Study CNTO1959PSO3004

Study CNTO1959PSO3004 was a Phase 3 multicenter, randomized, double-blind, placebo-controlled study of guselkumab in participants with moderate-to-severe plaque psoriasis. This study was only conducted in Japan. The target population was the same as for study CNTO1959PSO3001, with the exception of age

(this study included men or women 20 years of age and older).

- **Clinical Efficacy:** The study met all primary and major secondary efficacy endpoints, demonstrating substantial and sustained clinical improvement in Japanese participants.
- **Safety and Tolerability:** Guselkumab was generally well tolerated, with low incidences of serious adverse events and other adverse events of special interest.

1.9.Phase 3 Study CNTO1959PSO3005

Study CNTO1959PSO3005 was a Phase 3 multicenter, open-label study of guselkumab in participants with GPP or EP. This study was conducted only in Japan.

The target population included men or women 20 years of age and older, with a diagnosis of GPP or EP. Participants were required to be candidates for either systemic therapy or phototherapy for psoriasis and may have previously received some systemic therapies or phototherapy for GPP or EP. A total of 21 participants were enrolled and received SC guselkumab 50 mg at Weeks 0, 4, and 12, then q8w thereafter.

- **Clinical Efficacy:** Guselkumab demonstrated clinically meaningful efficacy in participants with generalized pustular psoriasis and erythrodermic psoriasis, with treatment responses maintained throughout the study.
- **Safety and Tolerability:** Treatment was generally well tolerated, and the observed safety profile was consistent with previous clinical experience.

1.10. Phase 3 Study CNTO1959PSO3006

Study CNTO1959PSO3006 was a Phase 3, randomized, double-blind, multicenter, placebo-controlled study evaluating the efficacy, safety, PK, immunogenicity, usability, and acceptability of guselkumab delivered using the PFS-S device in participants with moderate-to-severe plaque-type psoriasis. The target population was the same as for study CNTO1959PSO3001.

- **Clinical Efficacy**: The study met its primary and secondary efficacy endpoints, confirming the effectiveness of Guselkumab administered using the prefilled syringe device.
- **Safety and Tolerability:** Guselkumab was well tolerated, with a safety profile consistent with previous psoriasis studies.

1.11. Phase 3b Study CNTO1959PSO3008

Study CNTO1959PSO3008 was a Phase 3b, randomized, open-label, efficacy assessor-blinded, single country, multicenter, active comparator-controlled study of guselkumab in adult participants with moderate-to-severe plaque-type psoriasis who have not yet received any systemic therapy.

The target population included adult men and women with a diagnosis of plaque-type psoriasis for at least 6 months before the first administration of the study drug.

- **Clinical Efficacy**: Guselkumab demonstrated superior efficacy compared with the active comparator and maintained clinical benefits following treatment.
- **Safety and Tolerability:** Guselkumab showed a favorable safety profile and was generally better tolerated than the comparator treatment.

1.12. Phase 3 Study CNTO1959PSO3009

Study CNTO1959PSO3009 was a Phase 3, randomized, double-blind, multicenter, active-controlled study evaluating the comparative efficacy of guselkumab and secukinumab in participants with moderate-to-severe plaque-type psoriasis. The target population was the same as for study CNTO1959PSO3001, with the exception that participants who had ever received secukinumab were prohibited.

- **Clinical Efficacy**: Guselkumab demonstrated non-inferior and superior efficacy compared with the active comparator for the primary endpoint.
- **Safety and Tolerability:** The safety profile was consistent with previous studies, with no new safety signals identified.

1.13. Phase 3 Study CNTO1959PSO3011 (PROTOSTAR)

Study CNTO1959PSO3011 (PROTOSTAR) is an ongoing Phase 3, multicenter, randomized, placebo- and active comparator-controlled study evaluating the efficacy, safety, and PK of subcutaneously administered guselkumab for the treatment of chronic plaque psoriasis in pediatric participants ≥6 to <18 years of age.

The main study is being conducted in 2 parts. Part 1 is a randomized placebo- and active-comparator controlled study and Part 2 is an open-label study. Part 1 also has 2 parts: in Part 1a at least 60 participants ages ≥12 to <18 years will be randomized in a 2:1:1 ratio to receive guselkumab, placebo, or etanercept, and in Part 1b at least 30 participants ages ≥6 to < 18 years will be enrolled.

- **Clinical Efficacy** : This pediatric study is ongoing and efficacy analyses are not yet available.
- **Safety and Tolerability:** Available interim data indicate that guselkumab is generally well tolerated in the pediatric population.

1.14. Phase 3b Study CNTO1959PSO3012 (GUIDE)

Study CNTO1959PSO3012 (GUIDE) is an ongoing Phase 3b, multicenter, randomized, double-blind, parallel-group study evaluating further therapeutic strategies with guselkumab in participants with moderate-to-severe plaque-type psoriasis.

The target population is comprised of adults with a diagnosis of plaque-type psoriasis (approximately 40% participants with disease duration ≤2 years calculated from date at which first symptoms (plaque) were reported by the participant to date of screening visit). Participants must have moderate-to-severe plaque-type psoriasis defined by PASI >10 or affected BSA >10% and additionally a DLQI >10.

- **Clinical Efficacy**: The study demonstrated high rates of disease control, including maintenance of response with extended dosing intervals in selected participants.
- **Safety and Tolerability:** Interim analyses indicate a safety profile consistent with previous studies.

1.15. Phase 3b Study CNTO1959PSO3013

Study CNTO1959PSO3013 was a Phase 3b, multicenter, interventional, randomized, placebo-controlled study evaluating the efficacy and safety of guselkumab for the treatment of palmoplantar non-pustular psoriasis. The target population was comprised of participants aged ≥18 years who had a confirmed diagnosis of moderate-to-severe palmoplantar-non-pustular psoriasis with PASI score ≥3 and <10 and ppIGA ≥3, with palms and/or soles affected and at least 1 plaque at a body site other than the palms or soles (any size) for at least 6 months, to confirm a diagnosis of chronic psoriasis.

- **Clinical Efficacy**: Guselkumab demonstrated improvements in palmoplantar psoriasis outcomes, with

sustained clinical benefits over time.

- **Safety and Tolerability:** No new safety concerns were identified and the safety profile remained consistent with previous studies.

1.16. Phase 3b Study CNTO1959PSO3017 (SPECTREM)

CNTO1959PSO3017 (SPECTREM) is an ongoing Phase 3b, multicenter, randomized, placebo-controlled, double-blind study designed to evaluate the efficacy and safety of guselkumab in participants with low BSA moderate plaque psoriasis with special site involvement.

The target population consists of participants who are ≥18 years old, have a diagnosis of plaque psoriasis for at least 6 months with overall IGA 3 (moderate), and have BSA 2% to 15% with at least 1 plaque outside of special sites and with involvement of at least 1 special site (scalp, genital, intertriginous, and face) of moderate severity or higher.

- **Clinical Efficacy**: The study is ongoing and efficacy data are not yet available.
- **Safety and Tolerability:** Interim safety findings remain consistent with the established safety profile of Guselkumab.

