Title Page

A PHASE 2A DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO EVALUATE THE EFFICACY, SAFETY, AND TOLERABILITY OF KAN-101 IN PARTICIPANTS WITH CELIAC DISEASE

Study Intervention Number:	KAN-101
Study Intervention Name:	NA
US IND Number:	19492
EudraCT/EU CT Number:	2023-507240-37-00
ClinicalTrials.gov ID:	NCT 06001177
Pediatric Investigational Plan Number:	NA
Protocol Number:	KAN-101-03
Phase:	Phase 2a
Sponsor Legal Address:	Anokion SA 50 Hampshire Street, Suite 402, Cambridge, MA 02149, USA

Brief Title:

A Study of the Efficacy, Safety, and Tolerability of KAN-101 in Participants With Celiac Disease

Document History

Document	Version Date	Summary of Changes and Rationale
Original protocol	06 September 2023	N/A
Amendment 1	20 March 2024	Global Amendment: The rationale for the amendment is related to the PART 1 questions received from the EU CTA, submitted 27 Nov 2023. Cover Page of the protocol and synopsis: added the NCT number. Justification: removed TBD. Section 1.0, Schedule of assessments, added abbreviations under the SOA, and Tables 1, 2,3, and 4 Justification: To provide protocol clarity based on the responses to the questions received from EU CTA review. Section 4.3, Justification for dose; updated with information to support dose frequency. Justification: To provide protocol clarity based on the responses to the questions received from EU CTA review. Section 8.2.4.1, Histology assessments; updated section to provide approximate rate of screen failures related to histology requirements. Justification: To provide protocol clarity based on the responses to the questions received from EU CTA review. Section 8.4.4, Regulatory reporting requirements for serious adverse events, SAEs; Updated section with regulatory authorities US FDA, and EU Eudra Vigilance.

Document	Version Date	Summary of Changes and Rationale
		Justification: To provide protocol clarity based on the responses to the questions received from EU CTA review. Section 9.5, Interim Analyses, (IA) and synopsis updated to provide rationale for having the IA. Justification: To provide protocol clarity based on the responses to the questions received from EU CTA review. Section 9.6 and synopsis Sample size determination; corrected a typo from 99% to 94% approximate power, and 0.4 to 0.5 for standard deviation. Added dropout rate of 30% to determine a difference of 0.5 evaluable subjects, in the full analysis set. Justification: To provide protocol clarity based on the responses to the questions received from EU CTA review. Section 10.0, Appendix 1, Supporting documentation and operational considerations; Updated section with, "In addition to the safety reporting responsibilities to the Sponsor in Section 10.3.4, and in accordance with local regulations." Justification: To provide protocol clarity based on the responses to the questions received from EU CTA review. Appendix 9.0, Infusion- related reactions; updated, If the reaction has not resolved within "6 hours of study drug preparation", also added In

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		cases where infusion has started but cannot be completed with 6 hours of study drug preparation, the remainder of the infusion will not be administered and study intervention will be permanently discontinued. Justification: To provide protocol clarity based on the responses to the questions received from EU CTA review. Section 10.1.11, Publication policy, updated to see section 10.1.6 Justification: To provide protocol clarity based on the responses to the questions received from EU CTA review. References, Section 11.0, added reference Adelman DC, Murray J, Wu TT, et al. Measuring change in small intestinal histology in patients with celiac disease. The American Journal of Gastroenterology. 2018. 113:339-47. Justification: To provide protocol clarity based on the responses to the questions received from EU CTA review. Section 10.1.12 Sponsor's Medically Qualified Individual; updated to replace emergency contact cards with a study information card. Justification: The process for contacting a medically qualified individual has changed from a medical escalation process via a Pfizer Call Center to direct clinical

Document	Version Date	Summary of Changes and Rationale
		team contact using a Study Team Contact List Inclusion of PACL 1; Dated 05 January 2024; Section 5.0, Inclusion criteria #4 updated to match the synopsis. Removed details about laboratory ranges as not needed, also updated Appendix 2, Table 3; protocol required lab assessments Justification: Due to differences in lab ranges, it was decided to go with the lab labels, of negative and weak positive. Typos corrected.
		Section 5.2 Clarified Exclusion Criteria 12 Justification: To provide protocol clarity based on the responses to the questions received from EU CTA review Section 10.11 Added ASA Physical Status Classification System as a reference. Justification: To provide protocol clarity based on the responses to the questions received from EU CTA review References: Added American Socienty of Anesthesiologists. Statement on ASA Physical Status Classification System. 2020. Justification:To provide protocol clarity based on the responses to the

Document	Version Date	Summary of Changes and Rationale
		questions received from EU CTA review List of abbreviations updated. Justification: Added appendix 11

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1. PROTOCOL SUMMARY

1.1. Synopsis

Protocol Title:

A Phase 2a Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Tolerability of KAN-101 In Participants With Celiac Disease

Brief Title:

A Study of the Efficacy, Safety, and Tolerability of KAN-101 in Participants With Celiac Disease

Regulatory Agency Identification Number(s):

US IND Number:	19492
EudraCT/EU CT Number:	2023-507240-37-00
ClinicalTrials.gov ID:	NCT 06001177
Pediatric Investigational Plan Number:	NA
Protocol Number:	KAN-101-03
Phase:	Phase 2a

Rationale:

The sponsor is initiating this Phase 2a study of KAN-101 in adult participants with celiac disease (CeD) to investigate the ability of KAN-101 to protect intestinal mucosa from gluten-induced histological damage.

Objectives, Endpoints, and Estimands:

Objectives	Endpoints	Estimands
Primary:	**Primary:**	**Primary:**
• Assess the ability of KAN-101 to attenuate gluten challenge (GC)-induced changes in duodenal histology as measured by changes in villus-height:crypt depth (Vh:Cd) ratio after a 2-week GC.	• Changes from baseline in Vh:Cd ratio as assessed by esophagogastroduodenoscopy (EGD) with biopsy after 2-week GC (at Day 29)	**Estimand 1:** The primary estimand is the hypothetical estimand, which estimates the treatment effect of KAN-101 vs placebo for change from baseline in the ratio of Vh:Cd under the scenario of no intercurrent events. It includes the following 5 attributes: • Population: Participants who receive all 3 doses of study intervention and complete at least 7 days of GC. • Variable: the ratio of Vh:Cd change from baseline at Day 29. • Treatment conditions: KAN-101 or placebo. • Intercurrent Events: Prohibited medication. All data collected after any intercurrent events will be excluded.

Objectives	Endpoints	Estimands
		• Population level summary: The LSM difference of the change from baseline in the ratio of Vh:Cd between KAN-101 and placebo.
Secondary:	**Secondary:**	**Secondary:**
• Examine the impact of KAN-101 on biomarker response (interleukin-2 [IL-2]) in peripheral blood following GC	• IL-2 change from Day 15 (first day of GC) pre GC to Day 15 post GC.	**Estimand 2** is the hypothetical estimand, which estimates the treatment effect of KAN-101 vs Placebo for IL-2 under the scenario of no intercurrent events. It includes the following 5 attributes: • Population: Participants who receive all 3 doses of study intervention and complete at least 7 days of GC. • Variable: log transformed IL-2 change from pre GC to post GC at Day 15. • Treatment conditions: KAN-101 or placebo. • Intercurrent Events: Prohibited medication, incomplete GC on Day 15. All data collected after any intercurrent events will be excluded. • Population level summary: The least-squares mean (LSM) difference of the change from pre GC to post GC at Day 15 (log transformed) between KAN-101 and placebo.
• Determine the effects of KAN-101 on histologic features (intraepithelial lymphocytes [IELs] density) in duodenum biopsies following 2-week GC.	• Changes from baseline in IEL density in duodenum biopsy after 2-week GC (at Day 29)	**Estimand 3** is the hypothetical estimand, which estimates the treatment effect of KAN-101 vs placebo for change from baseline in duodenal IEL density under the scenario of no intercurrent events. It includes the following 5 attributes: • Population: Participants who receive all 3 doses of study intervention and complete at least 7 days of GC. • Variable: IEL change from baseline at Day 29. • Treatment conditions: KAN-101 or placebo. • Intercurrent Events: Prohibited medication. All data collected after any intercurrent events will be excluded. • Population level summary: The LSM difference of the change from baseline in IEL between KAN-101 and placebo.
• Assess the safety and tolerability of KAN-101 in participants with CeD.	• Incidence and severity of treatment emergent AEs as assessed by the Common Terminology Criteria for Adverse Events (CTCAE) v6.0 (or higher)	Not applicable.
	• Incidence and titer of KAN-101 anti-drug antibodies (ADA)	Not applicable.
• Assess the pharmacokinetics (PK) of multiple doses of KAN-101 in participants with CeD.	• Plasma concentration of KAN-101, and associated KAN-101 parameters: AUC_{inf}, AUC_{last}, C_{max}, T_{max} and $t_{½}$	Not applicable.

Dose Selection: Based on KAN-101-01 study results, 0.6 mg/kg of KAN-101 administered in 3 doses 3 days apart, will be evaluated. The frequency of dosing in the study is supported by the nonclinical, experimental autoimmune encephalomyelitis (EAE) mouse model that demonstrated that dosing every 3 days over one week was more effective than once per week dosing. Clinical biomarker data from the KAN-101-01 first-in-human (FIH) study also suggest that this dosing regimen is effective and appropriate in adults with CeD.

Overall Design:

Study KAN-101-03 is a multi-center, double-blind, placebo-controlled Phase 2a study to examine whether KAN-101 confers protection from GC-induced histological changes in the duodenum and to further evaluate the safety/tolerability of KAN-101 in adult participants (≥18 years) with CeD. Fifty-two participants (26 participants per arm) will be randomized 1:1 to the following arms: **0.6 mg/kg KAN-101 (Arm 1)** and **Placebo (Arm 2)**. This study comprises 4 periods:

Screening period: The study screening period is ≤42 days. During the screening period, eligibility will be confirmed by EGD with duodenal biopsy. The EGD with biopsy will only be performed once all other inclusion criteria are fulfilled. Histology results must be received prior to dosing to confirm eligibility.

Treatment period: The study treatment period is 7 days (Day 1 to Day 7). Study intervention will be administered to enrolled participants in the clinic intravenously (IV) on Day 1, Day 4, and Day 7. Post infusion each treatment day, participants will be monitored in the clinic for at least 4 hours for adverse reactions.

GC: Participants will undergo a 2-week GC in which they will ingest 9 g/day of gluten protein in the form of 12 g vital wheat gluten. All participants will return to the clinic on Day 15 for the first day of GC. The Day 15 GC will be performed in the clinic under supervision and blood samples will be collected at least 5 minutes prior to GC and 4 hours after the completion of the Day 15 GC for biomarker assessment. Materials will be sent home with the participant to complete the GC daily for the next 2 weeks (through Day 28). The study site will call the participant on Day 16 and Day 21 to collect data on any AEs or CM over the telephone. Symptom monitoring and compliance with the GC will be conducted via eDiary.

Observation and Follow-up period: Participants will be observed and followed for safety for the duration of the study (42 days [Day 1 to Day 42]). The second EGD with duodenal biopsy will be conducted on Day 29. Participants will return to the clinic on Day 42 for a final follow-up visit including safety assessment and labs, celiac serology, and exploratory biomarker sample collections.

If participants are unable to return to the clinic for protocol-specified visits, alternative methods for safety assessments and data collection may be employed to ensure the safety of the trial participants when appropriate.

Data Safety Monitoring Board (DSMB): This study will utilize a DSMB that will be composed of at least 2 physicians, one of which will be a CeD medical expert, and 1 biostatistician. DSMB members will be independent from the conduct of the study. The DSMB safety monitoring plan will be detailed in the DSMB charter. The primary responsibility of the DSMB is to safeguard study participants by reviewing and assessing the cumulative clinical safety data being collected during the performance of the study. The DSMB will meet periodically throughout the study to review cumulative safety data.

Number of Participants: It is anticipated that the study will enroll approximately 52 treated participants.

Study Population: Key inclusion and exclusion criteria are listed below.

Key Inclusion Criteria

Participants must meet the following key inclusion criteria to be eligible for enrollment into the study:

1. Adults aged 18 to 70 years inclusive.
2. Previously documented diagnosis of CeD based on positive serology (eg, tissue transglutaminase IgA antibody and/or DGP IgG) AND intestinal histology consistent with ≥ Marsh Type II or with evidence of villous atrophy.
3. HLA-DQ2.5 genotype (HLA-DQA1*05 and HLA-DQB1*02) (homozygotes or heterozygotes).
4. Negative or weak positive for transglutaminase IgA and negative or weak positive for DGP-IgA/IgG during screening.
5. Have followed a gluten-free diet for ≥12 months immediately prior to study entry (self-reported).
6. Screening intestinal biopsy demonstrating Vh:Cd ratio of 2.3 or higher.

Key Exclusion Criteria

Participants with any of the following key characteristics/conditions will be excluded:

1. Refractory CeD, defined as severe persistent or recurrent malabsorptive signs or symptoms with substantial villous atrophy (eg, documented Marsh score 3c in source data) despite strict adherence to a GFD for at least 12 months in absence of other disorders.
2. Selective IgA deficiency.
3. Positive for HLA-DQ8 genotype (DQA1*03, DQB1*0302) even if DQ2.5 is also present.

4. Known wheat allergy.
5. Diagnosis of type-I diabetes.
6. History of dermatitis herpetiformis.
7. Pregnant or breastfeeding.
8. Known history of severe hypersensitivity reactions or anaphylaxis to gluten.
9. Active gastrointestinal disease other than CeD (eg, inflammatory bowel disease, any forms of colitis except well-controlled microscopic colitis, uncontrolled IBS, peptic ulcer disease, eosinophilic esophagitis, and active GI infections).
10. Previous treatment with tolerance-inducing therapies for CeD.

Study Arms and Duration:

Study Intervention(s)		
Intervention Name	KAN-101	Placebo (Saline Solution)
Arm Name (group of participants receiving a specific treatment or no treatment)	KAN-101 (Arm 1)	Placebo (Arm 2)
Type	Drug	Drug
Dose Formulation	Solution for infusion	Solution for infusion
Unit Dose Strength(s)	CCI [redacted]	NA
Dosage Level(s)	CCI [redacted]	Placebo
Route of Administration	IV	IV
Use	Experimental	Placebo
IMP or NIMP/AxMP	IMP	Placebo
Sourcing	Provided centrally by the sponsor. Further details are presented in the IPM.	Provided locally by the site. Further details are presented in the IPM.
Packaging and Labeling	Study intervention will be provided in glass vials, 1 vial per carton. Each vial and carton will be labeled as required per country requirements. Study intervention will be prepared per IPM instructions and labeled in a	Placebo will be prepared per IPM instructions and labeled in a blinded manner per country and site requirements.

Study Intervention(s)		
	blinded manner per country and site requirements.	

IMP or NIMP/AxMP: Investigational medicinal product, Non investigational medicinal product, auxiliary medicinal product, IPM: Investigational product manual

Statistical Methods:

Sample Size Determination: The total sample size is expected to be approximately 52 treated participants.

A total sample size of 26 participants in each treatment group will have approximately 94%power to detect a difference in LSM of 0.50 in change in ratio of Vh:Cd between treatment and placebo, assuming that the common standard deviation is 0.45. Details of the analyses will be described in the statistical analysis plan.

Analysis Population

All participants who receive any portion of study intervention will be included in the Safety Analysis Set. All safety data will be summarized for participants in the Safety Analysis Set.

The Full Analysis Set will consist of all randomized participants who receive all 3 doses of study intervention and complete at least 7 days of GC.

The Per Protocol Set will include all participants from the FAS who complete all 14 days of GC and biopsies (Baseline [Day 1] and Day 29) and without major protocol violations that might affect study intervention on the primary endpoint. The PPS will be used in sensitivity analyses of the primary and secondary endpoints.

The Pharmacokinetic Analysis Set will contain all participants who received any portion of study intervention and have at least one post-dose drug concentration value.

Interim Analysis:

A planned IA will be performed when approximately 13 participants from each group have completed the Day 29 visit and histology assessments.

Unless a safety concern arises, no decision to stop the trial will be made based on this interim analysis. The results of the IA will be used for future strategic planning for the overall KAN-101 program.

Primary Statistical Analysis

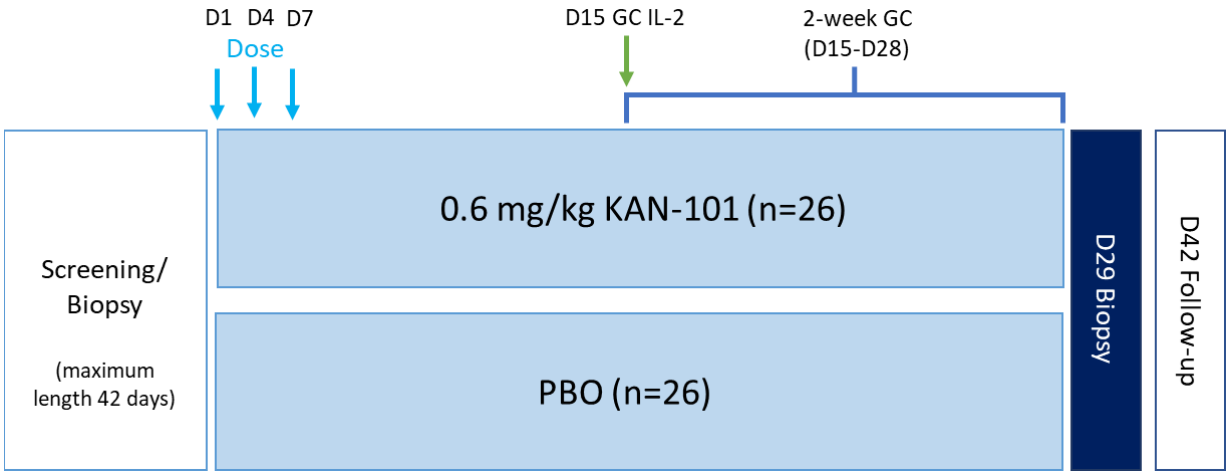
The primary endpoint change from baseline in the ratio of Vh:Cd will be analyzed using an analysis of covariance ANCOVA model with treatment as a factor and baseline as a covariate. Descriptive statistics will be used in general to summarize study results, ie, statistics for continuous variables will include number of observations, mean, standard

deviation, median, first, second, and third quartiles, minimum, and maximum; statistics for binary and categorical variables will include count and percentage. The CV, GM will also be included for continuous endpoints, where appropriate.

Ethical Considerations:

The overall potential benefit/risk of KAN-101 is considered favorable. Considering the measures and mitigations to minimize risk to study participants, the potential risks identified in association with participation in the study and with KAN-101 are justified by the anticipated benefits that may be afforded to participants with CeD.

1.2. Schema



1.3. Schedule of Activities

The SoA table provides an overview of the protocol visits and procedures. Refer to the STUDY ASSESSMENTS AND PROCEDURES section of the protocol for detailed information on each procedure and assessment required for compliance with the protocol.

The investigator may schedule visits (unplanned visits) in addition to those listed in the SoA table, in order to conduct evaluations or assessments required to protect the well-being of the participant.

Table 1. Schedule of Assessments

Abbreviations used in this table may be found in Appendix 12.	Scr.	Treatment Period			Gluten Challenge (Day 15 to 28)			Biopsy	FU	ET	Notes
Visit Identifier	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**	**ET**	• Day relative to start of study intervention (Day 1). • See Section 8.4.3 for follow-up AE and SAE assessments. • D16 and D21 are phone call visits (See Section 8.1.1) for collection of AEs and concomitant medications.
Type (Site or Phone Call)	**Site**	**Site**	**Site**	**Site**	**Site**	**Phone**	**Phone**	**Site**	**Site**	**Site**	
Study Day (D)	**Up to -42 days**	**D1**	**D4**	**D7**	**D15**	**D16**	**D21**	**D29**	**D42**	**ET**	
Visit Window (days)						**+2**	**±2**	**+3**	**+3**		
Screening Assessments											
Informed consent	X										• Informed consent should be obtained prior to undergoing any study-specific procedures. See Section 10.1.3 for additional information.
Medical history & demographics	X										• Includes disease history (symptoms at diagnosis and length of time on GFD) and GC history (within previous 12 months).
Inclusion/exclusion	X	X									
HIV, HBV, HCV testing	X										• See Exclusion Criterion #19 (See Appendix 2 for additional information).
HLA genotype	X										• HLA genotype will be assessed via central laboratory. For rescreening, HLA does not need to be repeated.

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Visit Identifier	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**	**ET**	• Day relative to start of study intervention (Day 1). • See Section 8.4.3 for follow-up AE and SAE assessments. • D16 and D21 are phone call visits (See Section 8.1.1) for collection of AEs and concomitant medications.
Type (Site or Phone Call)	**Site**	**Site**	**Site**	**Site**	**Site**	**Phone**	**Phone**	**Site**	**Site**	**Site**	
Study Day (D)	**Up to -42 days**	**D1**	**D4**	**D7**	**D15**	**D16**	**D21**	**D29**	**D42**	**ET**	
Visit Window (days)						**+2**	**±2**	**+3**	**+3**		
CeD serology	X								X	X	• CeD serology (tTG-IgA and DGP IgG) will be assessed via central laboratory (see Appendix 2 for additional information). For rescreening, CeD serology only needs to be repeated if >3 months have elapsed from last assessment.
12-lead ECG	X										• Not required for participants who have had an ECG within 3 months prior to screening.
Set up eDiary	X										
Clinical Procedures											
Physical examination	X							X	X	X	• See Section 8.3.5.
Pregnancy test	X	X			X			X	X	X	• Test at screening must be serum; serum or urine tests are acceptable at other visits. Screening and pre-dosing pregnancy tests must be negative before study intervention is administered. D15 pregnancy test must be negative before 2-week GC is initiated. See Section 8.3.6.
Contraception check	X	X	X	X	X			X	X	X	• See Section 5.3.1
Vital signs	X	X	X	X	X			X	X	X	• At screening only, includes height and weight. • Vital signs (pulse rate, temperature, respiratory rate, diastolic and systolic blood pressure) should be assessed before, during, and after dosing and before sample collection. See Section 8.3.2 for additional information.

Table 1. Schedule of Assessments

Abbreviations used in this table may be found in Appendix 12.	Scr.	Treatment Period			Gluten Challenge (Day 15 to 28)			Biopsy	FU	ET	Notes
Visit Identifier	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**	**ET**	• Day relative to start of study intervention (Day 1). • See Section 8.4.3 for follow-up AE and SAE assessments. • D16 and D21 are phone call visits (See Section 8.1.1) for collection of AEs and concomitant medications.
Type (Site or Phone Call)	**Site**	**Site**	**Site**	**Site**	**Site**	**Phone**	**Phone**	**Site**	**Site**	**Site**	
Study Day (D)	**Up to -42 days**	**D1**	**D4**	**D7**	**D15**	**D16**	**D21**	**D29**	**D42**	**ET**	
Visit Window (days)						**+2**	**±2**	**+3**	**+3**		
Prior/concomitant meds/procedures, incidental gluten exposure	X	X	X	X	X	X	X	X	X	X	• See Section 6.9 for additional information. • Incidental gluten exposure checked daily; entered into eDiary and reviewed at study visits.
EGD with biopsy (approx. 6 duodenal biopsies)	X							X		X	• EGD should only be performed after the participant has qualified with all other inclusion/exclusion criteria. • For rescreening, EGD does not need to be repeated if 1) <3 months have elapsed from last screening assessment, 2) the participant has continued GFD and 3) the participant has not undergone a GC. • Only participants who have completed all 3 doses of study intervention and at least 7 days of GC should undergo EGD with biopsy at D29 or at ET visit (if participant discontinues prior to D29).
PGIS		X			X			X	X	X	• Day 1 PGIS should be completed pre-dose (at least 5 minutes prior to infusion).
PGIC					X			X	X	X	
GC					D15-28 daily						• GC completed in clinic on D15 and at home for the next 13 days (D16 to D28). • Participants who withdraw from treatment and do not receive 3 full doses should not receive GC.
CDSD v2.1	To be completed daily										• PRO (CDSD© v2.1) will be completed via eDiary for at least 7 consecutive days during screening. • For re-screening: CDSD v2.1 only needs to be repeated if >3 months have elapsed from end of last PRO administration.

Table 1. Schedule of Assessments

Abbreviations used in this table may be found in Appendix 12.	Scr.	Treatment Period			Gluten Challenge (Day 15 to 28)			Biopsy	FU	ET	Notes
Visit Identifier	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**	**ET**	• Day relative to start of study intervention (Day 1). • See Section 8.4.3 for follow-up AE and SAE assessments. • D16 and D21 are phone call visits (See Section 8.1.1) for collection of AEs and concomitant medications.
Type (Site or Phone Call)	**Site**	**Site**	**Site**	**Site**	**Site**	**Phone**	**Phone**	**Site**	**Site**	**Site**	
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Visit Window (days)						**+2**	**±2**	**+3**	**+3**		
Safety Assessments											
Serious and non-serious AE monitoring	X	X	X	X	X	X	X	X	X	X	• See Section 8.4 for additional information.
Laboratory tests (safety)	X	X	X	X	X			X	X	X	• Includes hematology, chemistry, urinalysis, and coagulation. See Appendix 2 for a list of Clinical Laboratory tests to be done. For collection volumes, see the study laboratory manual. • Day 1,4, & 7 collection should be done pre-dose (at least 5 minutes prior to infusion). Day 15 collections should be done prior to the GC.
Study Intervention Administration and Randomization											• See Section 6 for additional information.
Randomization		X									
Study Intervention Administration		X	X	X							• See Section 6.1.1. Participants will be observed for at least 4 hours in clinic following IV infusion.
Additional Blood Samples											
PK blood sample		X		X							• PK sampling will be done pre-dose (at least 5 minutes prior to infusion) and end of infusion (+2) minutes. Additional sampling will be done at 2.5 hours (±5 minutes) and 4 hours (±5 minutes) after infusion start.

Table 1. Schedule of Assessments

Abbreviations used in this table may be found in Appendix 12.	Scr.	Treatment Period			Gluten Challenge (Day 15 to 28)			Biopsy	FU	ET	Notes
Visit Identifier	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**	**ET**	• Day relative to start of study intervention (Day 1). • See Section 8.4.3 for follow-up AE and SAE assessments. • D16 and D21 are phone call visits (See Section 8.1.1) for collection of AEs and concomitant medications.
Type (Site or Phone Call)	**Site**	**Site**	**Site**	**Site**	**Site**	**Phone**	**Phone**	**Site**	**Site**	**Site**	
Study Day (D)	**Up to -42 days**	**D1**	**D4**	**D7**	**D15**	**D16**	**D21**	**D29**	**D42**	**ET**	
Visit Window (days)						**+2**	**±2**	**+3**	**+3**		
ADA sample		X		X				X	X	X	• D1 & D7 samples should be taken pre-dose (at least 5 minutes prior to infusion).
Plasma biomarker (includes IL-2) sample		X	X	X	X			X	X	X	• See Section 8.2.2 for additional information. • D1, D4, and D7 samples should be taken pre-dose (at least 5 minutes prior to infusion) and 4 hours post end of infusion ± 15 minutes. Day 15 sample should be collected prior to GC and at 4 hours (± 15 minutes) after GC. • A single sample is collected on D29, D42, and ET. • Participants who withdraw from treatment and do not receive 3 full doses should not have plasma samples collected at D15, D29, and D42.

ADA – Anti-Drug Antibody; AE – Adverse Event; CDSD – Celiac Disease Symptom Diary; CeD – Celiac Disease; D - Day; DGP IgG – Deamidated Gliadin Peptide, Immunoglobulin G; ECG – Electrocardiogram ;eDiary – Electronic Diary; EGD – Esophagogastroduodenoscopy; ET – Early Termination; FU – Follow Up; GC – Gluten Challenge; GFD – Gluten Free Diet; HBV – Hepatitis B Virus; HCV – Hepatitis C Virus; HIV – Human Immunodeficiency Virus; HLA – Human Leukocyte Antigens; IL-2 – Interleukin-2;IV – Intravenous; PGIC – Patient Global Impression of Change; PGIS – Patient Global Impression of Severity; PK – Pharmacokinetics; PRO – Patient Reported Outcome; SAE – Serious Adverse Event; Scr – Screening; tTG, IgA – Tissue Transglutaminase Immunoglobulin A; V - Visit

2. INTRODUCTION

2.1. Study Rationale

The sponsor is initiating this Phase 2a study of KAN-101 in adult participants with CeD to investigate the ability of KAN-101 to protect intestinal mucosa from gluten-induced histological damage.

2.2. Background

2.2.1. Celiac Disease

CeD is an inherited autoimmune disorder that affects the digestive process of the small intestine. When a patient with CeD consumes gluten, that individual's immune system responds by attacking the small intestine, thereby inhibiting the absorption of nutrients. CeD can present with a variety of GI symptoms, including diarrhea, bloating, flatulence and abdominal pain, and non-GI symptoms such as anemia and vitamin deficiencies (Halfdanarson et al, 2007; Rubio-Tapia et al, 2013). Undiagnosed and untreated CeD has been linked to the development of other autoimmune disorders, nutritional disorders such as osteoporosis and infertility, and neurological conditions (Green et al, 2001; Green & Jabri, 2006).

It has been recently estimated that 0.7% of the world-wide population has CeD, with global prevalence rates on the rise (Singh et al, 2018). CeD is strongly associated with the Human Leukocyte Antigen *(HLA)-DQA1* and *HLA-DQB1* loci (*HLA-1*05*, *HLA-DQB1*02*; commonly referred to as HLA-DQ2.5) which is present in approximately 90% of CeD patients (Sollid et al, 1989; Sollid et al, 2012). The pathology observed in CeD patients is driven by the adaptive immune response specific to proteins generated in the digestive system after ingestion of gluten, which results in autoimmune-like pathology in the small intestine (Sollid & Jabri, 2013). Diagnosis is typically made by a combination of positive IgA, tTG, and/or IgG, DGPs, and small intestinal biopsy demonstrating villous abnormalities while on a gluten-containing diet or following a GC (Halfdanarson et al, 2007; Rubio-Tapia et al, 2013).

There is currently no pharmaceutical treatment approved for the management of CeD. Patients manage their symptoms by strict adherence to a GFD, which often presents a substantial logistical and financial burden (See et al, 2015). The effectiveness of the GFD is limited not only by motivation, access, and expense, but by uncertainty related to potential gluten content of certain medications and supplements. Adherence to the strict GFD is also limited by the ubiquity of gluten contamination in many gluten-free foods. Several studies have shown incomplete histological normalization of small bowel mucosa despite a strict GFD, with persistent villous atrophy seen in up to 79% of treated patients (See et al, 2015). In addition to adherence challenges, some patients report persistent, life-affecting symptoms despite attempting to adhere to the GFD. Patients with CeD who adhere to a strict GFD continue to have a heavy burden of care.

Thus, there remains a strong unmet medical need for pharmacologic interventions to help alleviate the growing disease burden of CeD.

2.2.2. KAN-101

KAN-101 is composed of a synthetic liver-targeting CCI [redacted] to a synthetic CCI [redacted] peptide domain of wheat alpha gliadin (KAN0009) recognized by the HLA-DQ2.5 haplotype. KAN0009 does not bind to the HLA-DQ8 molecule. KAN-101 is a liquid formulation drug product administered parenterally via an IV infusion.

KAN-101 harnesses natural tolerogenic pathways in the liver (Thomson & Knolle, 2010) to reprogram pathogenic immune cells to become tolerant toward specific antigens. KAN-101 specifically targets the immune cells that drive CeD and leaves the otherwise healthy components of the immune system intact to perform their natural, protective functions. The proposed mechanism of action of KAN-101 is receptor-mediated internalization of the molecule into liver cells, and the induction of immune tolerance through subsequent KAN0009 gliadin peptide antigen presentation on the major histocompatibility complex (MHC; class I and II). After KAN-101 internalization into liver cells, the KAN0009 peptide is released from the GP portion and processed intracellularly for presentation by MHC and signaling to gliadin-specific T cells for the induction of immune tolerance and subsequent amelioration of gut pathology.

The mechanisms by which KAN-101 induces immunologic tolerance are mediated by:

- Deletion of antigen-specific T cells
- Induction of anergy/clonal exhaustion of antigen-specific T cells
- Induction of regulatory T cells which control the antigen-specific T cell response.

For more information on the nonclinical findings, please see the KAN-101 IB.

2.2.3. Clinical Overview

KAN-101 was evaluated in a FIH Phase 1 study in participants with CeD on a GFD (KAN-101-01). KAN-101-01 was a 2-part, multicenter study designed to examine the safety and tolerability of SAD (Part A) and MAD (Part B) of KAN-101. A total of 41 participants received at least 1 dose of KAN-101 (0.15 mg/kg, 0.3 mg/kg, 0.6 mg/kg, 1.2 mg/kg, and 1.5 mg/kg) during the study. KAN-101 is also currently being evaluated in a two-part Phase 1b/Phase 2 study (KAN-101-02).

Study KAN-101-01

In Study KAN-101-01 administration of KAN-101 was effective at inducing T-cell tolerance (Murray et al, 2023):

- Three doses of KAN-101, administered 3 days apart, at 0.15, 0.3 and 0.6 mg/kg dose levels was effective in inducing T cell tolerance to gliadin. KAN-101 treated participants exhibited minimal change or a decrease in the gliadin-specific T-cell response following GC while placebo patients exhibited an increase in the gliadin-specific T-cell response following GC.

- KAN-101 also modified the immediate immune reaction upon ingestion of gluten by CeD participants in a dose-dependent manner. Participants treated with 3 doses of 0.6 mg/kg KAN-101, administered 3 days apart, exhibited lower median plasma IL-2 levels within hours of GC compared to placebo or 0.15 and 0.3 mg/kg KAN-101 dose levels.

KAN-101 demonstrated an acceptable safety and tolerability profile after single and multiple doses at all dose levels tested in KAN-101-01. There were no deaths, SAEs, or Grade 3 TEAEs observed. TEAEs were consistent with CeD participants upon gluten ingestion (ie, nausea, emesis, abdominal pain, headache, and diarrhea). No clinically relevant trends were observed for changes in vital signs, physical examination, laboratory tests, or ECG results. There were no meaningful correlations between the frequency of TEAEs and study drug dose level. There was an increased frequency of participants who experienced GI AEs in the total drug-treated group than in the placebo group in KAN-101-01. No MTD of KAN-101 was identified and no meaningful safety differences were observed among treatment groups during the study.

Data from the KAN-101-01 study suggests rapid elimination with mean half-life ranging from 3.74 to 36.8 minutes across 0.15 mg/kg to 1.2 mg/kg doses, following single or repeat IV infusions of KAN-101. The mean KAN-101 maximum exposure (C_{max}) and systemic exposure (AUC) appeared to exhibit approximate dose proportionality across 0.15 to 1.2 mg/kg dose range. With repeat dosing, there was no accumulation of KAN-101 which was in concordance with the rapid elimination.

Study KAN-101-02

Study KAN-101-02 is an ongoing, 2-part study to evaluate the safety, tolerability, PK parameters, and plasma biomarker (IL-2) response of participants with CeD treated with KAN-101. KAN-101-02 Part A is a Phase 1b, open-label MAD study to evaluate safety, tolerability, and PK of two doses of KAN-101, administered three days apart, at 1.2 and 3.0 mg/kg dose levels. Part B is a Phase 2, double-blind, PBO-controlled parallel design study to characterize the biomarker response in peripheral blood following GC. In Part B, participants will be randomized 1:1:1:1 to 4 treatment groups: PBO, 0.6 mg/kg, 1.2 mg/kg, or 3.0 mg/kg KAN-101.

In the original protocol for KAN-101-02, 1.2 mg/kg 3.0 mg/kg and 6.0 mg/kg KAN-101 were planned to be evaluated in a MAD 3+3 design (Part A). Based upon emerging data from Part A reviewed by the KAN-101-02 independent DSMB, the protocol was amended (Amendment 1) to proceed to Part B following completion of the Part A 3.0 mg/kg dose cohort. The decision not to test 6.0 mg/kg was not due to any safety concerns or exposures which exceeded the NOAEL. Part B is ongoing and will evaluate 0.6 mg/kg, and 1.2 mg/kg, and 3.0 mg/kg will be evaluated in a dose-ranging design (Part B) in CeD participants on GFD.