1.17. Phase 3b Study CNTO1959PSO3018 (VISIBLE)

Phase 3b Study CNTO1959PSO3018 (VISIBLE) CNTO1959PSO3018 (VISIBLE) is an ongoing Phase 3b, multicenter, randomized, placebo-controlled, double-blind study designed to evaluate the efficacy and safety of guselkumab in participants of skin of color with predominant body moderate-to-severe plaque psoriasis (Cohort A) or predominant moderate-to-severe scalp psoriasis (Cohort B).

- **Clinical Efficacy**: The study is ongoing, and efficacy analyses are not yet available.
- **Safety and Tolerability:** Interim safety data indicate that Guselkumab continues to demonstrate a favorable tolerability profile.

2. Psoriatic Arthritis

.1. Phase 1 Study CNTO1959PSA1001

Study CNTO1959PSA1001 was a Phase 1, open-label, multicenter, interventional study to assess the relative PK and tissue distribution of Guselkumab and risankizumab in healthy participants and participants with PsA. Both Guselkumab 100 mg SC and risankizumab 150 mg SC were co-administered on Day 1 in an open-label fashion to the same healthy participants at symmetric anatomic locations.

- **Clinical Efficacy:** Efficacy was not evaluated in this pharmacokinetic and tissue distribution study.
- **Safety and Tolerability:** Guselkumab was generally well tolerated, with only mild adverse events reported and no new safety concerns identified.

.2. Phase 2a Study CNTO1959PSA2001

Study CNTO1959PSA2001 was a Phase 2a, multicenter, randomized, double-blind, placebo-controlled, 2-arm study evaluating the efficacy and safety of guselkumab in participants with active PsA.

The target population included adult men or women with a diagnosis of PsA for at least 6 months and who have had an inadequate response to current or prior standard therapies. Participants with prior exposure to

1 anti-TNFα agent were permitted but limited to approximately 20% of the study population. Participants were required to have active PsA with ≥3 tender and ≥3 swollen joint counts, a CRP level ≥0.3 mg/dL, and ≥3% of BSA involvement with plaque psoriasis.

- **Clinical Efficacy:** Guselkumab demonstrated significant improvements in joint symptoms, physical function, skin manifestations, enthesitis, dactylitis, and quality of life in participants with active PsA. Clinical benefits were maintained through approximately one year of treatment.
- **Safety and Tolerability:** Guselkumab was generally well tolerated, with a safety profile consistent with previous experience and no unexpected safety findings.

.3. Phase 2a Study CNTO1959PSA2003

study CNTO1959PSA2003 is an ongoing Phase 2a, randomized, double-blind, active-controlled, parallel-group, multicenter, proof-of-concept clinical study designed to evaluate the efficacy and safety of combination therapy with guselkumab+golimumab (guselkumab q4w + golimumab q4w) versus guselkumab monotherapy (guselkumab q4w + placebo q4w) in adults with active PsA who have a previous history of inadequate response to either 1 or 2 anti-TNFα therapy(ies) either due to primary nonresponse or loss of efficacy.

- **Clinical Efficacy:** This ongoing study is evaluating combination therapy versus guselkumab monotherapy in participants with inadequate response to anti-TNF therapy. Efficacy data are not yet available.
- **Safety and Tolerability:** Interim safety findings indicate that guselkumab remains generally well tolerated, with no new safety signals identified.

.4. Phase 3 Study CNTO1959PSA3001

Study CNTO1959PSA3001 was a Phase 3, multicenter, randomized, double-blind, placebo-controlled, 3-arm study of guselkumab in adults with active PsA. The target population included adult men and women with active PsA who had had an inadequate response to standard therapies (eg, non-biologic DMARDs, apremilast, NSAIDs, and anti-TNFα agents in a limited subset of participants)

- **Clinical Efficacy:** Both Guselkumab dosing regimens demonstrated robust efficacy in improving joint and skin manifestations of PsA, physical function, and health-related quality of life. Responses were maintained through one year of treatment**.**
- **Safety and Tolerability:** Across both Phase 3 studies, Guselkumab demonstrated a favorable and consistent safety profile. Adverse events were generally comparable to placebo, serious adverse events were infrequent, and no new safety concerns were identified during long-term follow-up.

.5. Phase 3 Study CNTO1959PSA3002

Study CNTO1959PSA3002 was a Phase 3, multicenter, randomized, double-blind, placebo-controlled, 3-arm study of guselkumab in adults with active PsA (defined as ≥5 swollen joints and ≥5 tender joints at screening and at baseline and CRP ≥0.6 mg/dL at screening) who were biologic naïve and who previously

had inadequate response to standard nonbiologic therapies (eg, nonbiologic DMARDs, apremilast, and NSAIDs).

The target population was adult men and women with active PsA who previously had inadequate response to standard, nonbiologic therapies (eg, nonbiologic DMARDs, apremilast, and NSAIDs). A total of 739 participants were randomized in a 1:1:1 ratio to receive guselkumab 100 mg q4w, guselkumab 100 mg at Weeks 0 and 4 then q8w, or placebo q4w from Week 0 to Week 20 and crossover at Week 24 to receive guselkumab 100 mg.

- **Clinical Efficacy:** Guselkumab provided sustained improvements in arthritis symptoms, skin disease, enthesitis, dactylitis, physical function, and quality of life. Clinical efficacy and inhibition of radiographic progression were maintained through two years of treatment.
- **Safety and Tolerability:** Across both Phase 3 studies, guselkumab demonstrated a favorable and consistent safety profile. Adverse events were generally comparable to placebo, serious adverse events were infrequent, and no new safety concerns were identified during long-term follow-up.

.6. Phase 3b Study CNTO1959PSA3003

Study CNTO1959PSA3003 was a Phase 3b study to evaluate the efficacy and safety of guselkumab SC administered in participants with active PsA and an inadequate response to anti-TNFα therapy. The target population consisted of adult men or women with moderately-to-severely active PsA who demonstrated an inadequate response or intolerance to anti-TNFα therapy.

- **Clinical Efficacy:** Guselkumab demonstrated significant improvements in signs and symptoms of PsA compared with placebo, achieving the primary endpoint and all key secondary efficacy endpoints.
- **Safety and Tolerability:** The safety profile was consistent with previous studies, with low rates of serious adverse events, serious infections, malignancies, and treatment discontinuations.

.7. Phase 3b Study CNTO1959PSA3004

Study CNTO1959PSA3004 is an ongoing Phase 3b study to evaluate the efficacy and safety of SC administered guselkumab in improving the signs and symptoms and inhibiting radiographic progression in participants with active PsA who are biologic naïve and have had inadequate response to current standard therapies (eg, DMARDs/apremilast, corticosteroids, NSAIDs).

- **Clinical Efficacy:** This ongoing study is evaluating the efficacy of Guselkumab in biologic-naïve participants with active PsA. Efficacy data are not yet available.
- **Safety and Tolerability:** Interim safety data remain consistent with the established safety profile of Guselkumab.

.8. Phase 3b Study CNTO1959PSA3005

Study CNTO1959PSA3005 is an ongoing Phase 3b, multicenter, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of guselkumab administered SC in participants with active PsA who had an inadequate response and/or intolerance to 1 prior anti-TNFα agent.