For more information on the nonclinical and previous clinical findings, please see the KAN-101 IB.

Based on nonclinical and clinical findings from the FIH study (KAN-101-01), as well as independent DSMB reviewed preliminary data from the ongoing Phase 1b/2 study in adults with CeD (KAN-101-02), the sponsor is initiating this Phase 2a study of KAN-101 in adult participants with CeD to investigate the ability of KAN-101 to protect intestinal mucosa from gluten-induced histological damage.

2.3. Benefit/Risk Assessment

More detailed information about the known and expected benefits and risks and reasonably expected AEs of KAN-101 is found in the IB, which contains the RSI, which is the SRSD for this study. Refer to the Study Intervention(s) table in Section 6.1 for a complete description of SRSDs.

2.3.1. Risk Assessment

Potential Risk of Clinical Significance	Summary of Data/Rationale for Risk	Mitigation Strategy
Study Intervention(s) [KAN-101 and placebo]		
Potential for exacerbation of gastrointestinal symptoms associated with CeD, which may include and are not necessarily limited to AEs of headache, dizziness, fatigue/lethargy, nausea, vomiting, abdominal pain, diarrhea, constipation, skin rash, and abdominal tenderness.	The potential risks are based on the mechanism of action of KAN-101 and other similar therapeutic investigational immunomodulatory therapies in CeD (Daveson et al, 2017; Truitt et al, 2019).	AEs and clinical laboratory results will be monitored on an ongoing basis and managed according to established standard of care.
Use of a placebo arm.	The use of a placebo represents a potential risk.	Participants who experience worsening of CeD may discontinue from the study and may receive standard of care treatment at the investigator's discretion.
IV infusions will be administered over 30 minutes every 3 days during study treatment period.	IRR are known risks associated with IV infusions.	IRR will be monitored and specific guidance on acute and prophylactic treatment of IRRs and recommendations for future infusions of KAN-101 are provided in Appendix 9.
Potential hypersensitivity reactions may occur and include skin reaction, mucosal tissue reaction, respiratory reaction, GI reactions, and CV reactions.	Similar to other biologic molecules.	Participants will be closely monitored on site for 4 hours post infusion for signs of any reaction.
KAN-101 is a liver targeting agent.	Although FIH Study KAN-101-01 and nonclinical data show that KAN-101 had no significant impact on the liver (eg, liver enzyme levels and histopathology). KAN-101's potential impact on liver enzymes and bilirubin will continue to be evaluated in the clinical setting.	Transaminase, ALP and total bilirubin levels will be closely monitored and are included in safety laboratory assessments. Participants with ALT, AST, or ALP >1.5 ×ULN are not eligible for enrollment in KAN-101-03.

Potential Risk of Clinical Significance	Summary of Data/Rationale for Risk	Mitigation Strategy
		Participants considered to have a potential case of Hy's law will lead to a cessation of clinical dosing and participant will be followed to resolution.
Study Procedures		
KAN-101-03 includes a multiple-day (Day 15-28 daily) GC comprising ingestion of 9g/day of gluten protein.	Known AEs associated with GC are expected, which may include and are not necessarily limited to AEs of headache, fatigue/lethargy, nausea, vomiting, abdominal pain, diarrhea, constipation, and skin rash. Histological damage will occur as a result of the prolonged GC and could result in altered absorption of nutrients or fluids. Symptoms of such damage could include diarrhea, weight loss, and iron deficiency anemia.	Participants will consume the GC in clinic on Day 15 and at home for the remain 13 days through Day 28 and will be monitored for AEs associated with GC and managed according to established standard of care. The histological damage does not persist long-term and is reversed upon GFD. Participants will be monitored for AEs, including symptoms of CeD and intestinal mucosal damage, and safety labs will be assessed throughout the study to identify any abnormalities that may occur.
KAN-101-03 includes 2 EGD with biopsy (Screening and Day 29).	EGD with biopsy carries a small risk of bowel perforation. Duodenal biopsies also carry the risk of duodenal hematoma.	EGD for the study will be performed by qualified and experienced gastroenterologists.
Other		
The COVID-19 pandemic may pose risks to study participation.	Participants may have increased risk of SARS-CoV-2 infection by undergoing a study procedure at a study facility.	Inclusion of COVID-19 specific screening procedures and assessments according to the SoA.

2.3.2. Benefit Assessment

There is no individual health benefit for participating in the study. However, participants contribute to the process of developing new therapies for CeD for which there remains a strong unmet medical need for pharmacologic interventions to help alleviate the growing disease burden.

2.3.3. Overall Benefit/Risk Conclusion

The overall potential benefit/risk of KAN-101 is considered favorable.

Considering the measures and mitigations to minimize risk to study participants, the potential risks, including the use of a placebo arm, identified in association with participation in the study and with KAN-101 are justified by the anticipated benefits that may be afforded to participants with CeD.

3. OBJECTIVES, ENDPOINTS, AND ESTIMANDS

Objectives	Endpoints	Estimands
Primary:	**Primary:**	**Primary:**
• Assess the ability of KAN-101 to attenuate GC-induced changes in duodenal histology as measured by changes in Vh:Cd ratio after a 2-week GC.	• Changes from baseline in Vh:Cd ratio as assessed by EGD with biopsy after 2-week GC (at Day 29).	**Estimand 1:** The primary estimand is the hypothetical estimand, which estimates the treatment effect of KAN-101 vs Placebo for change from baseline in Vh:Cd under the scenario of no intercurrent events. It includes the following 5 attributes: • Population: Participants who receive all 3 doses of study intervention and complete at least 7 days of GC. • Variable: the ratio of Vh:Cd change from baseline at Day 29. • Treatment conditions: KAN-101 or placebo. • Intercurrent Events: Prohibited medication. All data collected after any intercurrent events will be excluded. • Population level summary: The LSM difference of the change from baseline in Vh:Cd between KAN-101 and placebo.
Secondary:	**Secondary:**	**Secondary:**
• Examine the impact of KAN-101 on biomarker response (IL-2) in peripheral blood following GC	• IL-2 change from Day 15 (first day of GC) pre GC to Day 15 post GC	**Estimand 2** is the hypothetical estimand, which estimates the treatment effect of KAN-101 vs Placebo for IL-2 under the scenario of no intercurrent events. It includes the following 5 attributes: • Population: Participants who complete all 3 doses of study intervention and complete at least 7 days of GC.

Objectives	Endpoints	Estimands
		• Variable: log transformed IL-2 change from pre GC to post GC at Day 15. • Treatment conditions: KAN-101 or Placebo. • Intercurrent Events: Prohibited medication, incomplete GC on Day 15. All data collected after any intercurrent events will be excluded. • Population level summary: The LSM difference of the change from pre GC to post GC at Day 15 (log transformed) between KAN-101 and placebo.
• Determine the effects of KAN-101 on histologic features (IELs density) in duodenum biopsies following 2-week GC.	• Changes from baseline in IEL density in duodenum biopsy after 2-week GC (at Day 29)	**Estimand 3** is the hypothetical estimand, which estimates the treatment effect of KAN-101 vs placebo for change from baseline in duodenal IEL density under the scenario of no intercurrent events. It includes the following 5 attributes: • Population: Participants who complete all 3 doses of study intervention and complete at least 7 days of GC. • Variable: IEL change from baseline at Day 29. • Treatment conditions: KAN-101 or placebo. • Intercurrent Events: Prohibited medication. All data collected after any intercurrent events will be excluded. • Population level summary: The LSM difference of the change from baseline in IEL between KAN-101 and placebo.
• Assess the safety and tolerability of KAN-101 in participants with CeD.	• Incidence and severity of treatment emergent AEs as assessed by the CTCAE v6.0 (or higher)	Not applicable.
	• Incidence and titer of KAN-101 ADA.	Not applicable.
• Assess the PK of multiple doses of KAN-101 in participants with CeD.	• Plasma concentration of KAN-101, and associated KAN-101 parameters: AUCinf, AUClast, Cmax, Tmax and t½	Not applicable.
Tertiary/Exploratory:	**Tertiary/Exploratory:**	**Tertiary/Exploratory:**
• Evaluate changes in histological features (Marsh-Oberhuber score) after a 2-week GC	• Changes from baseline in Marsh-Oberhuber score assessed via EGD with biopsy after 2-week GC	Not applicable.

Objectives	Endpoints	Estimands
• Assess the impact of KAN-101 administration on the incidence of CeD symptoms before and during GC as measured using CDSD v2.1.	• Changes from baseline in symptoms PROs including: CDSD v2.1, PGIC and PGIS over time.	Not applicable.
• Assess whether KAN-101 affects the incidence and/or titer of post-GC celiac serology.	• Incidence and titer of tTG IgA and DGP IgG at Day 42.	Not applicable.

4. STUDY DESIGN

4.1. Overall Design

Study KAN-101-03 is a multi-center, double-blind, placebo-controlled Phase 2a study to examine whether KAN-101 confers protection from GC-induced histological changes in the duodenum and to further evaluate the safety/tolerability of KAN-101 in adult participants ≥18 years to 70 years with CeD. Fifty-two participants (26 participants per arm) will be randomized 1:1 to the following arms:

1. 0.6 mg/kg KAN-101 (Arm 1)
2. Placebo (Arm 2)

Kanyos Bio, Inc. a wholly owned subsidiary of Anokion, as the sponsor of the study, is delegating to Pfizer all obligations for conduct of Study, including responsibility for preparing the protocol, and overall conduct and oversight of the study, including contracting with study sites. For this study, a DSMB (see Section 10.1.5) will review cumulative safety data.

This study comprises 4 periods:

- **Screening period:** up to ≤42 days before treatment initiation
  - During the screening period, eligibility will be confirmed by EGD with duodenal biopsy. The EGD with biopsy will only be performed once all other inclusion criteria are fulfilled. Histology results must be received prior to dosing to confirm eligibility.
- **Treatment period:** The study treatment period is 7 days (Day 1 to Day 7). Study intervention (either KAN-101 or placebo) will be administered to enrolled participants in the clinic IV on Days 1, 4, and 7. Post infusion each treatment day, participants will be monitored in the clinic for at least 4 hours for adverse reactions.

- **Gluten Challenge (GC):** 14 days
    - Participants will undergo a 2-week GC in which they will ingest 9 g/day of gluten protein in the form of 12 g vital wheat gluten. All participants will return to the clinic Day 15 for the first day of the GC. The Day 15 GC will be performed in the clinic under supervision and blood samples will be collected at least 5 minutes prior to GC and 4 hours after the completion of the Day 15 GC for biomarker assessment. Materials will be sent home with the participant to complete the daily GC for the next 2 weeks (through Day 28). The study site will call the participant on Day 16 and Day 21 to collect data on any AEs and/or CM over the telephone. Symptom monitoring will be conducted via the eDiary.

- **Observation/follow-up period:** Participants will be followed for safety for 42 days (Day 1 to Day 42). The second EGD with duodenal biopsy will be conducted on Day 29. Participants will return to the clinic on Day 42 for a final follow-up visit including safety assessment and labs, celiac serology, and exploratory biomarker sample collections. See SoA for assessments to be performed at this visit.

Refer to Table 1 for the complete schedule of assessments. If participants are unable to return to the clinic for protocol-specified visits, alternative methods for safety assessments and data collection may be employed to ensure the safety of the trial participants when appropriate.

An interim analysis may be performed when approximately 13 evaluable participants from each group have completed the Day 29 visit and histology assessments. Further details and study stopping criteria are presented in Section 9.5.

4.2. Scientific Rationale for Study Design

Based on nonclinical and clinical findings from the FIH study (KAN-101-01), the sponsor is initiating this Phase 2a study of KAN-101 in adult participants with CeD to investigate the ability of KAN-101 to protect intestinal mucosa from gluten-induced histological damage.

4.2.1. Choice of Contraception/Barrier Requirements

KAN-101 has not been evaluated in EFD study. The effects of KAN-101 on conception, pregnancy, and lactation are unknown. Therefore, the use of a highly effective contraception is required for WOCBP, and all men who are not sterile (biologically or surgically) must commit to the use of 1 reliable method of birth control for at least 21 days after the last dose of study intervention (see Appendix 4 for further information).

The observed $t_{1/2}$ of KAN-101 ranges between 3.74 to 36.8 minutes across 0.15 mg/kg to 1.5 mg/kg doses with no accumulation observed for repeat dosing. Pre-clinical toxicology and clinical information for KAN-101 are summarized in the IB.

4.3. Justification for Dose

The proposed dose of KAN-101 is 0.6 mg/kg administered in 3 doses 3 days apart. The nonclinical Experimental Autoimmune Encephalomyelitis (EAE) mouse model also demonstrated that dosing every 3 days was significantly more effective in inducing tolerance and improving disease outcome than 3 doses administered weekly, or 3 doses administered daily. While KAN-101 is expected to be rapidly distributed from the bloodstream into the liver, which is the target organ, it appears to have fast clearance and lack of accumulation after exposure in plasma/serum in preclinical and clinical studies. The 0.6 mg/kg administered in 3 doses 3 days apart in the FIH KAN-101-01 study has been established to be safe and tolerable. The clinical efficacy biomarker data from the study KAN-101-01 study further supports this dosing regimen since plasma inflammatory IL-2 biomarker levels after gluten challenge were lower in the 0.6 mg/kg dose group (when compared with placebo) at all timepoints examined on D15.

The EAE model is an inflammatory and demyelinating disease model that recapitulates human multiple sclerosis pathology. EAE was chosen due to a lack of available celiac disease models. The EAE model data demonstrated that dosing every 3 days was more effective than weekly dosing, and it was also determined that 3 doses administered every 3 days were significantly more effective in inducing tolerance and improving disease outcome than 3 doses administered weekly, or 3 doses administered daily. This dosing frequency is further supported by the clinical efficacy biomarker data from the FIH study KAN-101-01 where plasma inflammatory IL-2 biomarker levels were monitored before and after gluten challenge for dose and placebo groups. The data showed that plasma IL-2 levels observed after gluten challenge were lower in the 0.6 mg/kg dose group compared with placebo at all timepoints examined on D15. Finally, KAN-101 is rapidly distributed from the bloodstream into the liver; serum and plasma concentrations are undetectable within 1 to 4 hours of dose administration in rats and cynomolgus monkeys. The half-life observed in the FIH study KAN-101-01 was on the order of 30 minutes. There is no evidence of accumulation with repeated dosing in either preclinical or clinical studies.

The doses tested in FIH KAN-101-01 study were 0.3, 0.6, and 1.2 mg/kg and no safety signals were observed. Additionally, the highest dose tested in the ongoing KAN-101-02 study is 3mg/kg and no safety signals have been observed. The dose proposed for this study is 0.6 mg/kg administered in 3 doses 3 days apart.

4.4. End of Study Definition

The end of the study is defined as the date of the last visit of the last participant in the study or last scheduled procedure shown in the SoA for the last participant in the trial globally.

A participant is considered to have completed the study if they have completed all periods of the study, including the last visit or the last scheduled procedure shown in the SoA.

5. STUDY POPULATION

This study can fulfill its objectives only if appropriate participants are enrolled, including participants across diverse and representative racial and ethnic backgrounds. If a prescreening tool is utilized for study recruitment purposes, it will include collection of

information that reflects the enrollment of a diverse participant population including, where permitted under local regulations, age, sex, race, and ethnicity. The following eligibility criteria are designed to select participants for whom participation in the study is considered appropriate. All relevant medical and nonmedical conditions should be taken into consideration when deciding whether a particular participant is suitable for this protocol.

Prospective approval of protocol deviations to recruitment and enrollment criteria, also known as protocol waivers or exemptions, is not permitted.

5.1. Inclusion Criteria

Participants are eligible to be included in the study only if all of the following criteria apply:

Age and Sex:

1. Participants aged 18 years to 70 inclusive (or the minimum age of consent in accordance with local regulations) at screening.
    - Refer to Appendix 4 for reproductive criteria for male (Section 10.4.1) and female (Section 10.4.2) participants.

Disease Characteristics:

2. Previous diagnosis of CeD, based on documentation in the source data:
    - Positive celiac serology (eg, tissue transglutaminase IgA antibody and/or deamidated DGP IgG)
        - AND
    - Intestinal histology consistent with ≥ Marsh Type II or with evidence of villous atrophy.
3. Have HLA-DQ2.5 genotype (HLA-DQA1*05 and HLA-DQB1*02) (homozygotes or heterozygotes).
4. Negative or weak positive for transglutaminase IgA AND negative or weak positive for DGP-IgA/IgG during screening.
5. Screening intestinal biopsy demonstrating Vh:Cd ratio of 2.3 or higher.

Other Inclusion Criteria:

6. Have followed a gluten-free diet for ≥12 months immediately prior to study entry (self-reported).
7. Capable of understanding the ICD, complying with protocol requirements, and has signed the ICD.

5.2. Exclusion Criteria

Participants are excluded from the study if any of the following criteria apply:

Medical Conditions:

1. Refractory CeD, defined as severe persistent or recurrent malabsorptive signs or symptoms with substantial villous atrophy (eg, documented Marsh score 3c in source data) despite strict adherence to a GFD for at least 12 months in the absence of other disorders.

2. Selective IgA deficiency.

3. Positive for HLA-DQ8 genotype (*DQA1*03, DQB1*0302*) even if DQ2.5 is also present.

4. Known wheat allergy.

5. Diagnosis of type-I diabetes.

6. History of dermatitis herpetiformis.

7. Pregnant or breastfeeding.

8. Known history of severe hypersensitivity reactions or anaphylaxis to gluten.

9. Active gastrointestinal disease other than CeD (eg, inflammatory bowel disease, any forms of colitis except well-controlled microscopic colitis, uncontrolled IBS, peptic ulcer disease, eosinophilic esophagitis, and active GI infections).

10. Clinical signs and symptoms consistent with COVID-19 or confirmed infection by appropriate laboratory test within the 2 weeks prior to screening or dosing.

    - *Note:* participants who experienced symptoms consistent with COVID-19 or confirmed infection during the screening period may be rescreened after 4 weeks.

11. Prior severe course of COVID-19 requiring extracorporeal membrane oxygenation or mechanical ventilation within the last 12 months.