➢ **Clinical Efficacy:** This ongoing study is evaluating Guselkumab in participants with inadequate response or intolerance to prior anti-TNF therapy. Efficacy data are not yet available.

➢ **Safety and Tolerability:** Interim analyses indicate a safety profile consistent with previous clinical studies.

➢ **Phase 3 CNTO1275JPA3001 (PSUMMIT-Jr)**

CNTO1275JPA3001 (PSUMMIT-Jr) is a Phase 3, open-label, multicenter study that will consist of 2 cohorts. This study will evaluate the PK, efficacy, safety, and immunogenicity of ustekinumab (Cohort 1) and guselkumab (Cohort 2) in participants aged ≥5 to <18 years with active jPsA.

➢ **Clinical Efficacy:** This ongoing pediatric PsA study is evaluating the efficacy of Guselkumab in participants aged 5 to <18 years. Efficacy data are not yet available.

➢ **Safety and Tolerability:** Available interim data indicate that Guselkumab is generally well tolerated in the pediatric population.

➢ **Palmoplantar Pustulosis**

.1 Phase 2 Study CNTO1959PPP2001

Study CNTO1959PPP2001 was a Phase 2, randomized, double-blind, placebo-controlled, parallel-group, multicenter study of guselkumab in participants with PPP in Japan. Eligible participants had a diagnosis of PPP, as defined by a PPSI score ≥7 at screening and baseline (Week 0), including active lesions on the palms or soles, along with inadequate response to the treatment with topical steroid and/or topical vitamin D3 derivative preparations and/or the phototherapy and/or systemic etretinate before or at screening.

➢ **Clinical Efficacy:** Guselkumab demonstrated significant improvements in disease severity compared with placebo, with clinically meaningful reductions in palmoplantar pustulosis disease activity and higher response rates. Treatment benefits were maintained throughout the study period.

➢ **Safety and Tolerability:**

Guselkumab was generally well tolerated, with an adverse event profile comparable to placebo. No new safety signals were identified, and safety assessments revealed no clinically meaningful concerns.

.2 Phase 3 Study CNTO1959PPP3001

Study CNTO1959PPP3001 was a Phase 3, multicenter, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of guselkumab for the treatment of participants with PPP being conducted in Japan.

The target population was adult men or women with a diagnosis of PPP (with or without pustulotic arthro-osteitis) for at least 24 weeks before screening, and who had an inadequate response to conventional therapies (topical treatment, and/or phototherapy, and/or systemic treatment). Participants must have a PPPASI total score ≥12 and a PPPASI severity score of pustules/vesicle on the palms or soles ≥2 at screening and baseline.

➢ **Clinical Efficacy:** The study met its primary efficacy endpoint, demonstrating superior improvement in disease severity with Guselkumab compared with placebo. Clinically meaningful improvements were also

observed across key secondary efficacy measures.

- **Safety and Tolerability:** Guselkumab was generally well tolerated throughout the study, with no new safety concerns identified and no treatment-related safety signals observed during long-term follow-up.

➢ Rheumatoid Arthritis

.1. Phase 2 Study CNTO1275ARA2001

Study CNTO1275ARA2001 was a Phase 2, multicenter, randomized, double-blind, placebo-controlled, parallel-group study evaluating the efficacy and safety of ustekinumab and guselkumab administered subcutaneously in participants with active RA despite concomitant MTX therapy.

- **Clinical Efficacy:**

The primary efficacy endpoint was not achieved, and no significant improvements were observed across the major secondary efficacy endpoints.

Further development of Guselkumab for this indication has been **discontinued**.

- **Safety and Tolerability:** Guselkumab was generally well tolerated, with a safety profile comparable to placebo. The incidence of serious adverse events and infections was low, and no new safety concerns were identified during the study.

➢ Crohn's Disease

.1. Phase 2/3 Study CNTO1959CRD3001 (GALAXI Program)

Study CNTO1959CRD3001 is an ongoing, operationally seamless Phase 2/3 program in participants with moderately-to-severely active Crohn's disease who have demonstrated an inadequate response or failure to tolerate previous conventional therapy or biologic therapy.

The program includes **3 separate studies** conducted under a single protocol: a 48-week Phase 2 dose-ranging study (GALAXI-1) and 2 identically designed, placebo-, and active-controlled (ustekinumab), 48-week, Phase 3, confirmatory studies (GALAXI-2 and GALAXI-3).

- **Clinical Efficacy:** The GALAXI clinical program demonstrated significant improvements in clinical, endoscopic, and patient-reported outcomes in participants with moderately-to-severely active Crohn's disease. Across Phase 2 and Phase 3 studies, guselkumab achieved primary and major secondary efficacy endpoints, with sustained clinical remission and endoscopic improvements observed during long-term follow-up. Efficacy outcomes were generally comparable or favorable relative to the active comparator and were maintained through extended treatment periods.
- **Safety and Tolerability:** Guselkumab was generally well tolerated, with a safety profile consistent across Phase 2, Phase 3, and long-term extension periods. Serious adverse events, serious infections, malignancies, major adverse cardiovascular events, and treatment discontinuations were infrequent. No new safety signals were identified during long-term follow-up.

.2. Phase 3 Study CNTO1959CRD3003

Study CNTO1959CRD3003 is an ongoing Phase 3, open-label, multicenter study to evaluate the safety and

efficacy of guselkumab in participants with moderately-to-severely active Crohn's disease who have demonstrated an inadequate response or failed to tolerate the previous conventional therapy (ie, 6-MP, AZA, or corticosteroids) or biologic therapy (ie, TNFα antagonists or vedolizumab).
Participants receive guselkumab treatment in an open-label fashion:

- Weeks 0, 4, and 8: Guselkumab 200 mg IV administration (Induction)
- q4w after Week 8 until the end of the study: Guselkumab 200 mg SC administration (Maintenance)

Participants may enter an LTE phase after the 48-week treatment phase.

➢ **Clinical Efficacy:** Guselkumab demonstrated clinically meaningful improvements in disease activity, including sustained reductions in disease severity and corticosteroid use through 48 weeks of treatment.

➢ **Safety and Tolerability:** Guselkumab was generally well tolerated, with no new safety concerns identified. Serious adverse events were infrequent, and no clinically significant safety signals were observed.

.3.Phase 3 Study CNTO1959CRD3004 (GRAVITI)

Study CNTO1959CRD3004 (GRAVITI) is an ongoing Phase 3, randomized, double-blind, placebo-controlled, parallel-group, multicenter study to evaluate the efficacy and safety of guselkumab SC induction therapy followed by SC maintenance therapy. In this treat-through study design, the main treatment phase included a 12-week induction period followed by a 12-week maintenance period. This was followed by the ongoing 72-week extension treatment phase in which participants continue to receive the same maintenance dose regimen they were receiving at Week 24. Of note, participants in the placebo group received rescue treatment with guselkumab from Week 16 onwards if rescue criteria were met.
The target population was adult participants with moderately-to-severely active Crohn's disease with colitis, ileitis, or ileocolitis previously confirmed by radiography, histology, and/or endoscopy

➢ **Clinical Efficacy:** The study met its primary efficacy endpoints, demonstrating significant improvements in clinical remission and endoscopic response compared with placebo. Benefits were also observed across key secondary efficacy endpoints and maintained through long-term follow-up.