12. Any medical or psychiatric condition including recent (within the past year) or active suicidal ideation/behavior or laboratory abnormality or significant complications with previous EGD or presence of significant risk factors for complications associated with EGD, such as ASA Physical Status III or higher (see Appendix 11), that may increase the risk of study participation or, in the investigator's judgement, make the participant inappropriate for the study.

Prior/Concomitant Therapy:

13. Previous treatment with tolerance-inducing therapies for CeD.

14. Current use or incomplete washout of any prohibited concomitant medication(s) or participants unwilling/unable to use a permitted concomitant medication(s). Refer to Section 6.9 Prior and Concomitant Therapy.

Prior/Concurrent Clinical Study Experience:

15. Previous administration with an investigational product (drug or vaccine) within 30 days (or as determined by the local requirement) or 5 half-lives preceding the first dose of study intervention used in this study (whichever is longer).

Diagnostic Assessments:

16. Renal impairment as defined by an eGFR in adults of <60 mL/min/1.73m^2. Based upon participant age at screening, eGFR is calculated using the recommended formulas in Section 10.7.2 to determine eligibility and to provide a baseline to quantify any subsequent kidney safety events.

17. Hepatic dysfunction defined as:

    - Total bilirubin ≥1.5 × ULN (except for Gilbert's syndrome)
    - AST ≥1.5 × ULN
    - ALT ≥1.5 × ULN
    - Alkaline phosphatase >1.5 × ULN

18. Hematologic abnormalities defined as:

    - ANC ≤1000 mm^3
    - Platelets ≤100 × 10^9/L
    - Hemoglobin ≤10 g/dL
    - WBC outside the normal range and assessed as clinically significant by the investigator.

19. Positive for HIV, hepatitis B, and/or hepatitis C.

    - For Hepatitis B, all participants will undergo testing for HBsAg and HBcAb during screening. Participants who are HBsAg positive are not eligible for the study. Participants who are HBsAg negative and HBcAb positive will be

reflex tested for HBsAb and HBV DNA. If HBsAb is positive and HBV DNA negative, they may be enrolled in the study; if HBsAb is negative and/or HBV DNA is positive, the participant is not eligible for the study.

- For Hepatitis C, all participants will undergo HCVAb during screening. Participants with positive HCVAb tests will be reflex tested for HCV RNA. Only participants with negative HCVAb or HCV RNA will be allowed to enroll.

- For HIV, known history of HIV based on documented history with positive serological test, or positive HIV serologic test at screening, tested at central lab.

20. Baseline standard 12-lead ECG that demonstrates clinically relevant abnormalities that may affect participant safety or interpretation of study results (eg, QTcF >450 ms, complete LBBB, signs of an acute or indeterminate-age myocardial infarction, ST-T interval changes suggestive of myocardial ischemia, second- or third-degree AV block, or serious bradyarrhythmias or tachyarrhythmias).

    - If the baseline uncorrected QT interval is >450 ms, this interval should be rate corrected using the Fridericia method only and the resulting QTcF should be used for decision making and reporting.

    - If QTcF exceeds 450 ms, or QRS exceeds 120 ms, the ECG should be repeated twice and the average of the 3 QTcF or QRS values used to determine the participant's eligibility.

    - Computer-interpreted ECGs should be overread by a physician experienced in reading ECGs before excluding a participant.

Other Exclusion Criteria:

21. Investigator site staff directly involved in the conduct of the study and their family members, site staff otherwise supervised by the investigator, and sponsor and sponsor delegate employees directly involved in the conduct of the study and their family members.

5.3. Lifestyle Considerations

The following guidelines are provided:

5.3.1. Contraception

The investigator or their designee, in consultation with the participant, will confirm that the participant is utilizing an appropriate method of contraception for the individual participant and their partner(s) from the permitted list of contraception methods (see Appendix 4, Section 10.4.4) and will confirm that the participant has been instructed in its consistent and correct use. The investigator or designee will advise the participant to seek advice about the

donation and cryopreservation of germ cells prior to the start of study intervention, if applicable.

At time points indicated in the SoA, the investigator or designee will inform the participant of the need to use highly effective contraception consistently and correctly and document the conversation and the participant's affirmation in the participant's chart. Participants need to affirm their consistent and correct use of at least 1 of the selected methods of contraception, considering that their risk for pregnancy may have changed since the last visit.

In addition, the investigator or designee will instruct the participant to call immediately if the selected contraception method is discontinued and document the requirement to use an alternate protocol-specified method, including if the participant will no longer use abstinence as the selected contraception method, or if pregnancy is known or suspected in the participant or partner.

5.3.2. Meals and Dietary Restrictions

Following a GFD is required for study entry (see Section 5.1).

Participants are required to continue to follow a GFD during the study; incidental gluten exposure will be collected daily as part of an eDiary and reviewed at every study visit (see Section 8.3.1).

Participant's use of herbal medicines and probiotics should be reported on the CRF and should remain stable during the study.

5.3.3. Caffeine, Alcohol, and Tobacco

Participants should avoid excessive consumption of alcohol prior to visits with safety lab assessments as specified in the SoA.

5.3.4. Activity

Participants should avoid strenuous physical activities prior to visits with safety lab assessments as specified in the SoA.

5.4. Screen Failures

Screen failures are defined as participants who consent to participate in the clinical study but are not subsequently randomized in the study. CRF reported data will include, but is not limited to, demographics, medical/CeD history, and prior CeD treatments. Non-CRF reported data include, but is not limited to HLA and CeD serology, biopsy results, and CDSD v2.1 data collected up to date of screen failure. Non-CRF reported data will be transferred to the sponsor's designee (Pfizer), for all screen failure participants. Rescreening

Individuals who do not meet the criteria for participation in this study (screen failure) may be rescreened.

Participants **cannot be rescreened** if they fail screening due to:

- HLA genotyping assessment at screening.
- Positive for HIV, HBV, or HCV.
- Screening histology assessment.

For rescreening: the following assessments **do not need to be repeated**:

- HLA genotype assessment
- CeD serology, if <3 months have elapsed from last screening assessment
- 12-lead ECG, if <3 months have elapsed since last screening assessment
- EGD with biopsy, if <3 months have elapsed from last screening assessment
- CDSD v2.1, if <3 months have elapsed from last PRO administration

6. STUDY INTERVENTION(S) AND CONCOMITANT THERAPY

Study interventions are all prespecified investigational and noninvestigational medicinal products/auxiliary medicinal products, medical devices, and other interventions (eg, surgical and behavioral) intended to be administered to the study participants during the study conduct.

For the purposes of this protocol, study intervention refers to KAN-101 or placebo.

6.1. Study Intervention(s) Administered

Study Intervention(s)		
Intervention Name	KAN-101	Placebo (Saline Solution)
Arm Name (group of participants receiving a specific treatment or no treatment)	KAN-101 (Arm 1)	Placebo (Arm 2)
Type	Drug	Drug
Dose Formulation	Solution for infusion	Solution for infusion
Unit Dose Strength(s)	CCI [redacted]	NA
Dosage Level(s)	CCI [redacted]	Placebo
Route of Administration	IV	IV
Use	Experimental	Placebo

Study Intervention(s)		
IMP or NIMP/AxMP	IMP	Placebo
Sourcing	Provided centrally by the sponsor. Further details are presented in the IPM.	Provided locally by the site. Further details are presented in the IPM.
Packaging and Labeling	Study intervention will be provided in glass vials, 1 vial per carton. Each vial and carton will be labeled as required per country requirements. Study intervention will be prepared per IPM instructions and labeled in a blinded manner per country and site requirements.	Placebo will be prepared per IPM instructions and labeled in a blinded manner per country and site requirements.
SRSD	IB	NA

Study Arm(s)		
Arm Title	Arm 1	Arm 2
Arm Type	Experimental	Placebo
Arm Description	Participants will receive 0.6 mg/kg IV KAN-101 every 3 days starting on Day 1 and ending on Day 7.	Participants will receive IV placebo every 3 days starting on Day 1 and ending on Day 7.
Associated Intervention Labels	KAN-101	Placebo

6.1.1. Administration

Inclusion and exclusion criteria (Section 5.1 and Section 5.2) should be reviewed prior to study intervention administration (see SoA).

KAN-101 (0.6 mg/kg) is mixed with saline to a final volume of 250 mL and administered by IV infusion over approximately 30 minutes.

Placebo will be 250 mL normal saline only. Placebo will be administered by IV infusion over approximately 30 minutes.

Administration of study intervention(s) at the site will be performed by an appropriately qualified and trained member of the study staff as allowed by local, state, and institutional guidance.

Following administration of study intervention(s) at the site, participants will be observed for at least 4 hours by an appropriately qualified and trained member of the study staff. Appropriate medication and other supportive measures for management of a medical emergency will be available in accordance with local guidelines and institutional guidelines.

For participants who may experience nausea and/or vomiting following study intervention administration on Day 1, antiemetics (eg, metoclopramide or ondansetron) may be administered 30 minutes before subsequent study intervention administration on Day 4 and/or Day 7 at the discretion of the investigator.

6.2. Preparation, Handling, Storage, and Accountability

This is a double-blind study. Further details regarding blinding of study intervention are presented in Section 6.4.

1. The investigator or designee must confirm that appropriate conditions (eg, temperature) have been maintained during transit for all study interventions received and any discrepancies are reported and resolved before use of the study intervention.

2. Only participants enrolled in the study may receive study intervention and only authorized site staff may supply, prepare, and/or administer study intervention.

3. All study interventions must be stored in a secure, environmentally controlled, and monitored (manual or automated recording) area in accordance with the labeled storage conditions with access limited to the investigator and authorized site staff. At a minimum, daily minimum and maximum temperatures for all site storage locations must be documented and available upon request. Data for nonworking days must indicate the minimum and maximum temperatures since previously documented upon return to business.

4. Any excursions from the study intervention label storage conditions should be reported to Pfizer upon discovery along with actions taken. The site should actively pursue options for returning the study intervention to labeled storage conditions, as soon as possible. Once an excursion is identified, the study intervention must be quarantined and not used until Pfizer provides permission to use the study intervention. Specific details regarding the excursion definition and information to report for each excursion will be provided to the site in the IPM or other specified location.

5. Any storage conditions stated in the SRSD will be superseded by the storage conditions stated on the label. See the IPM for storage conditions of the study intervention once diluted.

6. Study interventions should be stored in their original containers.

7. The investigator, institution, head of the medical institution (where applicable), or authorized site staff is responsible for study intervention accountability, reconciliation, and record maintenance (ie, receipt, reconciliation, and final disposition records), such as the IPAL or sponsor or sponsor delegate-approved equivalent. All study interventions will be accounted for using a study intervention accountability form/record.

8. Further guidance and information for the final disposition of unused study interventions are provided in the IPM. All destruction must be adequately documented. If destruction is authorized to take place at the investigator site, the investigator must ensure that the materials are destroyed in compliance with applicable environmental regulations, institutional policy, and any special instructions provided by Pfizer.

Upon identification of a product complaint, notify Pfizer within 1 business day of discovery as described in the IPM.

6.2.1. Preparation and Dispensing

See the IPM for instructions on how to prepare the study intervention for administration. Study intervention may only be prepared and dispensed by a member of the site's designated unblinded personnel and must be an appropriately qualified and experienced member of the study staff (eg, physician, nurse, physician's assistant, nurse practitioner, pharmacy assistant/technician, or pharmacist) as allowed by local, state, and institutional guidance. A second staff member will verify calculations and paperwork associated with preparation. No information regarding the preparation and dispensation of study intervention may be shared with site's designated blinded personnel. Blinding of site personnel is further described in Section 6.4.2. The study intervention will be administered in a blinded fashion to the participants.

6.3. Assignment to Study Intervention

Allocation of participants to treatment groups will proceed through the use of an IRT system. The site personnel (eg, study coordinator or specified designee) will be required to enter or select information including but not limited to the user's ID and password, the protocol number, and the participant number. The site personnel will then be provided with a randomization number corresponding to the assigned treatment group, and DU or container number(s) when study intervention is being supplied via the IRT system. The IRT system will provide a confirmation report containing the participant number, randomization number, and DU or container number assigned. The confirmation report must be stored in the site's files. Blinding of site personnel is described in Section 6.4.2.

Study intervention will be dispensed at the study visits summarized in the SoA.

The study-specific IRT reference manual and IPM will provide the contact information and further details on the use of the IRT system.

6.4. Blinding

This is a double-blind study.

6.4.1. Blinding of Participants

Participants and their caregivers will be blinded to their assigned study intervention.

6.4.2. Blinding of Site Personnel

Investigators and other site staff will be blinded to participants' assigned study intervention. Participants will be assigned to receive study intervention according to the assigned treatment group from the randomization scheme. Investigators will remain blinded to each participant's assigned study intervention throughout the course of the study.

Unblinded personnel include site staff involved in study intervention preparation and allocation (eg, data systems support and pharmacists).

In order to maintain this blind, an otherwise uninvolved third party will be responsible for the preparation and dispensing of all study intervention and will endeavor to ensure that there are no differences in the time taken to dispense or visual presentation, following randomization or dispensing.

In the event of a Quality Assurance audit, the auditor(s) will be allowed access to unblinded study intervention records at the site(s) to verify that randomization/dispensing has been done accurately.

6.4.3. Blinding of the Sponsor

Sponsor and sponsor-delegate staff will be blinded to participants' assigned study intervention, except for sponsor and sponsor-delegate-staff involved in the assignment or distribution of study intervention. Sponsor and sponsor-delegate staff who are not directly involved with the conduct of this study will prepare analyses and documentation containing unblinded data while the study is ongoing to support interactions with the DSMB.

6.4.4. Breaking the Blind

The IRT will be programmed with blind-breaking instructions. In case of an emergency, the investigator has the sole responsibility for determining if unblinding of a participant's treatment assignment is warranted. Participant safety must always be the first consideration in making such a determination. If the investigator decides that unblinding is warranted, the investigator should make every effort to contact the study medical monitor prior to unblinding a participant's treatment assignment unless this could delay further management of the participant. If a participant's treatment assignment is unblinded, Pfizer must be notified within 24 hours after breaking the blind. The date and reason that the blind was broken must be recorded in the source documentation and CRF.

The study-specific IRT reference manual and IPM will provide the contact information and further details on the use of the IRT system.

6.5. Study Intervention Compliance

The pharmacy will complete the Dose Calculation Worksheet which will be provided as part of the IPM. The use of the Dose Calculation Worksheet is preferred, but it does not preclude the use of an existing appropriate clinical site documentation system. The existing clinical site's documentation system should capture all pertinent/required information on the

preparation and administration of the dose. This may be used in place of the Dose Calculation Worksheet after approval from the sponsor and/or designee.

Compliance with the study intervention is defined as receiving 100% of the doses as specified per protocol.

6.6. Dose Modification

No dose modification is allowed.

6.7. Continued Access to Study Intervention After the End of the Study

No study intervention will be provided to participants at the end of their study participation. It is expected that participants will be treated as required with standard-of-care treatments, as advised by their usual care physician.

6.8. Treatment of Overdose

For this study, any dose of study intervention greater than the maximum dose of study intervention according to the protocol within a 24-hour time period will be considered an overdose.

There is no specific treatment for an overdose.

In the event of an overdose, the investigator/treating physician should:

1. Contact the study medical monitor within 24 hours.
2. Closely monitor the participant for any AEs/SAEs and laboratory abnormalities as medically appropriate and follow up until resolution, stabilization, the event is otherwise explained, or the participant is lost to follow-up (as defined in Section 7.3).
3. Document the quantity of the excess dose as well as the duration of the overdose in the CRF.
4. Overdose is reportable to the Pfizer **only when associated with an SAE.**
5. Obtain a blood sample for PK analysis as soon as overdose is identified but no later than 24 hours from the last over-dosed study intervention if requested by the study medical monitor (determined on a case-by-case basis).

Decisions regarding dose interruptions or modifications will be made by the investigator in consultation with the study medical monitor as needed based on the clinical evaluation of the participant.

6.9. Prior and Concomitant Therapy

All participants are required to maintain stable dosing of permitted prescribed and OTC medications for the duration of the study.

6.9.1. Prohibited During the Study

The following therapies are prohibited during the study:

- Any additional therapies to treat CeD.
- Other investigational agents, including biologic or non-biologic immunosuppressive or immunomodulatory therapies.
    - Washout period for chronic, systemic non-biologic immunosuppressive or immunomodulatory agents (eg, methotrexate, sulfasalazine, or corticosteroids such as prednisone, etc.) is 3 months prior to screening.
    - Washout period for biologic immunosuppressive or immunomodulatory agents (eg, adalimumab, etanercept, certolizumab) is 12 months prior to screening; except anti-severe acute respiratory syndrome coronavirus 2 monoclonal antibodies.
- Non-investigational systemic immunosuppressive and immunomodulatory therapies (eg, IV or oral corticosteroids). Corticosteroids administered topically or by inhalation or other ways may be allowed but should be discussed with medical monitor prior to enrollment in the study or initiation of new treatment.
- All vaccines between 4 weeks prior to dosing through 4 weeks from the last dose of study intervention; vaccines are permitted at all other times during the study.

6.9.2. Permitted During the Study

Hormonal contraceptives that meet the requirements of this study are allowed to be used in participants who are WOCBP (see Appendix 4).

HRT use by postmenopausal women is permitted if they meet requirements in Appendix 4.

Any other medication that is considered necessary for the participant's welfare that is not expected to interfere with the evaluation of KAN-101 may be given at the discretion of the investigator and documented on the CRF.

In cases involving concomitant therapies whose predicted interference with KAN-101 is unknown to the investigator, Pfizer should be contacted for discussion.

Any medication (including over-the-counter or prescription medications, vitamins, and/or herbal supplements) that the participant receives after enrollment through the last study visit must be recorded on the CRF. Participants should report any changes to permitted medications during the study to the investigator as soon as they occur. Medication changes must be documented in the participant's record and CRF.

Participants being treated for IBS symptomology will be allowed to continue current treatment (eg, dicyclomine) unless the drug is specifically prohibited; participants should be

on a stable dose for at least 4 weeks prior to entry and remain on a stable dose throughout the study.