➢ **Safety and Tolerability:** The safety profile was consistent with the established safety profile of Guselkumab. Rates of adverse events, serious adverse events, and treatment discontinuations remained low, with no new safety signals identified.

.4. Phase 3 Study CNTO1959CRD3007 (PROGRESS)

CNTO1959CRD3007 (PROGRESS) was a Phase 3, multicenter, randomized, placebo-controlled, prospective double-blind study designed to evaluate the efficacy and safety of SC guselkumab in reducing the recurrence of Crohn's disease in adult participants who have recently undergone a surgical resection for Crohn's disease. **The sponsor made an internal business decision to terminate the study, unrelated to safety or efficacy of guselkumab.** This planned Phase 3 study was terminated after 4 participants were enrolled, randomized, and treated for up to 16 weeks. No participants were evaluable for the primary

endpoint of endoscopic recurrence prior to or at Week 48 due to the early termination.

- **Safety and Tolerability:** Limited available data did not identify any new safety concerns and were consistent with the established safety profile of Guselkumab.

.5. Phase 3b Study CNTO1959CRD3008 (REASON)

CNTO1959CRD3008 (REASON) is an ongoing Phase 3b, multicenter, open-label study to evaluate transmural healing and the disease-modifying effect of guselkumab in adult participants with active Crohn's disease.

A target of approximately 112 participants will be enrolled. Eligible participants must be diagnosed with luminal Crohn's disease (confirmed by radiography, histology, and/or endoscopy) for a minimum of 3 months, have had an inadequate response with lost response to, or were intolerant to either conventional therapy or advanced therapy, or have medical contraindication to such therapies. Participants with active moderate-to-severely active Crohn's disease will be enrolled.

- **Clinical Efficacy:** efficacy data are not yet available.
- **Safety and Tolerability:** Interim safety findings remain consistent with the known safety profile of Guselkumab.

.6. Phase 3 Study CNTO1959PBCRD3007 (MACARONI-23)

CNTO1959PBCRD3007 (MACARONI-23) is part of an ongoing Phase 3, multicenter, randomized, 2-arm, clinical development program to investigate under a single protocol the efficacy, safety, and PK of guselkumab as 1 of the 2 different IL-23 inhibitors in pediatric Crohn's disease. The guselkumab cohort consists of a randomized, open-label induction, double-blind maintenance, parallel-group design.

The target study population is composed of pediatric participants of 2 to 30) who have an inadequate response to, loss of response to, or are intolerant to non-biological therapy for Crohn's disease (biologic-naïve, Bio-NF), and/or those who failed biologic and/or advanced therapy for Crohn's disease (eg, biologic/JAK inhibitor-failed, Bio-IR).

- **Clinical Efficacy:** This ongoing pediatric Crohn's disease study is evaluating the efficacy of Guselkumab in children and adolescents with moderate-to-severe disease. Efficacy data are not yet available.
- **Safety and Tolerability:** Available interim safety data indicate that guselkumab is generally well tolerated in the pediatric population.
- **Studies With Guselkumab as a Reference or Comparator Arm (78934804CRD2001 (DUET-CD)**

78934804CRD2001 (DUET-CD) is an ongoing Phase 2b, randomized, double-blind, placebo- and active-controlled, parallel-group, multicenter study to evaluate the efficacy and safety of induction and maintenance JNJ-78934804 (guselkumab/golimumab combination) therapy in participants with moderately-to-severely active Crohn's disease who have had an inadequate initial response, loss of response, or intolerance to 1 or more approved ADTs (ADT-IR). ADT is defined as a biologic (including

anti-TNFα, ustekinumab, risankizumab, or vedolizumab, as branded or as a biosimilar). This dose-ranging study includes participants 18 to 65 years of age (inclusive, at the time of consent) with moderately or severely active Crohn's disease (defined by a CDAI score ≥220 and ≤450) and either a mean daily abdominal pain score ≥2 (based on the unweighted CDAI component of abdominal pain) or a mean daily stool frequency count ≥4 (based on the unweighted CDAI component of the number of liquid or very soft stools), of at least 3 months duration, with colitis, ileitis, or ileocolitis previously confirmed in the past by radiology, histology and/or endoscopy. Participants must also have endoscopic evidence of active ileal and/or colonic Crohn's disease (screening SES-CD score >6 [or >4 for isolated ileal disease]) at the time of screening ileocolonoscopy. More details on this study can be found in the JNJ-78934804 (guselkumab/golimumab combination) IB

- **Clinical Efficacy:** This ongoing Phase 2b study is evaluating a combination therapy containing Guselkumab in participants with moderately-to-severely active Crohn's disease who have had an inadequate response or intolerance to prior advanced therapies. Efficacy data are not yet available.
- **Safety and Tolerability:** Interim safety findings from the ongoing study indicate an acceptable safety profile, with no new safety concerns identified to date.

➢ **Ulcerative Colitis**

.1. Phase 2a Study CNTO1959UCO2002 (VEGA)

Study CNTO1959UCO2002 (VEGA) was a Phase 2a, randomized, double-blind, active-controlled, parallel-group, multicenter, interventional proof-of-concept clinical study designed to evaluate the efficacy and safety of the combination of guselkumab and golimumab, administered separately but in combination as individual doses (guselkumab 200 mg IV and golimumab 200 mg SC at Week 0; golimumab 100 mg SC at Weeks 2, 6, and 10; guselkumab 200 mg IV at Weeks 4 and 8, followed by guselkumab 100 mg SC q8w through Week 38) in adults with moderately-to-severely active UC.

- **Clinical Efficacy:** Combination therapy with Guselkumab and golimumab demonstrated greater clinical efficacy than either monotherapy in participants with moderately-to-severely active ulcerative colitis. Improvements were observed across clinical, endoscopic, and histologic outcomes and were maintained during the maintenance phase.
- **Safety and Tolerability:** The combination regimen and subsequent guselkumab maintenance therapy were generally well tolerated, with a safety profile comparable to the individual monotherapies. No new safety concerns were identified.

.2. Phase 2b/3 Study CNTO1959UCO3001 (QUASAR)

Study CNTO1959UCO3001 (QUASAR) is an ongoing Phase 2b/3 clinical development program for guselkumab in UC conducted under a single protocol consisting of 3 separate studies:

- Induction Study 1 (Phase 2b Induction Dose-ranging Study).
- Induction Study 2 (Phase 3 Induction Study).

• Maintenance Study (Phase 3 Maintenance Study).

➢ **Clinical Efficacy:** The QUASAR development program demonstrated that Guselkumab achieved primary and key secondary efficacy endpoints during both induction and maintenance treatment phases. Significant improvements were observed in clinical response, clinical remission, and endoscopic outcomes, with durable efficacy maintained through long-term follow-up.

➢ **Safety and Tolerability** Guselkumab demonstrated a safety profile consistent with that established in approved indications. Adverse events, serious adverse events, infections, and treatment discontinuations occurred at low rates, and no new safety signals were identified.

.3. Phase 3 Study CNTO1959UCO3004 (ASTRO)

the CNTO1959UCO3004 (ASTRO) study is an ongoing randomized, double-blind, placebo-controlled, parallel-group, multicenter study to evaluate the efficacy and safety of guselkumab SC induction therapy in adult participants with moderately-to-severely active UC who have demonstrated an inadequate response to or intolerance of conventional (ie, 6-MP, AZA, or corticosteroids) or advanced therapy (ADT; ie, TNFα antagonists, vedolizumab, ozanimod, or approved JAK inhibitors).

➢ **Clinical Efficacy:** This ongoing Phase 3 study is evaluating subcutaneous induction therapy with Guselkumab in participants with moderately-to-severely active ulcerative colitis. Efficacy data are not yet available.

➢ **Safety and Tolerability:** Interim safety findings indicate that Guselkumab continues to be generally well tolerated, with no new safety concerns identified.

.4. Phase 3 study CNTO1959PUC3001 (QUASAR Jr)

The CNTO1959PUC3001 (QUASAR Jr) study is an ongoing randomized, open-label induction, double-blind maintenance, parallel-group, multicenter study in pediatric participants with moderately-to-severely active UC to evaluate the efficacy, safety, and PK of guselkumab.

The target population is composed of participants who are 2 to <18 years of age with moderately-to-severely active UC (as defined by a baseline modified Mayo [without PGA] score of 5 through 9 inclusive, with a screening Mayo endoscopy sub score of ≥2 as determined by a central review of the video endoscopy). Participants must have demonstrated an inadequate response and/or intolerance to advanced therapy (ie, TNFα antagonist, vedolizumab, ozanimod, or JAK inhibitor) and/or conventional therapies (ie, IV or oral corticosteroids, oral amino salicylates, or the immunomodulators, AZA, 6-MP, MTX) or be dependent upon corticosteroids. Participants who have a history of an inadequate response and/or intolerance to only oral amino salicylates will comprise a maximum of approximately 15% of the population.

Study enrollment will continue until 80 induction responders across the 2 maintenance arms have been attained.

➢ **Clinical Efficacy:** This ongoing pediatric study is evaluating the efficacy of Guselkumab in children

and adolescents with moderately-to-severely active ulcerative colitis. Efficacy data are not yet available.

- **Safety and Tolerability:** Available interim safety data indicate that Guselkumab is generally well tolerated in the pediatric population.

.5. Studies With Guselkumab as a Reference or Comparator Arm

78934804UCO2001 (DUET-UC) is a Phase 2a, randomized, double-blind, placebo- and active-controlled, parallel-group, multicenter study to evaluate the efficacy and safety of induction and maintenance JNJ-78934804 (guselkumab/golimumab combination) therapy in participants 18 to 65 years of age (inclusive, at the time of consent) with moderately-to-severely active UC as determined by a modified Mayo Score ≥5 and a final reported endoscopy subscore ≥2 obtained during the central review of the screening video endoscopy at baseline. Participants must also have demonstrated an inadequate initial response, loss of response, or intolerance to 1 or more approved ADTs (ADT-IR). ADT is defined as a biologic or a novel oral agent with biologic-like activity (including anti-TNFα therapies, ustekinumab, mirikizumab, vedolizumab, tofacitinib, filgotinib, upadacitinib, or ozanimod as branded or as a biosimilar). More details on this study can be found in the JNJ-78934804 (guselkumab/golimumab combination) IB

As of 12 July 2024, enrollment has completed.

- **Clinical Efficacy:** This ongoing Phase 2a study is evaluating a combination therapy containing Guselkumab in participants with moderately-to-severely active ulcerative colitis who have had an inadequate response or intolerance to prior advanced therapies. Efficacy data are not yet available.
- **Safety and Tolerability :** Interim safety findings indicate an acceptable safety profile, with no new safety concerns identified to date.

➢ Hidradenitis Suppurativa

.1. Phase 2 Study CNTO1959HDS2001 Study

CNTO1959HDS2001 was a Phase 2, multicenter, randomized, placebo-controlled, double-blind, proof-of-concept study evaluating the efficacy, safety, PK, and immunogenicity of guselkumab administered SC and IV for the treatment of moderate-to-severe HS in adult participants. The target population was adult men and women with moderate-to-severe HS of at least 1-year duration. Participants must also have had HS lesions in at least 2 distinct anatomic areas, had an inadequate response to an adequate course of oral antibiotics for treatment of HS, and had a total abscess and inflammatory nodule count of ≥3 at the screening and baseline visits.

- **Clinical Efficacy:** This Phase 2 proof-of-concept study evaluated Guselkumab in adults with moderate-to-severe hidradenitis suppurativa. Modest improvements were observed across key efficacy measures, including disease activity, lesion counts, and patient-reported outcomes. Clinical responses were generally maintained throughout the treatment period.
- **Safety and Tolerability :** Guselkumab was generally well tolerated, with a safety profile consistent with previous clinical experience. Serious adverse events were infrequent, no new safety signals were identified, and there were no reported cases of malignancy, major adverse cardiovascular events, or severe

hypersensitivity reactions during the study.

➢ Familial Adenomatous Polyposis

.1. Phase 1 Study CNTO1959COR1001

Study CNTO1959COR1001 was a Phase 1b, randomized, blinded, placebo-controlled, multicenter, proof-of-concept study to evaluate the preliminary clinical activity of guselkumab in participants with FAP. The study was designed to determine if guselkumab has clinical activity in the colorectum and duodenum, by reducing the number of polyps over a period of 24 weeks.

The target population was adult men and women diagnosed with phenotypic FAP with disease involvement of the colorectum; post-colectomy or subtotal colectomy with ileocolonic anastomosis, ileo-rectal anastomosis, or ileal pouch-anal anastomosis with at least a 1 cm rectal cuff; and polyps with a sum of diameters ≥10 mm in the rectum or pouch post screening biopsies.

➢ **Clinical Efficacy:** This proof-of-concept study evaluated the potential effect of guselkumab on colorectal and duodenal polyp burden in participants with familial adenomatous polyposis. The primary efficacy endpoint was not met, and no consistent or sustained reduction in polyp burden was demonstrated. Consequently, the study did not provide sufficient evidence to support a clinically meaningful treatment effect in this indication.

➢ **Safety and Tolerability:** Guselkumab was generally well tolerated, with no deaths reported during the study. The overall safety profile was consistent with previous clinical experience, and no new safety concerns were identified.

➢ Giant Cell Arteritis

.1. Phase 2 Study CNTO1959GCA2001

Study CNTO1959GCA2001 is an ongoing Phase 2, multicenter, randomized, placebo-controlled, double-blind, proof-of-concept study to evaluate guselkumab for the treatment of participants with new-onset or relapsing GCA. The study is designed to evaluate the efficacy, safety, PK, and immunogenicity of guselkumab in combination with a 26-week GC taper regimen.

The study design included a target of approximately 51 participants to be randomized 2:1 to receive guselkumab 200 mg or placebo SC q4w from Week 0 to Week 48.

➢ **Clinical Efficacy:** This Phase 2 proof-of-concept study evaluated Guselkumab in participants with new-onset or relapsing giant cell arteritis. The study did not meet its primary efficacy endpoint, although a numerical improvement was observed in the proportion of participants achieving glucocorticoid-free remission compared with placebo. Based on the interim efficacy results, further development of Guselkumab in this indication was discontinued.