Antidiarrheal (eg, loperamide), antiemetics (eg, metoclopramide or ondansetron), or acetaminophen may be used for symptomatic treatment if warranted unless the drug is specifically prohibited. These symptomatic treatments are optionally allowed as pre-treatment to study intervention administration at Day 4 and Day 7 at investigator discretion. If given at a study visit, use must be recorded on the CRF.

6.9.3. Rescue Medicine

There is no rescue therapy to reverse AEs observed with KAN-101; standard medical supportive care, such as antiemetics (eg, metoclopramide or ondansetron), may be provided to manage AEs.

7. DISCONTINUATION OF STUDY INTERVENTION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1. Discontinuation of Study Intervention

It may be necessary for a participant to permanently discontinue study intervention. Reasons for permanent discontinuation of study intervention include the following:

- An AE that requires permanent discontinuation of study treatment*;
- Noncompliance with the protocol;
- Investigator decision;
- Participant becomes pregnant;
- Participant death;
- Participant lost to follow-up;
- Termination of the study by the sponsor;
- Voluntary withdrawal of consent by the participant.

* Note: AEs leading to the discontinuation of study intervention will be followed until resolution, stabilization, the event is otherwise explained, or the participant is lost to follow-up.

Note that discontinuation of study intervention does not represent withdrawal from the study. If study intervention is permanently discontinued, the participant should remain in the study to be evaluated for safety. See the SoA for data to be collected at the time of discontinuation of study intervention and follow-up for any further evaluations that need to be completed.

In the event of discontinuation of study intervention, it must be documented on the appropriate CRF/in the medical records whether the participant is discontinuing further

receipt of study intervention or also from study procedures, further study follow-up, and/or future collection of additional information.

Participants who withdraw from treatment and do not receive 3 full doses should not undergo GC, have plasma samples taken for IL-2 on Day 15, Day 29, and Day 42, or receive a second EGD with biopsy.

7.1.1. Liver Injury

A participant who meets the criteria as described in Appendix 6 will be withdrawn from study intervention.

7.1.2. Pregnancy

Pregnancy tests are conducted as specified per the SoA and administration of study intervention or 2-week GC will only be initiated in the presence of a negative pregnancy test.

If a participant is confirmed to be pregnant (see Section 8.3.6) during any visit, conducting of GCs and further dosing with study intervention will be discontinued immediately and permanently.

Section 8.4.5.1 describes the follow-up activities if a participant meets EDP criteria.

7.1.3. COVID-19

If a participant has COVID-19 during the study, this should be reported as an AE or SAE (as appropriate) and appropriate medical intervention provided.

It is recommended that the investigator discuss temporary or permanent discontinuation of study intervention with the study medical monitor.

7.1.4. Temporary Discontinuation

In cases where a temporary discontinuation or dosing interruption is required, the total infusion should be completed within 6 hours of thawing the drug product. Any temporary discontinuations or interruptions of study intervention should be documented in the CRF.

See Appendix 9 for detailed guidance regarding infusion administration interruptions due to IRR.

7.2. Participant Discontinuation/Withdrawal From the Study

A participant may withdraw from the study at any time at their own request. Reasons for discontinuation from the study include the following:

- Investigator's decision;
- Participant death;
- Participant lost to follow-up;

- Termination of the study by Sponsor;
- Voluntary withdrawal of consent of participant.

At the time of discontinuing from the study, if possible, an early discontinuation visit should be conducted. See the SoA for assessments to be collected at the time of study discontinuation and follow-up and for any further evaluations that need to be completed.

In order to maintain this blind, an otherwise uninvolved third party will be responsible for administration of the study intervention. This includes ensuring that there are no differences in time or effort taken to administer the study intervention and no blinded site staff are able to view the administration.

The participant will be permanently discontinued from the study intervention and the study at that time.

If a participant withdraws from the study, they may request destruction of any remaining samples taken and not tested, and the investigator must document any such requests in the site study records and notify Pfizer accordingly.

If the participant withdraws from the study and also withdraws consent (see Section 7.2.1) for disclosure of future information, no further evaluations will be performed and no additional data will be collected. The sponsor or designee may retain and continue to use any data collected before such withdrawal of consent.

7.2.1. Withdrawal of Consent

Participants who request to discontinue receipt of study intervention will remain in the study and must continue to be followed for protocol -specified follow-up procedures. The only exception to this is when a participant specifically withdraws consent for any further contact with them or persons previously authorized by the participant to provide this information. Participants should notify the investigator in writing of the decision to withdraw consent from future follow-up, whenever possible. The withdrawal of consent should be explained in detail in the medical records by the investigator, as to whether the withdrawal is only from further receipt of study intervention or also from study procedures and/or posttreatment study follow-up, and entered on the appropriate CRF page. In the event that vital status (whether the participant is alive or dead) is being measured, publicly available information should be used to determine vital status only as appropriately directed in accordance with local law.

7.3. Lost to Follow-Up

A participant will be considered lost to follow-up if the participant repeatedly fails to return for scheduled visits and is unable to be contacted by the study site.

The following actions must be taken if a participant fails to return to the clinic for a required study visit:

- The site must attempt to contact the participant and reschedule the missed visit as soon as possible. Counsel the participant on the importance of maintaining the assigned visit schedule, and ascertain whether the participant wishes to and/or should continue in the study;
- Before a participant is deemed lost to follow-up, the investigator or designee must make every effort to regain contact with the participant (where possible, 3 telephone calls and, if necessary, a certified letter to the participant's last known mailing address or local equivalent methods). These contact attempts should be documented in the participant's medical record;
- Should the participant continue to be unreachable, the participant will be considered to have withdrawn from the study.

8. STUDY ASSESSMENTS AND PROCEDURES

8.1. Administrative Procedures

The investigator (or an appropriate delegate at the investigator site) must obtain a signed and dated ICD before performing any study-specific procedures.

Study procedures and their timing are summarized in the SoA. Protocol waivers or exemptions are not allowed.

Adherence to the study design requirements, including those specified in the SoA, is essential and required for study conduct.

All screening evaluations must be completed and reviewed to confirm that potential participants meet all eligibility criteria. The investigator will maintain a screening log to record details of all participants screened and to confirm eligibility or record reasons for screening failure, as applicable.

Every effort should be made to ensure that protocol-required tests and procedures are completed as described. However, it is anticipated that from time to time there may be circumstances outside the control of the investigator that make it unfeasible to perform the test. In these cases, the investigator must take all steps necessary to ensure the safety and well-being of the participant. When a protocol-required test cannot be performed, the investigator will document the reason for the missed test and any corrective and preventive actions that they have taken to ensure that required processes are adhered to as soon as possible. The study team must be informed of these incidents in a timely manner.

For samples being collected and shipped, detailed collection, processing, storage, and shipment instructions and contact information will be provided to the investigator site prior to initiation of the study.

The actual collection times of blood sampling may change. Additional blood samples may be taken for safety assessments at times specified by the sponsor or sponsor's designee, provided the total volume taken during the study does not exceed 550 mL within 60 days.

8.1.1. Telehealth Visits

Telehealth visits may be used to assess participant safety and collect data points. Telehealth includes the exchange of healthcare information and services via telecommunication technologies (eg, audio, video, videoconferencing software) remotely, allowing the participant and the investigator to communicate on aspects of clinical care, including medical advice, reminders, education, and safety monitoring. Assessments that may be performed during a telehealth visit are described in the SoA.

Study participants must be reminded to promptly notify site staff about any change in their health status.

8.2. Efficacy Assessments

Efficacy assessments are performed at times specified in the SoA.

8.2.1. Gluten Challenge

All eligible, enrolled participants that received all three doses of study intervention will undergo a 2-week GC at starting Day 15.

- Participants are required to fast for at least 6 hours (or overnight), except for water and any medications they might have previously been prescribed, prior to GC. This pertains to both the study clinic visit during which the GC is performed (see SoA) and the at-home GC.
- At the Day 15 study visit, a qualified staff member will prepare the GC.
- Participants will consume 9g of gluten protein PO in the clinic and the participant will be observed for at least 4 hours to monitor for hyperacute reactions requiring medical treatment and collection of biomarker samples.
- Materials will be sent home with the participant to complete the GC daily for the next 13 days.

Completion of the GC is defined as consumption of the entirety of the 9g GC within approximately 15 minutes.

- At the Day 15 visit, participants will consume the GC on site under the observation of site staff. Participants will complete the remaining days of GC at home and document the completion of the GC via the eDiary.

Compliance with the GC is defined as completion of all 14 days of the GC. Only participants fully compliant with the GC may be analyzed as part of the PPS (see Section 9.3).

Only participants who have completed at least 7 days of GC should undergo the second EGD with biopsy. For participants who:

- Continue in the study, the EGD with biopsy will take place at the Day 29 visit (see SoA).
- Discontinue early, the EGD with biopsy will take place at the ET visit (see SoA).

Any symptoms associated with the GC should be recorded as AEs (see Section 8.4). Any AEs associated with the GC study assessment are separate to AEs related to study intervention (KAN-101/placebo).

8.2.2. Plasma IL-2 Biomarker Assessment

Plasma samples will be collected to assess the magnitude of biomarker response of IL-2 pre- and post-GC in peripheral blood at times specified in the SoA.

Further details are presented in Section 8.7.

8.2.3. Patient Reported Outcomes

PROs will be collected via eDiary.

8.2.3.1. CDSD v2.1

The CDSD v2.1, a novel patient-reported outcome measure developed for use with participants with CeD, consists of five symptoms including diarrhea, abdominal pain, bloating, nausea, and tiredness. The CDSD v2.1 assesses severity, in five scales from "none" to "very severe", and frequency. The CDSD v2.1 will be assessed daily as part of the eDiary beginning during the screening period after signing the ICD.

The CDSD v2.1 should be completed for at least 7 consecutive days during screening at any time prior to the baseline visit (Day 1). After screening and through the end of the study, compliance with the CDSD v2.1 is defined as 80% completion.

8.2.3.2. PGIC

The PGIC is a patient-completed question to assess the overall impression of disease improvement experienced by the participant. The PGIC score ranges from "much better" to "much worse". The PGIC will be assessed at visits specified in SoA.

8.2.3.3. PGIS

The PGIS is a patient-completed question to assess the overall impression of disease severity experienced by the participant. The PGIS score ranges from "None" to "Very Severe". The PGIS will be assessed at visits specified in SoA.

8.2.4. Esophagogastroduodenoscopy With Biopsy

EGD with biopsies will be collected from participants at times specified in the SoA.

EGD with biopsy will be performed by a qualified gastroenterologist at each site. All study gastroenterologists will be trained on the study-specific procedures for obtaining the biopsy, including the location and number of biopsies to be obtained as well as the procedures for storing and shipping of samples.

Approximately 6 duodenal biopsies will be obtained per collection.

Endoscopy data obtained during screening may be used as the baseline histology in a participant undergoing re-screening if 1) the endoscopy data was obtained up to 3 months prior to re-screening, 2) the participant has continued GFD and 3) the participant has not undergone a GC.

8.2.4.1. Histological Assessments

Tissue samples collected during biopsy as specified in the SoA will be analyzed for histological state (including, but not limited to: villus height, crypt depth, Marsh score, and IEL count). Histology will be centrally read by qualified raters.

It is anticipated that approximately 50% of patients will have baseline histology that may be exclusionary for this trial (Vh:Cd <2.3). (Adelman et al, 2018). A baseline Vh:Cd ratio cutoff of 2.3 was chosen to ensure that participants with evidence of more moderate to severe villous atrophy are not enrolled into the study.

Management of Incidental Findings

An incidental finding is one unknown to the participant that has potential health or reproductive importance, which is discovered unexpectedly in the course of a research study, but is unrelated to the purpose and beyond the aims of the study.

Histology from EGD biopsy will be reviewed by a central review facility. The purpose of this review is to evaluate histology for celiac disease. Central histological review is not a complete medical review of the participant. If, during the central review process, an unexpected observation is identified and this finding could, in the opinion of the central reviewer, have a significant health or reproductive consequence, this finding may be shared with the study sponsor or sponsor's designee for disclosure to the PI. All follow-up testing and final diagnosis will be left to the discretion of the medical professionals at the site or those with an existing physician-participant relationship. The PI will be responsible for reporting any AEs identified from incidental findings as described in the AE reporting section. Identification of such incidental findings during the central review process should not be expected, and the site maintains responsibility for performing a general safety review of all histology as per site protocols.

8.3. Safety Assessments

Safety will be assessed through the monitoring of AEs, clinical signs and symptoms, vital signs and clinical laboratory evaluations.

All participants will be monitored continuously for AEs from screening until the safety follow-up visit on Day 42. AE severity will be assessed using the NCI CTCAE v6.0 or higher (see Appendix 10). The DSMB will review cumulative safety data periodically. Any Grade 4 AEs assessed as related to study drug will result in notification of the regulatory agencies in parallel with the DSMB.

Participants will be monitored in the clinic for at least 4 hours following IV study drug administration for IRR (see Appendix 9).

In relation to participant safety during the COVID-19 pandemic, current national laws and local recommendations should be strictly adhered to during the study.

Planned time points for all safety assessments are provided in the SoA. Unscheduled safety measurements may be obtained at any time during the study to assess any perceived safety issues.

8.3.1. Incidental Gluten Exposure Assessment

Incidental gluten exposure will be assessed daily as part of the participant's eDiary. Assessment of any incidental gluten exposure will be reviewed at all study visits.

8.3.2. Vital Signs

Any untoward vital sign findings that are identified during the active collection period and meet the definition of an AE or SAE (Appendix 3) must be reported according to the processes in Sections 8.4.1 to 8.4.3.

Vital signs will be monitored before, during and after study intervention infusions to assess for IRR (see Appendix 9).

Vital signs will be taken before collection of laboratory tests. Height and weight will also be measured and recorded at screening only and captured on the CRF.

BP and PR assessment consists of a single measure of PR and a single BP. Sitting BP and PR measurement will be assessed with a completely automated device. Manual techniques will be used only if an automated device is not available. BP and PR measurement should be preceded by at least 5 minutes of rest with the participant in a sitting position, in a quiet setting without distractions.

Oral temperature and respiratory rate will be assessed. Temperature and respiratory rate findings collected during the study will be considered source data and will not be required to be reported, unless otherwise noted.

8.3.3. Electrocardiograms

A standard 12-lead ECG utilizing limb leads (with a 10-second rhythm strip) should be collected at screening using an ECG machine that automatically calculates the HR and measures PR interval, QT interval, QTcF, and QRS complex. Alternative lead placement methodology using torso leads (eg, Mason-Likar) should not be used given the potential risk

of discrepancies with ECGs acquired using standard limb lead placement. The ECG should be performed prior to blood draws and after the participant has rested quietly for at least 5 minutes in a supine position.

Unscheduled ECGs are permitted per the investigator's discretion.

In some cases, it may be appropriate to repeat abnormal ECGs to rule out improper lead placement as contributing to the ECG abnormality. If a machine-read QTc value is prolonged, as defined above, repeat measurements may not be necessary if a qualified medical provider's interpretation determines that the QTcF values are in the acceptable range.

ECG values of potential clinical concern are listed in Appendix 8.

8.3.4. Clinical Safety Laboratory Assessments

See Appendix 2 for the list of clinical safety laboratory tests to be performed and the SoA for the timing and frequency. All protocol required- laboratory assessments, as defined in Appendix 2, must be conducted in accordance with the laboratory manual and the SoA. Unscheduled clinical laboratory measurements may be obtained at any time during the study to assess any perceived safety issues.

The investigator must review the laboratory report, document this review, and record any clinically significant changes occurring during the study in the AE section of the CRF. Clinically significant abnormal laboratory test findings are those that are not associated with any underlying disease, unless judged by the investigator to be more severe than expected for the participant's condition.

All laboratory tests with values considered clinically significant and abnormal during participation in the study or within the follow-up period after the last dose of study intervention should be repeated until the values return to normal or baseline or are no longer considered clinically significant by the investigator or study medical monitor.

If such values do not return to normal/baseline within a period of time judged reasonable by the investigator, the etiology should be identified and Pfizer notified.

See Appendix 6 for suggested actions and follow-up assessments in the event of potential DILI.

See Appendix 7 for instructions for laboratory testing to monitor kidney function and reporting laboratory test abnormalities.

8.3.4.1. Alternative Facilities for Clinical Safety Laboratory Assessment

Protocol-specified safety laboratory evaluations will be conducted at a central laboratory.

Non-protocol-specified laboratory evaluations as ordered by the investigator may be conducted at a local laboratory.

If a local laboratory is used, qualified study site personnel must order, receive, and review results. Site staff must collect the local laboratory reference ranges and certifications/ accreditations for filing at the site. Laboratory test results are to be provided to the site staff as soon as possible. The local laboratory reports should be filed in the participant's source documents/medical records. Relevant data from the local laboratory report should be recorded on the CRF.

8.3.5. Physical Examinations

A complete physical examination will include, at a minimum, assessments of the cardiovascular, respiratory, gastrointestinal, and neurological systems.

Investigators should pay special attention to clinical signs related to previous serious illnesses.

Physical examination findings collected during the study will be considered source record and will not be required to be reported, unless otherwise noted. Any untoward physical examination findings that are identified during the active collection period and meet the definition of an AE or SAE (Appendix 3) must be reported according to the processes in Sections 8.4.1 to 8.4.3.

8.3.6. Pregnancy Testing

A serum pregnancy test is required at screening. Following screening, pregnancy tests may be urine or serum tests, and must have a sensitivity of at least 25 mIU/mL. Pregnancy tests will be performed in WOCBP (see Appendix 4) at the times listed in the SoA. Following a negative pregnancy test result at screening, appropriate contraception must be commenced and a second negative pregnancy test result will be required at the baseline visit prior to the starting the study intervention. Pregnancy tests will also be done whenever 1 menstrual cycle is missed during the active treatment period (or when potential pregnancy is otherwise suspected) and at the end of the study. Pregnancy tests may also be repeated if requested by IRBs/ECs or if required by local regulations. If a urine test cannot be confirmed as negative (eg, an ambiguous result), a serum pregnancy test is required. In such cases, the participant must be excluded if the serum pregnancy result is positive.

8.4. Adverse Events, Serious Adverse Events, and Other Safety Reporting

The definitions of an AE and an SAE can be found in Appendix 3.