➢ **Safety and Tolerability:** Guselkumab was generally well tolerated, with a safety profile consistent with previous clinical studies and approved indications. No new safety concerns were identified, and a decision was made to **terminate the study due to interim efficacy data.** The clinical study report which includes

final safety data (through Week 60 and LTE) is not yet available

➢ Lupus Nephritis

.1. Phase 2 Study CNTO1959LUN2001

Study CNTO1959LUN2001 was a Phase 2 multicenter, randomized, double-blind, placebo-controlled, parallel-group study of guselkumab in participants with active LN. The original study design included a target of approximately 60 participants receiving background treatment with MMF/MPA and GCs to be randomized to 1 of 2 treatment groups to receive guselkumab 400 mg or placebo IV at Weeks 0, 4, and 8 and guselkumab 200 mg or placebo SC q4w from Week 12 through Week 48. Participants who completed the assessments at the Week 52 visit and achieved CRR had the option to participate in the LTE of the study.

➢ **Clinical Efficacy:** This Phase 2 study evaluated Guselkumab in participants with active lupus nephritis receiving standard background therapy. The study was terminated early due to enrollment challenges, resulting in a limited sample size. Consequently, the available data were insufficient to draw meaningful conclusions regarding the efficacy of Guselkumab in this indication

➢ **Safety and Tolerability:** Guselkumab was generally well tolerated, with a safety profile consistent with previous clinical studies and established experience. No new safety signals were identified, and adverse events, serious adverse events, and treatment discontinuations occurred at low and comparable rates between treatment groups.

➢ Systemic Sclerosis

.1. Phase 2a Study CNTO1959SSC2001

Study CNTO1959SSC2001 is an ongoing Phase 2a multicenter, randomized, placebo-controlled, double-blind, proof-of-concept study of guselkumab in participants with SSc. A target of 56 participants was randomly assigned in a 1:1 ratio to receive guselkumab 400 mg or matching placebo IV administration at Weeks 0, 4, and 8, followed by guselkumab 200 mg or matching placebo SC administration q4w from Week 12 until Week 48. Participants who completed 52 weeks in the main study were enrolled in the open-label LTE until week 104.

➢ **Clinical Efficacy:** This ongoing Phase 2a proof-of-concept study demonstrated that guselkumab significantly improved skin fibrosis and disease severity compared with placebo, achieving the primary efficacy endpoint. Improvements were observed early during treatment and were sustained through 52 weeks. Favorable effects were also observed across additional measures of disease activity, physical function, and clinical outcomes.

➢ **Safety and Tolerability:** Guselkumab was generally well tolerated, with a safety profile consistent with previous clinical experience. Serious adverse events and treatment discontinuations were infrequent, and no new safety concerns were identified. No clinically meaningful increases in infections, malignancies, cardiovascular events, tuberculosis, or other adverse events of special interest were observed during the study period.

➢ Celiac Disease

.1. Phase 1b Study 64304500CLD1001

Study 64304500CLD1001 was a Phase 1b, randomized, double-blind, placebo-controlled, multicenter, interventional study in both men and women with biopsy-proven celiac disease. **A decision was made to terminate the celiac disease study.** This decision was unrelated to safety as no participants had been treated with guselkumab in the study.

➢ Pregnancy

Pregnancy exposures have been reported in participants enrolled in ongoing and completed clinical studies of Guselkumab across multiple indications. Available data include both maternal and paternal exposures. Review of the reported pregnancy outcomes did not identify any fetal abnormalities or congenital malformations associated with Guselkumab exposure.

The cumulative pregnancy data available to date have not identified any new safety concerns related to pregnancy exposure. Ongoing monitoring and evaluation of pregnancy outcomes continue as part of the overall safety assessment of Guselkumab.

➢ Healthy Participants

Seven Phase 1 studies of guselkumab in healthy participants have been completed (CNTO1959PSO1001, CNTO1959NAP1001, CNTO1959NAP1002, CNTO1959CRD1001, CNTO1959CRD1002, CNTO1959CRD1003, and CNTO1959EDI1001). As of 12 July 2024, Phase 1 study CNTO1959PSO1008 is ongoing.

Study design	Safety and tolerability results
Study CNTO1959PSO1001 was a randomized, double-blind, placebo-controlled, ascending-dose study of guselkumab following a single IV or SC administration in healthy participants (Part 1) and in participants with moderate-to-severe plaque psoriasis (Part 2). In Part 1 of CNTO1959PSO1001 in healthy participants,	no deaths, SAEs, or AEs that resulted in study drug discontinuation occurred. Seven (19.4%) of 36 guselkumab-treated participants had infections compared with 3 (27.3%) of 11 participants in the placebo group. No guselkumab-treated participants in Part 1 had a malignancy, ISR, or AE of hypersensitivity or allergic reaction. Safety results from Part 2 of study PSO1001 in participants with moderate-to-severe plaque psoriasis are presented in the relevant section before.
Study CNTO1959NAP1001 was an open-label, randomized, parallel Phase 1 study assessing PK comparability between the lyophilized formulation used in Phase 1 and Phase 2 studies and the liquid	No deaths or discontinuations due to AEs occurred. No AEs of malignancy, anaphylaxis or serum sickness reaction were reported. Treatment-emergent SAEs of spontaneous abortion were

formulation to be used in Phase 3, as well as the comparability between the liquid formulation delivered by a PFS with PFS-U and with PFS-FID in healthy participants.	reported in 2 participants, 1 event each in the SC lyophilized formulation group and the IV liquid formulation group. Overall, 34 (28.1%) participants reported ISRs during the study. The proportion of participants with ISRs was higher in the group that received guselkumab with the PFS-FID (51.2%) compared with the other groups (25.0% and 7.5% in the PFS-U and SC lyophilized formulation groups, respectively)
Study CNTO1959NAP1002 was an open-label, single-dose study to characterize the elimination of guselkumab in healthy participants. Eight participants received a single IV infusion of 10 mg/kg guselkumab over 60 minutes. The participants returned to the study site for follow-up visits including safety assessments through Day 85.	No deaths, SAEs, or discontinuations due to an AE occurred during the study. Overall, there were no clinically meaningful changes in clinical laboratory tests, vital signs, physical examinations, ECGs, or concomitant medication use during the study. The findings in the study are comparable to those reported in healthy participants in the previous studies
Study CNTO1959CRD1001 was a Phase 1, non-randomized, open-label, sequential-cohort, single-dose study conducted in China to evaluate the PK of guselkumab or ustekinumab following a single IV administration or SC administration in healthy Chinese participants. A total of 60 healthy participants of Chinese ancestry (both male and female) participated in 5 sequential treatment cohorts. In each cohort, 12 participants were enrolled.	No treatment-emergent deaths, SAEs or AEs leading to discontinuations were reported during the study
Study CNTO1959CRD1002 was a Phase 1, randomized, double-blind, placebo-controlled study to assess safety, tolerability, and PK of guselkumab after single IV administrations in Japanese healthy male participants.	No deaths, other serious TEAEs, or TEAEs leading to the study agent discontinuation were reported during the study. Frequently reported TEAEs were categorized in the SOCs Infections and infestations (27.8% in guselkumab treatment group) and Gastrointestinal disorders (16.7% in guselkumab treatment group): nasopharyngitis was the most

	frequently reported TEAE and occurred in 4 (22.2%) of 18 participants in the guselkumab treatment group. No infusion reactions were reported during the study.
Study CNTO1959CRD1003 was a randomized, open-label, 2-part, parallel-group, adaptive-design, study to evaluate the PK bioequivalence of 200 mg guselkumab administered by a single SC injection with 2 mL PFS-U or 2 mL PFS-Y with 200 mg guselkumab administered by 2 SC injections with standard 1 mL PFS-U in healthy participants. In Parts 1 and 2, 440 healthy participants (stratified by weight)	There were no deaths reported in the study and no TEAEs leading to early termination of study participation. No newly identified malignancies or cases of active TB were reported in the study. Of 436 treated participants, 299 (68.6%) participants reported at least 1 AE during the study, of which 250 (57.3%) participants experienced AEs that were assessed as related to the study intervention by the investigator. Three participants experienced SAEs in the study. One participant from the Reference Device (2×1.0 mL PFS-U) group experienced an SAE sepsis due to tubo-ovarian abscess, leading to an exploratory laparotomy, left salpingo-oophorectomy, supracervical hysterectomy and extensive lysis of adhesions, assessed by investigator as related to the study intervention, followed by a post-operative ileus, assessed by investigator as not related to the study intervention. Two other participants from the Test Device 1 (1×2.0 mL PFS-U) group experienced SAEs: 1 participant experienced an SAE appendicitis and underwent surgical removal, which was assessed by the investigator as related to the study intervention, and 1 participant with drug exposure during pregnancy experienced an SAE of pregnancy ending in spontaneous abortion, assessed by the investigator as not related to study intervention. The most frequently reported TEAEs included: injection site pain (17.2%) followed by headache (16.7%), injection site erythema (10.3%), back pain (7.8%), and injection site induration

	(5.0%)
Study CNTO1959EDI1001 was a Phase 1, open-label, randomized, parallel-group study to assess the bioequivalence of the IV formulation of guselkumab using prefilled syringes assembled in an UltraSafe Plus™ Passive Needle Guard and IV formulation of guselkumab using final vialed product in healthy participants.	No deaths or AEs leading to treatment discontinuation were reported. No malignancies or TB related events were reported during the study. Of the 140 participants treated in this study, 74 (52.9%) participants (35 [50.0%] participants from guselkumab PFS-U IV group and 39 [55.7%] participants from guselkumab FVP IV group) reported ≥1 AEs. Majority of the AEs in both treatment groups were assessed as mild in severity. One (0.7%) participant from the guselkumab PFS-U IV 100 mg/mL formulation treatment arm experienced an SAE of gastroesophageal reflux disease that was assessed by the investigator as related to the study intervention. The highest number of participants (≥10%) in the study had TEAEs in the SOC Nervous system disorders (12.1%) followed by General disorders and administration site conditions and Infections and infestations (10.0% each). Headache (11.4%) followed by myalgia (5.7%) and influenza-like illness, vessel puncture site hematoma, vessel puncture site pain, rhinitis, and oropharyngeal pain (2.9% each) were the most commonly reported TEAEs (≥2.5%) by preferred term in the study.
Study CNTO1959PSO1008 is an ongoing Phase 1, open-label, randomized, parallel, multicenter, single-dose study to evaluate the relative bioavailability of 100 mg guselkumab administered by a single SC injection with 1.0 mL PSF-Y with the approved 1.0 mL PFS-U in healthy participants.	As of 12 July 2024, no major AEs have been reported.

17. Immunogenicity (Anti-drug Antibodies)

- The immunogenicity data from the completed Phase 1 to 3 studies show a generally low incidence of antibodies to guselkumab through up to 5 years of continuous treatment.

- No apparent impact of antibodies to guselkumab on the PK of guselkumab was observed based on comparison of PK between participants who were positive for antibodies to guselkumab and participants who were negative for antibodies to guselkumab. Overall, the development of antibodies to guselkumab did not appear to be associated with a reduction in the clinical efficacy of guselkumab and had no discernible impact on ISRs or possible serious hypersensitivity reactions. However, the limited number of participants who developed antibodies to guselkumab and who had ISRs precludes drawing a definite conclusion regarding the impact of antibodies to guselkumab on the incidence of ISR.

- **Protocol: Phase:** III

Objective(s):

- Objectives To evaluate the clinical efficacy of guselkumab in fistulizing, perianal Crohn's disease
- To assess the overall safety of guselkumab

Rationale:

Guselkumab (TREMFYA®) is a fully human immunoglobulin G1 lambda (IgG1) monoclonal antibody (mAb) that binds to the p19 subunit of human IL-23 with high specificity and affinity, without blocking IL-12. Binding of guselkumab to the IL-23p19 subunit blocks the subsequent binding of extracellular IL-23 to the cell surface IL-23 receptor, inhibiting IL-23 specific intracellular signaling and subsequent activation and cytokine production. Guselkumab inhibits the biological activity of IL-23 in all in vitro assays examined. A rapidly growing body of evidence suggests that dysregulated IL-23/IL-17 responses contribute to chronic inflammation underlying the pathophysiology of many immune-mediated diseases (Uhlig 2006), including psoriasis, multiple sclerosis, rheumatoid arthritis, and inflammatory bowel disease. Guselkumab is approved for the treatment of adults with moderate to severe plaque psoriasis in the United States, European Union, Canada, Japan, and several other countries and regions worldwide. In addition, guselkumab has been approved for the treatment of psoriatic arthritis, generalized pustular psoriasis, erythrodermic psoriasis, and palmoplantar pustulosis in Japan. Submissions for regulatory approval of the psoriatic arthritis indication are currently under review in several other countries globally. Guselkumab is being developed as a potential treatment for a variety of other diseases including Crohn's disease and familial adenomatous polyposis. A Phase 2/3 pivotal study program of guselkumab for moderate to severely active Crohn's disease, known as GALAXI, is currently ongoing and may provide similar data to ustekinumab, based on pre-specified 'other' endpoints; however, GALAXI does not include the use of MRI per EMA guidance. This Phase 3 study aims to evaluate the efficacy and safety of guselkumab in the treatment of adult participants with active fistulizing, perianal Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or biologic therapy or have medical contraindications to such therapies. The

primary endpoint is combined clinical and radiological remission.