AEs may arise from symptoms or other complaints reported to the investigator by the participant (or, when appropriate, by a caregiver, surrogate, or the participant's legally authorized representative), or they may arise from clinical findings of the investigator or other healthcare providers (clinical signs, test results, etc).

The investigator and any qualified designees are responsible for detecting, documenting, and recording events that meet the definition of an AE or SAE and remain responsible to pursue and obtain adequate information both to determine the outcome and to assess whether the

event meets the criteria for classification as an SAE or caused the participant to discontinue the study intervention (see Section 7.1).

During the active collection period as described in Section 8.4.1, each participant will be questioned about the occurrence of AEs in a nonleading manner.

In addition, the investigator may be requested by the sponsor or designee to obtain specific follow -up information in an expedited fashion.

8.4.1. Time Period and Frequency for Collecting AE and SAE Information

The time period for actively eliciting and collecting AEs and SAEs ("active collection period") for each participant begins from the time the participant provides informed consent, which is obtained before undergoing any study -related procedure and/or receiving study intervention, through and including a minimum of 28 calendar days, except as indicated below, after the last administration of the study intervention.

Follow-up by the investigator continues throughout the active collection period and until the AE or SAE or its sequelae resolve or stabilize at a level acceptable to the investigator.

When a clinically significant AE remains ongoing at the end of the active collection period, follow-up by the investigator continues until the AE or SAE or its sequelae resolve or stabilize at a level acceptable to the investigator and the sponsor concurs with that assessment.

For participants who are screen failures, the active collection period ends when screen failure status is determined.

If the participant withdraws from the study and also withdraws consent for the collection of future information, the active collection period ends when consent is withdrawn.

If a participant permanently discontinues or temporarily discontinues study intervention because of an AE or SAE, the AE or SAE must be recorded on the CRF and the SAE reported using the CT SAE Report Form.

Investigators are not obligated to actively seek information on AEs or SAEs after the participant has concluded study participation. However, if the investigator learns of any SAE, including a death, at any time after a participant has concluded study participation, and they consider the event to be reasonably related to the study intervention, the investigator must promptly report the SAE to Pfizer Safety using the CT SAE Report Form.

8.4.1.1. Reporting SAEs to the Pfizer Safety

All SAEs occurring in a participant during the active collection period as described in Section 8.4.1 are reported to the Pfizer Safety on the CT SAE Report Form immediately upon awareness and under no circumstance should this exceed 24 hours, as indicated in Appendix 3. The investigator will submit any updated SAE data to Pfizer Safety within 24 hours of its being available.

8.4.1.2. Recording Nonserious AEs and SAEs on the CRF

All nonserious AEs and SAEs occurring in a participant during the active collection period, which begins after obtaining informed consent as described in Section 8.4.1, will be recorded on the AE section of the CRF.

The investigator is to record on the CRF all directly observed and all spontaneously reported AEs and SAEs reported by the participant.

As part of ongoing safety reviews conducted by the sponsor, any nonserious AE that is determined by the sponsor to be serious will be reported by Pfizer Safety as an SAE. To assist in the determination of case seriousness, further information may be requested from the investigator to provide clarity and understanding of the event in the context of the clinical study.

8.4.2. Method of Detecting AEs and SAEs

The method of recording, evaluating, and assessing causality of AEs and SAEs and the procedures for completing and transmitting SAE reports are provided in Appendix 3.

Care will be taken not to introduce bias when detecting AEs and/or SAEs. Open-ended and nonleading verbal questioning of the participant is the preferred method to inquire about AE occurrences.

8.4.3. Follow-Up of AEs and SAEs

After the initial AE or SAE report, the investigator is required to proactively follow each participant at subsequent visits/contacts. For each event, the investigator must pursue and obtain adequate information until resolution, stabilization, the event is otherwise explained, or the participant is lost to follow-up (as defined in Section 7.3).

In general, follow-up information will include a description of the event in sufficient detail to allow for a complete medical assessment of the case and independent determination of possible causality. Any information relevant to the event, such as concomitant medications and illnesses, must be provided. In the case of a participant death, a summary of available autopsy findings must be submitted as soon as possible to Pfizer Safety.

Further information on follow-up procedures is provided in Appendix 3.

8.4.4. Regulatory Reporting Requirements for SAEs

Prompt notification by the investigator to Pfizer Safety of an SAE is essential so that legal obligations and ethical responsibilities toward the safety of participants and the safety of a study intervention under clinical investigation are met.

The sponsor or sponsor's designee has a legal responsibility to notify both the local regulatory authority and other regulatory agencies about the safety of a study intervention under clinical investigation. The sponsor or sponsor's designee will comply with

country-specific regulatory requirements relating to safety reporting to the regulatory authority (such as the US FDA and EU EudraVigilance), IRBs/ECs, and investigators.

Investigator safety reports must be prepared for SUSARs according to local regulatory requirements and Pfizer Safety policy and forwarded to investigators as necessary.

An investigator who receives SUSARs or other specific safety information (eg, summary or listing of SAEs) from Pfizer Safety will review and then file it along with the SRSD(s) for the study and will notify the IRB/EC, if appropriate according to local requirements.

8.4.5. Environmental Exposure, Exposure During Pregnancy or Breastfeeding, and Occupational Exposure

Environmental exposure occurs when a person not enrolled in the study as a participant receives unplanned direct contact with or exposure to the study intervention. Such exposure may or may not lead to the occurrence of an AE or SAE. Persons at risk for environmental exposure include healthcare providers, family members, and others who may be exposed. An environmental exposure may include EDP, EDB, and occupational exposure.

Any such exposures to the study intervention under study are reportable to the Pfizer within 24 hours of investigator awareness.

8.4.5.1. Exposure During pregnancy

An EDP occurs if:

- A female participant is found to be pregnant while receiving or after discontinuing study intervention during the mandatory contraception period (see Appendix 4).
- A male participant who is receiving or has discontinued study intervention inseminates a female partner during the mandatory contraception period (see Appendix 4).
- A female nonparticipant is found to be pregnant while being exposed or having been exposed to study intervention because of environmental exposure. Below are examples of environmental EDP if they occur within 21 days after exposure:
  - A female family member or healthcare provider reports that she is pregnant after having been exposed to the study intervention by ingestion, inhalation, or skin contact.
  - A male family member or healthcare provider who has been exposed to the study intervention by ingestion, inhalation, or skin contact then inseminates his female partner prior to or around the time of conception.

The investigator must report EDP to Pfizer within 24 hours of the investigator's awareness, irrespective of whether an SAE has occurred. The initial information submitted should

include the anticipated date of delivery (see below for information related to termination of pregnancy).

- If EDP occurs in a participant/participant's partner, the investigator must report this information to Pfizer on the CT SAE Report Form and an EDP Supplemental Form, regardless of whether an SAE has occurred. Details of the pregnancy will be collected after the start of study intervention and until 12 weeks after the last dose.

- If EDP occurs in the setting of environmental exposure, the investigator must report information to Pfizer using the CT SAE Report Form and EDP Supplemental Form. Since the exposure information does not pertain to the participant enrolled in the study, the information is not recorded on a CRF; however, a copy of the completed CT SAE Report Form is maintained in the investigator site file.

Follow-up is conducted to obtain general information on the pregnancy and its outcome for all EDP reports with an unknown outcome. The investigator will follow the pregnancy until completion (or until pregnancy termination) and notify Pfizer of the outcome as a follow-up to the initial-EDP Supplemental Form. In the case of a live birth, the structural integrity of the neonate can be assessed at the time of birth. In the event of a termination, the reason(s) for termination should be specified and, if clinically possible, the structural integrity of the terminated fetus should be assessed by gross visual inspection (unless preprocedure test findings are conclusive for a congenital anomaly and the findings are reported).

Abnormal pregnancy outcomes are considered SAEs. If the outcome of the pregnancy meets the criteria for an SAE (ie, ectopic pregnancy, spontaneous abortion, intrauterine fetal demise, neonatal death, or congenital anomaly in a live-born baby, a terminated fetus), the investigator should follow the procedures for reporting SAEs. Additional information about pregnancy outcomes that are reported to Pfizer as SAEs follows:

- Spontaneous abortion including miscarriage and missed abortion should be reported as an SAE;

- Neonatal deaths that occur within 1 month of birth should be reported, without regard to causality, as SAEs. In addition, infant deaths after 1 month should be reported as SAEs when the investigator assesses the infant death as related or possibly related to exposure to the study intervention.

Additional information regarding the EDP may be requested by Pfizer. Further follow-up of birth outcomes will be handled on a case-by-case basis (eg, follow--up on preterm infants to identify developmental delays). In the case of paternal exposure, the investigator will provide the participant with the Pregnant Partner Release of Information Form to deliver to his partner. The investigator must document in the source documents that the participant was given the Pregnant Partner Release of Information Form to provide to his partner.

8.4.5.2. Exposure During Breastfeeding

An EDB occurs if:

- A female participant is found to be breastfeeding while receiving or after discontinuing study intervention during the mandatory contraception period (see Appendix 4).
- A female nonparticipant is found to be breastfeeding while being exposed or having been exposed to study intervention (ie, environmental exposure) within the last 21 days. An example of environmental EDB is a female family member or healthcare provider who reports that she is breastfeeding after having been exposed to the study intervention by ingestion, inhalation, or skin contact.

The investigator must report EDB to Pfizer within 24 hours of the investigator's awareness, irrespective of whether an SAE has occurred. The information must be reported using the CT SAE Report Form. When EDB occurs in the setting of environmental exposure, the exposure information does not pertain to the participant enrolled in the study, so the information is not recorded on a CRF. However, a copy of the completed CT SAE Report Form is maintained in the investigator site file.

8.4.5.3. Occupational Exposure

The investigator must report any instance of occupational exposure to Pfizer within 24 hours of the investigator's awareness using the CT SAE Report Form, regardless of whether there is an associated SAE. Since the information about the occupational exposure does not pertain to a participant enrolled in the study, the information is not recorded on a CRF; however, a copy of the completed CT SAE Report Form must be maintained in the investigator site file.

8.4.6. Cardiovascular and Death Events

Not applicable.

8.4.7. Disease-Related Events and/or Disease-Related Outcomes Not Qualifying as AEs or SAEs

Not applicable.

8.4.8. Adverse Events of Special Interest

Not applicable.

8.4.8.1. Lack of Efficacy

The investigator must report signs, symptoms, and/or clinical sequelae resulting from lack of efficacy. Lack of efficacy or failure of expected pharmacological action is reportable to Pfizer **only if associated with an SAE**.

8.4.9. Medical Device Deficiencies

Not applicable.

8.4.10. Medication Errors

Medication errors may result from the administration or consumption of the study intervention by the wrong participant, or at the wrong time, or at the wrong dosage strength.

Medication errors are recorded and reported as follows:

Recorded on the Medication Error Page of the CRF	Recorded on the Adverse Event Page of the CRF	Reported on the CT SAE Report Form to Pfizer Safety Within 24 Hours of Awareness
All (regardless of whether associated with an AE)	Any AE or SAE associated with the medication error	Only if associated with an SAE

Medication errors include:

- Medication errors involving participant exposure to the study intervention;
- Potential medication errors or uses outside of what is foreseen in the protocol that do or do not involve the study participant.
- Administration of a quantity of study intervention per administration or cumulative, which is above the maximum dose according to the protocol.
- Unintentional error in dispensing or administration of study intervention not in accordance with the protocol.

Whether or not the medication error is accompanied by an AE, as determined by the investigator, such medication errors occurring to a study participant are recorded on the medication error page of the CRF which is a specific version of the AE page and, if applicable, any associated serious and nonserious AEs, are recorded on the AE page of the CRF.

In the event of a medication dosing error, Pfizer should be notified within 24 hours.

Medication errors should be reported to the Pfizer within 24 hours on a CT SAE Report Form **only when associated with an SAE.**

8.5. Pharmacokinetics

Blood samples will be collected for measurement of plasma concentrations of KAN-101 as specified in the SoA. Instructions for the collection and handling of biological samples will be provided in the laboratory manual. The actual date and time (24-hour clock time) of each sample will be recorded. Samples collected for measurement of plasma concentrations of study intervention will be analyzed using a validated analytical method in compliance with applicable SOPs.

The actual times for PK assessment may change, and if needed, additional PK samples may be taken at times specified by sponsor or designee, provided the total blood volume taken during the study does not exceed 550 mL during any period of 56 consecutive days. All efforts will be made to obtain the samples at the exact nominal time relative to dosing. Collection of samples within 2 minutes for samples that are planned at less than 1 hour, and within 5 minutes for samples planned between 1-7 hours after dose administration of the nominal time respectively relative to dosing will not be captured as a protocol deviation, as long as the exact time of the collection is noted on the source document and the CRF/DCT.

Samples will be used to evaluate the PK of KAN-101. Samples collected for analyses of KAN-101 plasma concentration may also be used to evaluate safety or efficacy aspects related to concerns arising during or after the study, for metabolite identification and/or evaluation of the bioanalytical method, or for other internal exploratory purposes, and not reported in the CSR.

The PK samples must be processed and shipped as indicated in the instructions provided to the investigator site to maintain sample integrity. Any deviations from the PK sample handling procedure (eg, sample collection and processing steps, interim storage or shipping conditions), including any actions taken, must be documented and reported to Pfizer. On a case-by-case basis, the sponsor or designee may make a determination as to whether sample integrity has been compromised.

Genetic analyses will not be performed on these whole blood samples unless consent for this was included in the informed consent. Participant confidentiality will be maintained.

Drug concentration information that may unblind the study will not be reported to investigator sites or blinded personnel until the study has been unblinded.

Any changes in the timing or addition of time points for any planned study assessments must be documented and approved by the relevant study team member and then archived in the sponsor and site study files but will not constitute a protocol amendment. The IRB/EC will be informed of any safety issues that require alteration of the safety monitoring scheme or amendment of the ICD.

8.6. Genetics

8.6.1. Specified Genetics

To determine study eligibility, all participants will be assessed via central laboratory for HLA-DQ2.5 genotype (see Inclusion Criteria, Section 5.1).

Details on processes for collection and shipment of these samples can be found in the study laboratory manual.

8.7. Biomarkers

Collection of samples for biomarker research is also part of this study.

The following samples for biomarker research are required and will be collected from all participants in the study at times specified in the SoA:

- Plasma (including for plasma IL-2 biomarker efficacy assessment; see Section 8.2.2).

Plasma samples collected will be analyzed for cytokine responses including but not limited to IL-2.

Details on processes for collection and shipment of these samples can be found in the study laboratory manual.

8.7.1. Residual Research Samples for Biomarkers

Any remaining residual samples not used for protocol-specified assessments will be retained as local regulations and IRB/ECs allow.

- Samples include, but are not limited to:
  - Plasma
  - Histopathology samples

Residual research samples may be used for research related to the study intervention(s) or celiac disease. Genes and other analytes (eg, proteins, RNA, nondrug metabolites) may be studied using the residual samples.

See Appendix 5 for information regarding genetic research. Details on processes for collection and shipment of these samples can be found in the study laboratory manual.

8.8. Immunogenicity Assessments

Blood samples will be collected for determination of ADA as specified in the SoA. Instructions for the collection and handling of biological samples will be provided in the laboratory manual. The actual date and time (24-hour clock time) of each sample will be recorded.

Samples collected for determination of ADA may also be used for additional characterization of the immune response and/or evaluation of the bioanalytical method, or for other internal exploratory purposes. These data will be used for internal exploratory purposes.

Genetic analyses will not be performed on these whole blood samples unless consent for this was included in the informed consent. Participant confidentiality will be maintained.

Samples will be analyzed using a validated analytical method in compliance with applicable SOPs.

The immunogenicity samples must be processed and shipped as indicated in the instructions provided to the investigator site to maintain sample integrity. Any deviations from the immunogenicity sample handling procedure (eg, sample collection and processing steps,

interim storage, or shipping conditions), including any actions taken, must be documented and reported to Pfizer. On a case-by-case basis, the sponsor may make a determination as to whether sample integrity has been compromised.

Immunogenicity information that may unblind the study will not be reported to investigator sites or blinded personnel until the study has been unblinded.

Any changes in the timing or addition of time points for any planned study assessments must be documented and approved by the relevant study team member and then archived in the sponsor and site study files but will not constitute a protocol amendment. The IRB/EC will be informed of any safety issues that require alteration of the safety monitoring scheme or amendment of the ICD.

8.9. Health Economics

Health economics will not be assessed in this study.

9. STATISTICAL CONSIDERATIONS

Detailed methodology for summary and statistical analyses of the data collected in this study is outlined here and further detailed in the SAP, which will be maintained by the sponsor or sponsor's designee. The SAP may modify what is outlined in the protocol where appropriate; however, any major modifications of the primary endpoint definitions or their analyses will also be reflected in a protocol amendment.

9.1. Statistical Hypotheses

The hypotheses for the primary and secondary endpoints are:

- H_0: The mean values are the same between the treatment groups
- H_1: The mean values are not the same between the treatment groups

9.2. Estimands

9.2.1. Primary Estimand

Estimand 1 will be used for the primary endpoint main analysis.

Estimand 1: The primary estimand is the hypothetical estimand, which estimates the treatment effect of KAN-101 vs placebo for change from baseline in the ratio of Vh:Cd under the scenario of no intercurrent events. It includes the following 5 attributes:

- Population: Participants who receive all 3 doses of study intervention and complete at least 7 days of GC;
- Variable: the ratio of Vh:Cd change from baseline to Day 29;
- Treatment condition: KAN-101 or placebo;

- Intercurrent events: Prohibited medication. All data collected after any intercurrent events will be excluded;
- Population-level summary: The LSM difference of the change from baseline in Vh:Cd between KAN-101 group and placebo.

9.2.1.1. Secondary Estimands

Estimand 2 is hypothetical, which estimates the treatment effect of KAN-101 compared with placebo for IL-2 under the scenario of no intercurrent events. It includes the following 5 attributes:

- Population: Participants who complete all 3 doses of study intervention and complete at least 7 days of GC;
- Variable: log transformed IL-2 change from pre GC to post GC at Day 15 (first day of GC);
- Treatment condition: KAN-101 or placebo;
- Intercurrent events: prohibited medication, incomplete GC on Day 15. All data collected after any intercurrent events will be excluded;
- Population-level summary: the LSM difference (log transformed) of the change from pre GC to post GC at Day 15 (first day of GC) between KAN-101 group and placebo.