Design:

- The FUZION study is a Phase 3, multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of guselkumab in participants aged ≥18 years with fistulizing, perianal Crohn's disease. Eligible participants must be diagnosed with Crohn's disease (confirmed by clinical evaluation and a combination of endoscopic, histological, radiological, and/or biochemical investigations) for a minimum of 3 months, and must have at least one active draining perianal fistula with or without a seton in place at screening, confirmed by a blinded central review of the screening MRI results.
- The study consists of a screening period of up to 6 weeks prior to baseline data collection, a 48-week randomized treatment period with 3 treatment groups, and a post-intervention safety follow-up (as a site visit or telephone contact) 16 weeks after the participant's last dose of study intervention (Week 64 ±7 days). The total duration of the study for each participant will be approximately 70 weeks.
- The use of concomitant therapies used at baseline for fistulizing, perianal Crohn's disease such as immunomodulators (ie, azathioprine [AZA], 6-mercaptopurine [6-MP], or methotrexate [MTX]), 5-aminosalicylic acid (5ASA), antibiotic therapy, oral corticosteroids, or procedures such as drainage, fistula curettage and/or seton placement if clinically indicated, is permitted during the screening phase, provided they follow the specifications detailed in Section 6.8. Participants with a currently draining fistula are permitted to be enrolled. Participants should not initiate or change any other concomitant Crohn's disease-specific medical therapies, other than those they are permitted to receive, as per the protocol.
- During the study period, efficacy, safety, PK, PD, immunogenicity, and biomarkers will be assessed per the Schedule of Activities. Key safety assessments will include adverse events (AEs), clinical laboratory tests (hematology and chemistry), vital signs, physical examination, screening electrocardiogram (ECG), monitoring for hypersensitivity reactions, injection-site reactions, and early detection of active tuberculosis (TB).
- Participants enrolled in the study will be randomized (2:2:1) to one of 3 treatment groups:

Group 1: A total of 112 participants will receive guselkumab 200 mg IV at Weeks 0, 4 and 8. At Week 12, participants will switch to guselkumab 200 mg SC q4w through to Week 48.

Group 2: A total of 112 participants will receive guselkumab 200 mg IV at Weeks 0, 4 and 8. At Week 16, participants will switch to guselkumab 100 mg SC q8w through to Week 48.

Group 3: A total of 56 participants will receive placebo IV at Weeks 0, 4 and 8. At Week 12, participants will switch to placebo SC q4w through to Week 20. At Week 24, the participants' fistula status will be clinically assessed, and participants receiving placebo will continue treatment in the study based on their clinically assessed fistula response status:

Placebo responders: Continue placebo SC q4w from Week 24 through to Week 48.

Placebo non-responders: Receive guselkumab 400 mg SC q4w from Week 24 through Week 32. At Week 36, participants will switch to guselkumab 200 mg SC q4w through to Week 48.

In addition, placebo administrations (IV and SC) will be given, as appropriate, to maintain the blind throughout the duration of the study. Clinically assessed fistula response is defined as a ≥50% reduction from baseline in number of open or draining perianal fistulas. Participants in all treatment groups will be assessed for **their fistula response status at Week 24**. No dose modifications are planned/permitted for participants in any of the study groups before assessment of the primary endpoint at Week 24. At Week 24, non-responders in the guselkumab or placebo groups may receive one blinded dose adjustment as an escape, and will be analyzed as failures.

Design of Long-term Extension up to Week 96

- The LTE will be conducted approximately from Week 48 through Week 96. At the Week 48 time-point, participants who complete the 48-week treatment period and who, and in the opinion of the investigator, will continue to benefit from the study intervention (ie, based on Week 48 clinical evaluations), may be eligible to enter the LTE. During the LTE, participants will continue to receive the blinded study intervention in the LTE until study unblinding, which will occur after the Week 48 database lock (DBL). The sponsor and sites will remain blinded until the Week 48 DBL except for the screening eligibility review, which will be shared with the sites.
- Upon study unblinding after the Week 48 DBL, participants receiving placebo will be discontinued from study intervention and will complete a SFU visit at that time-point. Participants receiving guselkumab will continue to receive their assigned regimens for the remaining duration of the LTE through Week 96.

Benefit/risk assessment

- Guselkumab has undergone extensive nonclinical and clinical development as summarized in the latest version of the IB and described briefly in Section 2.2. The collective efficacy and safety results of the Phase 1, Phase 2, and Phase 3 clinical studies in healthy volunteers and patients with plaque psoriasis established a favorable benefit-risk profile for guselkumab in the treatment of plaque psoriasis and regulatory approval for the plaque psoriasis indication. This clinical experience provided support for the ongoing development of guselkumab in other inflammatory diseases such as psoriatic arthritis, generalized pustular psoriasis, erythrodermic psoriasis, palmoplantar pustulosis, and ulcerative colitis.
- Available animal and human data support the critical role of IL-23 in the pathogenesis of Crohn's disease, and studies with other anti-IL-23 monoclonal antibodies suggest that selective targeting of IL-23 may achieve higher levels of efficacy than that observed with other mechanisms of action, in patients with Crohn's disease. Available results from the GALAXI 1 study show that guselkumab IV induction demonstrated greater improvements compared to placebo across the key clinical efficacy and endoscopic outcome measures at Week 12. The safety profile of guselkumab in the GALAXI 1 study population is consistent with the safety profile of guselkumab established from clinical trials across investigational and approved indications.
- Potential risks of guselkumab, including those of serious infection and malignancy, are being

addressed via judicious inclusion/exclusion criteria, frequent study visits to allow for close monitoring of patient safety, guidelines for participant management (including monitoring of clinical laboratory tests and treatment discontinuation criteria), detailed description of allowed and prohibited concomitant medications, and comprehensive medical monitoring of data by the sponsor during the conduct of the studies.

- In summary, the collective nonclinical and clinical evidence for the critical role of IL-23 in the pathogenesis of Crohn's disease, the benefit-risk profile of guselkumab established to date in psoriasis and other immune-mediated diseases, and the GALAXI 1 results provide a strong scientific and clinical rationale for pursuing development of guselkumab in patients with fistulizing, perianal Crohn's disease and for the investigation of guselkumab in this study. Taking into account the measures taken to minimize risk to participants of this study, the potential risks identified in association with guselkumab are justified by the anticipated benefits that may be afforded to participants with active fistulizing, perianal Crohn's disease.

- ***Recommendation &/ or*** **Questions & Answers:-----**

- **Abbreviation**

CD	Crohn's Disease
CT	Clinical Trial
CM	Conditioned Media
CFR	Code of Federal Regulations
EC	Ethics Committee
ECG	Electrocardiogram
EDA	Egyptian Drug Authority
ELISA	Enzyme-Linked Immunosorbent Assay
GLP	Good Laboratory Practice
IB	Investigator's Brochure
IL	Interleukin
IL-12	Interleukin-12
IL-23	Interleukin-23
IL-23R	Interleukin-23 Receptor
IV	Intravenous
KEA	Kinetic Exclusion Assay
mAb	Monoclonal Antibody
µg/mL	Microgram per milliliter

mg/kg	Milligram per kilogram
NaCl	Sodium Chloride
NHP	Non-Human Primate
NK	Natural Killer
NKL	Natural Killer Leukemic (cell line)
NK92MI	Human NK cell line
NOAEL	No Observed Adverse Effect Level
OECD	Organization for Economic Co-operation and Development
PBMCs	Peripheral Blood Mononuclear Cells
PI	Principal Investigator
PK	Pharmacokinetics
pM	Picomolar
QTcB	Corrected QT interval (Bazett's formula)
REC	Research Ethics Committee
rhIL-23	Recombinant Human Interleukin-23
SC	Subcutaneous
STAT3	Signal Transducer and Activator of Transcription 3
Th17	T helper 17 cells
USP	United States Pharmacopeia