Estimand 3 is the hypothetical estimand, which estimates the treatment effect of KAN-101 vs placebo for change from baseline in duodenal IEL density under the scenario of no intercurrent events. It includes the following 5 attributes:

- Population: Participants who complete all 3 doses of study intervention and complete at least 7 days of GC;
- Variable: IEL change from baseline to Day 42;
- Treatment conditions: KAN-101 or placebo;
- Intercurrent Events: Prohibited medication. All data collected after any intercurrent events will be excluded;
- Population level summary: The LSM difference of the change from baseline in IEL between KAN-101 and placebo.

9.2.2. Multiplicity Adjustment

There is no multiplicity adjustment for multiple endpoints. The alpha spending for the planned interim analysis is described in the Interim Analysis section (Section 9.5).

9.3. Analysis Sets

For purposes of analysis, the following analysis sets are defined:

Participant Analysis Set	Description
Enrolled	All participants who sign the ICD.
Full analysis set (FAS)	All participants who are randomly assigned to study intervention and receive all 3 doses of study intervention, and complete at least 7 days of GC. Participants will be analyzed according to the intervention they are randomized.
Per protocol set (PPS)	The PPS will include all participants from the FAS who complete all 14 days of GC and biopsies, and without major protocol violations that might affect the evaluation of the effect of study intervention on the primary endpoint. The PPS will be used in sensitivity analyses of the primary and secondary endpoints. Specific reasons for warranting exclusion from this population will be documented prior to database lock.
Safety analysis set	All participants who receive any portion of study intervention. Participants will be analyzed according to the intervention they actually received.
PK analysis set	All participants who receive any portion of study intervention and have at least one post-dose concentration value.

9.4. Statistical Analyses

The SAP will be developed and finalized before any analyses are performed and will describe the analyses and procedures for accounting for missing, unused, and spurious data. This section is a summary of the planned statistical analyses of the primary and secondary endpoints.

9.4.1. General Considerations

Descriptive statistics will be used in general to summarize study results by treatment groups KAN-101 and Placebo, ie, count and percent will be presented for binary endpoints and categorical endpoints; statistics for continuous variables will include number of observations, mean, standard deviation, minimum, first, second, and third quartiles, and maximum. The CV and GM will also be included, where appropriate. Graphics may be used to present the data.

9.4.1.1. Analyses for Continuous Endpoints

For continuous endpoints with baseline, the change from baseline will be analyzed by time point using ANCOVA model with treatment as the factor, baseline as a covariate. Continuous endpoints without baseline will be analyzed by time point using ANOVA model

with treatment as a factor. Comparison of KAN-101 to placebo (providing LSM of the treatments, LSM of the treatment difference, p-value and 95% CI) will be generated.

9.4.1.2. Missing Data Handling

No imputation for missing efficacy and safety data.

9.4.2. Primary Endpoints/Estimands Analysis

9.4.2.1. Definition of Endpoints

The primary endpoint is change from baseline in the ratio of Vh:Cd as assessed by EGD with biopsy after 2-week GC (at Day 29).

9.4.2.2. Main Analytical Approach

Primary endpoint will be analyzed using ANCOVA model as described in Section 9.2.1 based on Estimand 1.

9.4.2.3. Sensitivity/Supportive Analytical Approach

PP analysis will be performed for change from baseline in the ratio of Vh:Cd at Day 29 visit using ANCOVA model as described in Section 9.2.1 for PPS. If number of participants in PPS is too small (eg, less than 50% of FAS), PP analysis may not be performed.

9.4.3. Secondary Endpoints Analysis

9.4.3.1. Change in IL-2 from pre GC to post GC at Day 15 (First Day of GC)

Change in IL-2 (log transformed) will be analyzed using ANCOVA model as described in Section 9.2.1 based on Estimand 2 (see Section 9.2.1). PP analysis will be performed for change in IL-2 (log transformed) using ANCOVA model as described in Section 9.2.1 for PPS as well.

9.4.3.2. Changes from baseline in IEL in duodenum biopsy at Day 29 Visit

Change in IEL will be analyzed using ANCOVA model based on Estimand 3 (see Section 9.2.1). PP analysis will be performed for change in IEL using ANCOVA model as described in Section 9.2.1 for PPS as well.

9.4.3.3. Incidence and severity of TEAEs and Incidence and titer of KAN-101 ADA

- See Section 9.4.6.

9.4.3.4. Plasma concentration of KAN-101, and associated KAN-101 parameters: AUCinf, AUClast, Cmax, Tmax and t½

PK concentration and PK parameters will be descriptively summarized by treatment group. The PK parameters to be assessed, their definition, and method of determination are detailed in Section 9.4.5. Actual PK sampling times will be used in the derivation of PK parameters.

9.4.4. Tertiary/Exploratory Endpoints Analysis

Results of the below exploratory endpoint analyses will be summarized descriptively, analyzed, utilized for internal purposes, and may not be described in the CSR. The following exploratory endpoints will be collected:

- Change from baseline in Marsh-Oberhuber assessed via EGD with biopsy score after the 2-week GC.
- PROs, including CDSD v2.1, PGIC, and PGIS, will be summarized to track CeD symptoms over the duration of the study.
- Incidence and titer of tTG IgA and DGP IgG at Day 42.

Further details for exploratory analyses may be presented in the SAP and/or an exploratory SAP.

9.4.5. Pharmacokinetic Analysis

Actual PK sampling times will be used in the derivation of PK parameters. The plasma concentration of KAN-101 will be listed and descriptively summarized by nominal PK sampling time and treatment group. Individual subject, mean, and median profiles of the plasma concentration-time data will be plotted by treatment group using actual (for individual) and nominal (for median) times, respectively. Mean and median profiles will be presented on both linear and log scales.

Table 2. PK Parameters Analyzed

Parameter	Definition	Method of Determination
AUC_{last}	Area under the plasma concentration-time profile from time 0 to the time of the last quantifiable concentration (Clast)	Linear/Log trapezoidal method
AUC_{inf}	Area under the plasma concentration-time profile from time 0 extrapolated to infinite time	AUC_{last} + (Clast/K_{el}), where Clast is the predicted plasma concentration at the last quantifiable time point estimated from the log-linear regression analysis
C_{max}	Maximum plasma concentration	Observed directly from data
T_{max}	Time to reach C_{max}.	Observed directly from data.
$t_{½}$[a]	Terminal phase half-life	$Log_e(2)/k_{el}$, where k_{el} is the terminal phase rate constant calculated by a linear regression of the loglinear -concentration time- curve. Only those data points judged to describe the terminal log-linear decline will be used in the regression

a. If data permit

Please see Appendix 11 for abbreviations

The PK parameters in Table 2 will be summarized descriptively by treatment group in accordance with sponsor or sponsor's designee data standards. Summary statistics will also include the geometric mean and coefficient of variation for all parameters except T_{max}.

9.4.6. Safety Analyses

All the safety data will be summarized descriptively through appropriate data tabulations, descriptive statistics, and/or graphical presentations. All safety analyses will be performed on the safety population.

9.4.7. Other Analyses

Immunogenicity assessments will be summarized descriptively.

Pharmacogenetics and biomarker data from Residual Research Samples may be collected during or after the trial and retained for future analyses; the results of such analyses are not planned to be included in the CSR.

9.5. Interim Analyses

An IA will be conducted to assess efficacy after approximately 13 participants from each group have completed through the Day 29 visit including histology assessments. .

Unless a safety concern arises, no decision to stop the trial will be made based on this interim analysis. The results of the IA will be used for future strategic planning for the overall KAN-101 program.

Before any interim analysis is performed, the details of the objectives, decision criteria, dissemination plan, and method of maintaining the study blind (if applicable) as per the sponsor's or sponsor designee's SOPs will be documented and approved in a DSMB charter. In addition, the analysis details will be documented and approved in the SAP or a separate interim statistical analysis plan.

9.6. Sample Size Determination

A sufficient number of participants will be screened to achieve approximately 52 treated participants (26 per study arm). The sample size calculation is based on the primary efficacy estimand and its endpoint, changes from baseline in the ratio of Vh:Cd at Day 29 visit. With a 2-sided type I error rate of 5%, the study will have approximately 94% power under a sample size of 26 participants per arm to detect a treatment difference in LSM of 0.50 in change in ratio of Vh:Cd between treatment arms, assuming that the common standard deviation is 0.5. If 30% of subjects dropout without the primary endpoint assessment, even if the dropout is unevenly distributed between the two groups (eg, 20% dropout in KAN-101 group, 40% in placebo group), the study will still have 82% power to detect the treatment difference of 0.5 with evaluable participants (ie, full analysis set).

10. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1. Appendix 1: Regulatory, Ethical, and Study Oversight Considerations

10.1.1. Regulatory and Ethical Considerations

This study will be conducted in accordance with the protocol and with the following:

- Consensus ethical principles derived from international guidelines, including the Declaration of Helsinki and CIOMS International Ethical Guidelines;
- Applicable ICH GCP guidelines;
- Applicable laws and regulations, including applicable privacy laws.

The protocol, protocol amendments, ICD, SRSD(s), and other relevant documents (eg, advertisements) must be reviewed and approved by the sponsor, submitted to an IRB/EC by the investigator, and reviewed and approved by the IRB/EC before the study is initiated.

Any amendments to the protocol will require IRB/EC approval before implementation of changes made to the study design, except for changes necessary to eliminate an immediate hazard to study participants.

Protocols and any substantial amendments to the protocol will require health authority approval prior to initiation except for changes necessary to eliminate an immediate hazard to study participants.

In addition to the safety reporting responsibilities to the Sponsor in Section 10.3.4, and in accordance with local regulations, the investigator may be responsible for the following:

- Providing written summaries of the status of the study to the IRB/EC annually or more frequently in accordance with the local regulatory requirements, policies, and procedures established by the IRB/EC;
- Notifying the IRB/EC of SAEs or other significant safety findings as required by IRB/EC procedures;
- Providing oversight of the conduct of the study at the site and adherence to requirements of 21 CFR, ICH GCP guidelines, the IRB/EC, European regulation 536/2014 for clinical studies, and all other applicable local regulations.

10.1.1.1. Reporting of Safety Issues and Serious Breaches of the Protocol or ICH GCP

In the event of any prohibition or restriction imposed (ie, clinical hold) by an applicable regulatory authority in any area of the world, or if the investigator is aware of any new information that might influence the evaluation of the benefits and risks of the study intervention, Pfizer should be informed immediately.

In addition, the investigator will inform Pfizer *i*mmediately of any urgent safety measures taken by the investigator to protect the study participants against any immediate hazard, and of any serious breaches of this protocol or of the ICH GCP guidelines that the investigator becomes aware of.

10.1.2. Financial Disclosure

Investigators and subinvestigators will provide the sponsor or sponsor's designee with sufficient, accurate financial information as requested to allow the sponsor or sponsor's designee to submit complete and accurate financial certification or disclosure statements to the appropriate regulatory authorities. Investigators are responsible for providing information on financial interests during the course of the study and for 1 year after completion of the study.

10.1.3. Informed Consent Process

The investigator or the investigator's representative will explain the nature of the study, including the risks and benefits, to the participant or their legally authorized representative and answer all questions regarding the study. The participant or their legally authorized representative should be given sufficient time and opportunity to ask questions and to decide whether or not to participate in the trial.

Participants must be informed that their participation is voluntary. Participants or their legally authorized representative (if allowed by local regulations) will be required to sign a statement of informed consent that meets the requirements of 21 CFR 50, local regulations, ICH guidelines, privacy, and data protection requirements, where applicable, and the IRB/EC or study center.

The investigator must ensure that each participant or their legally authorized representative is fully informed about the nature and objectives of the study, the sharing of data related to the study, and possible risks associated with participation, including the risks associated with the processing of the participant's personal data.

The participant or their legally authorized representative must be informed that their personal study-related data will be used by the sponsor or sponsor's designee in accordance with local data protection law. The level of disclosure must also be explained to the participant or their legally authorized representative.

The participant or their legally authorized representative must be informed that their medical records may be examined by Clinical Quality Assurance auditors or other authorized personnel appointed by the sponsor, by appropriate IRB/EC members, and by inspectors from regulatory authorities.

The investigator further must ensure that each study participant or their legally authorized representative is fully informed about their right to access and correct their personal data and to withdraw consent for the processing of their personal data.

The medical record must include a statement that written informed consent was obtained before the participant was enrolled in the study and the date on which the written consent was obtained. The authorized person obtaining the informed consent must also sign the ICD.

Participants or their legally authorized representative must be reconsented to the most current version of the IRB/EC-approved ICD(s) during their participation in the study as required per local regulations.

A copy of the ICD(s) must be provided to the participant or their legally authorized representative (if allowed by local regulations).

Participants who are rescreened are required to sign a new ICD.

10.1.4. Data Protection

All parties will comply with all applicable laws, including laws regarding the implementation of organizational and technical measures to ensure protection of participant data.

Participants' personal data will be stored at the study site in encrypted electronic and/or paper form and will be password protected or secured in a locked room to ensure that only authorized study staff have access. The study site will implement appropriate technical and organizational measures to ensure that the personal data can be recovered in the event of disaster. In the event of a potential personal data breach, the study site will be responsible for determining whether a personal data breach has in fact occurred and, if so, providing breach notifications as required by law.

To protect the rights and freedoms of participants with regard to the processing of personal data, participants will be assigned a single, participant-specific numerical code. Any participant records or data sets that are transferred to the sponsor or sponsor's designee will contain the numerical code; participant names will not be transferred. All other identifiable data transferred to the sponsor or sponsor's designee will be identified by this single, participant-specific code. The study site will maintain a confidential list of participants who participated in the study, linking each participant's numerical code to their actual identity and medical record ID. In case of data transfer, the sponsor or sponsor's designee will protect the confidentiality of participants' personal data consistent with the clinical study agreement and applicable privacy laws.

Information technology systems used to collect, process, and store study-related data are secured by technical and organizational security measures designed to protect such data against accidental or unlawful loss, alteration, or unauthorized disclosure or access.

The sponsor or sponsor's designee maintains SOPs on how to respond in the event of unauthorized access, use, or disclosure of sponsor or sponsor's designee information or systems.

10.1.5. Committees Structure

10.1.5.1. Data Monitoring Committee

This study will use a DSMB. The DSMB is independent of the study team and includes only external (at least 2 physicians, one of which will be a CeD medical expert, and 1 biostatistician independent from the conduct of the study) members. The DSMB charter describes the role of the DSMB in more detail. The DSMB safety monitoring plan will be detailed in the DSMB charter.

The primary responsibility of the DSMB is to safeguard study participants by reviewing and assessing the cumulative clinical safety data being collected during the performance of the study. The DSMB will meet periodically throughout the study to review cumulative safety data. The DSMB will be responsible for ongoing monitoring of the safety of participants in the study according to the charter. The recommendations made by the DSMB will be forwarded to the appropriate authorized sponsor personnel for review and final decision. The sponsor or sponsor's designee will communicate such decisions, which may include summaries of aggregate analyses of safety data, to regulatory authorities and investigators, as appropriate.

10.1.6. Dissemination of Clinical Study Data

The sponsor fulfills its commitment to publicly disclose clinical study results through posting the results of studies on www.clinicaltrials.gov (ClinicalTrials.gov), the EudraCT/CTIS, and other public registries and websites in accordance with applicable local laws/regulations. In addition, the sponsor reports study results outside of the requirements of local laws/regulations pursuant to its SOPs.

In all cases, study results are reported by the sponsor in an objective, accurate, balanced, and complete manner and are reported regardless of the outcome of the study or the country in which the study was conducted.

www.clinicaltrials.gov

The sponsor posts clinical trial results on www.clinicaltrials.gov for Kanyos Bio, Inc.-sponsored interventional studies (conducted in patients) that evaluate the safety and/or efficacy of a product, regardless of the geographical location in which the study is conducted. These results are submitted for posting in accordance with the format and timelines set forth by US law.

EudraCT/CTIS

The sponsor posts clinical trial results on EudraCT/CTIS for Kanyos Bio, Inc.-sponsored interventional studies in accordance with the format and timelines set forth by EU requirements.

Documents within marketing applications

The sponsor complies with applicable local laws/regulations to publish clinical documents included in marketing applications. Clinical documents include summary documents and CSRs including the protocol and protocol amendments, sample CRFs, and SAPs. Clinical documents will have personally identifiable information anonymized.

Data sharing

The sponsor provides researchers secure access to participant-level data or full CSRs for the purposes of "bona-fide scientific research" that contributes to the scientific understanding of the disease, target, or compound class. The sponsor will make data from these trials available 18 months after study completion. Participant-level data will be anonymized in accordance with applicable privacy laws and regulations. CSRs will have personally identifiable information anonymized.

Data requests are considered from qualified researchers with the appropriate competencies to perform the proposed analyses. Research teams must include a biostatistician. Data will not be provided to applicants with significant conflicts of interest, including individuals requesting access for commercial/competitive or legal purposes.

10.1.7. Data Quality Assurance

All participant data relating to the study will be recorded on printed or electronic CRF unless transmitted to the sponsor or designee electronically (eg, laboratory data). The investigator is responsible for verifying that data entries are accurate and correct by physically or electronically signing the CRF.

Guidance on completion of CRFs will be provided in the CRF Completion Requirements document.

The investigator must ensure that the CRFs are securely stored at the study site in encrypted electronic and/or paper form and are password protected or secured in a locked room to prevent access by unauthorized third parties.

The investigator must permit study-related monitoring, audits, IRB/EC review, and regulatory agency inspections and provide direct access to source records and documents. This verification may also occur after study completion. It is important that the investigator(s) and their relevant personnel are available during the monitoring visits and possible audits or inspections and that sufficient time is devoted to the process.

Monitoring details describing strategy, including definition of study-critical data items and processes (eg, risk-based initiatives in operations and quality such as risk management and mitigation strategies and analytical risk-based monitoring), methods, responsibilities, and requirements, including handling of noncompliance issues and monitoring techniques (central, virtual, or on-site monitoring), are provided in the data management plan and monitoring plan maintained and utilized by the sponsor or designee.

The sponsor or designee is responsible for the data management of this study, including quality checking of the data.

Records and documents, including signed ICDs, pertaining to the conduct of this study must be retained by the investigator for 15 years after study completion unless local regulations or institutional policies require a longer retention period. No records may be destroyed during the retention period without the written approval of the sponsor. No records may be transferred to another location or party without written notification to the sponsor. The investigator must ensure that the records continue to be stored securely for as long as they are maintained.

When participant data are to be deleted, the investigator will ensure that all copies of such data are promptly and irrevocably deleted from all systems.

The investigator(s) will notify the sponsor or its agents immediately of any regulatory inspection notification in relation to the study. Furthermore, the investigator will cooperate with the sponsor or its agents to prepare the investigator site for the inspection and will allow the sponsor or its agent, whenever feasible, to be present during the inspection. The investigator site and investigator will promptly resolve any discrepancies that are identified between the study data and the participant's medical records. The investigator will promptly provide copies of the inspection findings to the sponsor or its agent. Before response submission to the regulatory authorities, the investigator will provide the sponsor or its agents with an opportunity to review and comment on responses to any such findings.

10.1.8. Source Documents

Source documents provide evidence for the existence of the participant and substantiate the integrity of the data collected. Source documents are filed at the investigator site.

Data reported on the CRF or entered in the eCRF that are from source documents must be consistent with the source documents or the discrepancies must be explained. The investigator may need to request previous medical records or transfer records, depending on the study. Also, current medical records must be available.

In this study, the CRF will serve as the source document. A document must be available at the investigative site that identifies those data that will be recorded on the CRF and for which the CRF will be the source document.

Definition of what constitutes source document and its origin can be found in the Source Document Locator, which is maintained by the sponsor or sponsor's designee (Pfizer).

Description of the use of the computerized system is documented in the data management plan, which is maintained by the sponsor or sponsor's designee.

The investigator must maintain accurate documentation (source record) that supports the information entered in the CRF.

The sponsor or designee will perform monitoring to confirm that data entered into the CRF by authorized site personnel are accurate, complete, and verifiable from source documents; that the safety and rights of participants are being protected; and that the study is being conducted in accordance with the currently approved protocol and any other study agreements, ICH GCP guidelines, and all applicable regulatory requirements.

10.1.9. Use of Medical Records

There may be instances when copies of medical records for certain cases are requested by the sponsor or sponsor designee, where ethically and scientifically justified and permitted by local regulations, to ensure participant safety.

Due to the potential for a participant to be re-identified from their medical records, the following actions must be taken when medical records are sent to the sponsor or sponsor designee:

- The investigator or site staff must redact personal information from the medical record. The personal information includes, but is not limited to, the following: participant names or initials, participant dates (eg, birth date, date of hospital admission/discharge, date of death), participant identification numbers (eg, Social Security number, health insurance number, medical record number, hospital/institution identifier), participant location information (eg, street address, city, country, postal code, IP address), participant contact information (eg, telephone/fax number, email address).

- Each medical record must be transmitted to the sponsor or sponsor designee using systems with technical and organizational security measures to ensure the protection of personal data (eg, Florence is the preferred system if available).

- There may be unplanned situations where the sponsor may request medical records (eg, sharing medical records so that the sponsor can provide study-related advice to the investigator). The medical records should be submitted according to the procedure described above.

10.1.10. Study and Site Start and Closure

The study start date is the date of the first participant's first visit.

The sponsor reserves the right to close the study site or terminate the study at any time for any reason at the sole discretion of the sponsor, including (but not limited to) regulatory authority decision, change in opinion of the IRB/EC, or change in benefit-risk assessment. Study sites will be closed upon study completion. A study site is considered closed when all required documents and study supplies have been collected and a study-site closure visit has been performed.

The investigator may initiate study-site closure at any time upon notification to the sponsor or designee (Pfizer) if requested to do so by the responsible IRB/EC or if such termination is required to protect the health of study participants.

Reasons for the early closure of a study site by the sponsor may include but are not limited to:

- Failure of the investigator to comply with the protocol, the requirements of the IRB/EC or local health authorities, the sponsor's procedures, or the ICH GCP guidelines;
- Inadequate recruitment of participants by the investigator;
- Discontinuation of further study intervention development.

If the study is prematurely terminated or suspended, the sponsor or designee shall promptly inform the investigators, the ECs/IRBs, the regulatory authorities, and any CRO(s) used in the study of the reason for termination or suspension, as specified by the applicable regulatory requirements. The investigator shall promptly inform the participant and should assure appropriate participant therapy and/or follow-up.

Study termination is also provided for in the clinical study agreement. If there is any conflict between the contract and this protocol, the contract will control as to termination rights.

10.1.11. Publication Policy

Publication by the clinical study site(s) of any data from this study must be carried out in accordance with the Clinical Site Agreement, see 10.1.6 for details related to study results related to publication.

10.1.12. Sponsor's Medically Qualified Individual

The sponsor will designate a medically qualified individual (MQI, also known as the medical monitor) to advise the investigator on study-related medical questions. The contact information for the study medical monitor is documented in the Study Team Contact List located in the Investigator Site File. Participants are provided with a Pfizer study information card at the time of informed consent, which includes contact information for their investigator in case of study-related medical questions. The study information card contains, at a minimum, (a) study number, (b) participant's study identification number, and (c) principal investigator contact information.

10.2. Appendix 2: Clinical Laboratory Tests

The following laboratory tests will be performed at times defined in the SoA section of this protocol. Additional laboratory results may be reported on these samples as a result of the method of analysis or the type of analyzer used by the clinical laboratory, or as derived from calculated values. These additional tests would not require additional collection of blood. Unscheduled clinical laboratory measurements may be obtained at any time during the study to assess any perceived safety issues.

Clinical laboratory tests should be performed prior to KAN-101/placebo infusion when applicable.

Table 3. Protocol-Required Laboratory Assessments

Hematology	Chemistry	Urinalysis	Other
Hemoglobin Hematocrit RBC count Platelet count WBC count Total neutrophils (Abs, %) Eosinophils (Abs,%) Monocytes (Abs,%) Basophils (Abs,%) Lymphocytes (Abs,%) PT aPTT INR	Urea and creatinine Serum cystatin C eGFR Glucose (fasting) Calcium Sodium Potassium Chloride Total CO_2 (bicarbonate) AST, ALT Total and direct bilirubin Alkaline phosphatase Uric acid Albumin Total protein Magnesium Amylase Lipase Phosphorus	Local dipstick: pH Glucose (qual) Protein (qual) Blood (qual) Ketones Nitrites Leukocyte esterase Laboratory: Microscopy and culture[a]	At screening: FSH[b] Pregnancy test (β-hCG)[c] HBsAg and HBcAb. HBsAb and HBV DNA as reflex tests Hepatitis C antibody and HCV RNA as reflex test HIV HLA genotype and CeD serology (eg, HLA-DQ2.5 and HLA-DQ8 testing[d], tTG and DGP IgA/IgG) Biomarker: IL-2 PK/ADA

ALT: alanine aminotransferase, AST: aspartate aminotransferase, B-hCG: β-human chorionic gonadotropin, estimated glomerular filtration rate, DGP: deamidated gliadin peptide(s),DNA: deoxyribonucleic acid, FSH: follicle-stimulating hormone, DGP: deamidated gliadin peptide(s), HBV:Hepatitis B virus, HCV:Hepatitis C virus, HBsAb:Hepatitis surface antibody, HBcAb: hepatitis B core antibody, HBsAg: hepatitis B surface antigen, HIV; human immunodeficiency virus, HLA: human leukocyte antigen, IgA/IgG: immunoglobulin A, immunoglobulin G, and IgA/IgG: immunoglobulin A, immunoglobulin G
Please also see Appendix D for abbreviations

a. Only if Urinary Tract Infection is suspected and urine dipstick is positive for nitrites or leukocyte esterase or both.
b. For confirmation of postmenopausal status only.
c. A serum pregnancy test is required at screening. Following screening, local urine testing will be standard for the protocol unless serum testing is required by local regulation or IRB/EC. Serum or urine β-hCG for female participants of childbearing potential.
d. For re-screening, the HLA does not need to be repeated and CeD serology (the tTG and DGP antibody tests) should only be repeated if >3 months have elapsed from previous assessment.

The investigator must review the laboratory report, document this review, and record any clinically relevant changes occurring during the study in the AE section of the CRF.

Laboratory/analyte results that could unblind the study and have been collected for the purpose of the study will not be reported to investigator sites or other blinded personnel until the study has been unblinded.

10.3. Appendix 3: Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-Up, and Reporting

10.3.1. Definition of AE

AE Definition
• An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. • Note: An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study intervention.

Events Meeting the AE Definition
• Any abnormal laboratory test results (hematology, clinical chemistry, or urinalysis) or other safety assessments (eg, ECG, radiological scans, vital sign measurements), including those that worsen from baseline, considered clinically significant in the medical and scientific judgment of the investigator. Any abnormal laboratory test results that meet any of the conditions below must be recorded as an AE: Is associated with accompanying symptoms. Requires additional diagnostic testing or medical/surgical intervention. Leads to a change in study dosing (outside of any protocol-specified dose adjustments) or discontinuation from the study, significant additional concomitant drug treatment, or other therapy. • Exacerbation of a chronic or intermittent preexisting condition, including an increase in either frequency and/or intensity of the condition. • New condition detected or diagnosed after study intervention administration, even though it may have been present before the start of the study. • Signs, symptoms, or the clinical sequelae of a suspected drug-drug interaction. • Signs, symptoms, or the clinical sequelae of a suspected overdose of either study intervention or a concomitant medication. Overdose per se will not be reported as an AE or SAE unless it is an intentional overdose taken with possible suicidal/self-harming intent. Such overdoses should be reported regardless of sequelae.

Events NOT Meeting the AE Definition
• Any clinically significant abnormal laboratory findings or other abnormal safety assessments that are associated with the underlying disease, unless judged by the investigator to be more severe than expected for the participant's condition. • The disease/disorder being studied or expected progression, signs, or symptoms of the disease/disorder being studied, unless more severe than expected for the participant's condition. • Medical or surgical procedure (eg, endoscopy, appendectomy): the condition that leads to the procedure is the AE. • Situations in which an untoward medical occurrence did not occur (social and/or convenience admission to a hospital). • Anticipated day-to-day fluctuations of preexisting disease(s) or condition(s) present or detected at the start of the study that do not worsen.

10.3.2. Definition of an SAE

An SAE is defined as any untoward medical occurrence that, at any dose, meets one or more of the criteria listed below:
a. Results in death
b. Is life-threatening The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event. It does not refer to an event that hypothetically might have caused death if it were more severe.
c. Requires inpatient hospitalization or prolongation of existing hospitalization In general, hospitalization signifies that the participant has been admitted (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's office or outpatient setting. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred or was necessary, the AE should be considered serious. Hospitalization for elective treatment of a preexisting condition that did not worsen from baseline is not considered an AE.

d. Results in persistent or significant disability/incapacity

- The term disability means a substantial disruption of a person's ability to conduct normal life functions.
- This definition is not intended to include experiences of relatively minor medical significance, such as uncomplicated headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (eg, sprained ankle), that may interfere with or prevent everyday life functions but do not constitute a substantial disruption.

e. Is a congenital anomaly/birth defect

f. Is a suspected transmission via a Kanyos Bio, Inc. product of an infectious agent, pathogenic or nonpathogenic

The event may be suspected from clinical symptoms or laboratory findings indicating an infection in a participant exposed to a Kanyos Bio, Inc. product. The terms "suspected transmission" and "transmission" are considered synonymous. These cases are considered unexpected and handled as serious expedited cases by pharmacovigilance personnel. Such cases are also considered for reporting as product defects, if appropriate.

g. Other situations:

- Medical or scientific judgment should be exercised by the investigator in deciding whether SAE reporting is appropriate in other situations, such as significant medical events that may jeopardize the participant or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These events should usually be considered serious.
- Examples of such events include invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization, or development of drug dependency or drug abuse.

10.3.3. Recording/Reporting and Follow-Up of AEs and/or SAEs During the Active Collection Period

AE and SAE Recording/Reporting

The table below summarizes the requirements for recording AEs on the CRF and for reporting SAEs on the CT SAE Report Form to Pfizer Safety throughout the active collection period. These requirements are delineated for 3 types of events: (1) SAEs; (2) nonserious AEs; and (3) exposure to the study intervention under study during pregnancy or breastfeeding, and occupational exposure.

It should be noted that the CT SAE Report Form for reporting of SAE information is not the same as the AE page of the CRF. When the same data are collected, the forms must be completed in a consistent manner. AEs should be recorded using concise medical terminology and the same AE term should be used on both the CRF and the CT SAE Report Form for reporting of SAE information.

Safety Event	Recorded on the CRF	Reported on the CT SAE Report Form to Pfizer Safety Within 24 Hours of Awareness
SAE	All	All
Nonserious AE	All	None
Exposure to the study intervention under study during pregnancy or breastfeeding	All AEs or SAEs associated with EDP or EDB Note: Instances of EDP or EDB not associated with an AE or SAE are not captured in the CRF	All instances of EDP are reported (whether or not there is an associated SAE)* All instances of EDB are reported (whether or not there is an associated SAE)**
Environmental or occupational exposure to the product under study to a nonparticipant (not involving EDP or EDB)	None. Exposure to a study nonparticipant is not collected on the CRF	The exposure (whether or not there is an associated AE or SAE) must be reported***

* **EDP** (with or without an associated AE or SAE): any pregnancy information is reported to Pfizer Safety using the CT SAE Report Form and EDP Supplemental Form; if the EDP is associated with an SAE, then the SAE is reported to Pfizer Safety using the CT SAE Report Form.
** **EDB** is reported to Pfizer Safety using the CT SAE Report Form, which would also include details of any SAE that might be associated with the EDB.
*** **Environmental or occupational exposure:** AEs or SAEs associated with occupational exposure are reported to Pfizer Safety using the CT SAE Report Form.

- When an AE or SAE occurs, it is the responsibility of the investigator to review all documentation (eg, hospital progress notes, laboratory reports, and diagnostic reports) related to the event.
- The investigator will then record all relevant AE or SAE information in the CRF.
- It is **not** acceptable for the investigator to send photocopies of the participant's medical records to Pfizer Safety in lieu of completion of the CT SAE Report Form/AE or SAE CRF page.
- There may be instances when copies of medical records for certain cases are requested by the sponsor/Pfizer Safety. In this case, all participant identifiers, with the exception of the participant number, will be redacted on the copies of the medical records before submission to Pfizer Safety.
- The investigator will attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. Whenever possible, the diagnosis (not the individual signs/symptoms) will be documented as the AE or SAE.

Assessment of Intensity

The investigator will make an assessment of intensity for each AE and SAE reported during the study and assign it to 1 of the categories listed below (as defined by the NCI CTCAE system).

GRADE	Clinical Description of Intensity
1	MILD AE
2	MODERATE AE
3	SEVERE AE
4	LIFE-THREATENING; urgent intervention indicated
5	DEATH RELATED TO AE

Further details regarding the CTCAE are presented in Appendix 10.

An event is defined as "serious" when it meets at least 1 of the predefined outcomes as described in the definition of an SAE, NOT when it is rated as severe.

Assessment of Causality

- The investigator is obligated to assess the relationship between study intervention and each occurrence of each AE or SAE. The investigator will use clinical judgment to determine the relationship.

- A "reasonable possibility" of a relationship conveys that there are facts, evidence, and/or arguments to suggest a causal relationship, rather than a relationship cannot be ruled out.
- Alternative causes, such as underlying disease(s), concomitant therapy, and other risk factors, as well as the temporal relationship of the event to study intervention administration, will be considered and investigated.
- The investigator will also consult the IB and/or product information, for marketed products, in their assessment.
- For each AE or SAE, the investigator **must** document in the medical notes that they have reviewed the AE or SAE and have provided an assessment of causality.
- There may be situations in which an SAE has occurred and the investigator has minimal information to include in the initial report to Pfizer Safety. However, **it is very important that the investigator always make an assessment of causality for every event before the initial transmission of the SAE data to Pfizer Safety.**
- The investigator may change their opinion of causality in light of follow-up information and send an SAE follow-up report with the updated causality assessment.
- The causality assessment is one of the criteria used when determining regulatory reporting requirements.
- If the investigator does not know whether or not the study intervention caused the event, then the event will be handled as "related to study intervention" for reporting purposes, as defined by Pfizer Safety. In addition, if the investigator determines that an SAE is associated with study procedures, the investigator must record this causal relationship in the source documents and CRF, and report such an assessment in the dedicated section of the CT SAE Report Form and in accordance with the SAE reporting requirements.

Follow-Up of AEs and SAEs

- The investigator is obligated to perform or arrange for the conduct of supplemental measurements and/or evaluations, as medically indicated or as requested by the sponsor/Pfizer Safety, to elucidate the nature and/or causality of the AE or SAE as fully as possible. This may include additional laboratory tests or investigations, histopathological examinations, or consultation with other healthcare providers.

- If a participant dies during participation in the study or during a recognized follow-up period, the investigator will provide Pfizer Safety with a copy of any postmortem findings, including histopathology.
- New or updated information will be recorded in the originally submitted documents.
- The investigator will submit any updated SAE data to Pfizer Safety within 24 hours of receipt of the information.

10.3.4. Reporting of SAEs

SAE Reporting to Pfizer Safety via an Electronic DCT

- The primary mechanism for reporting an SAE to Pfizer Safety will be the electronic DCT.
- If the electronic system is unavailable, then the site will use the paper SAE DCT (see next section) to report the event within 24 hours.
- The site will enter the SAE data into the electronic DCT (eg, eSAE or PSSA) or paper form (as applicable) as soon as the data become available.
- After the study is completed at a given site, the electronic DCT will be taken off-line to prevent the entry of new data or changes to existing data.
- If a site receives a report of a new SAE from a study participant or receives updated data on a previously reported SAE after the electronic DCT has been taken off-line, then the site can report this information on a paper SAE form (see next section) or to Pfizer Safety by telephone.

SAE Reporting to Pfizer Safety via the CT SAE Report Form

- Facsimile transmission of the CT SAE Report Form is one of the preferred methods to transmit this information to Pfizer Safety.
- In circumstances when the facsimile is not working, an alternative method should be used, eg, secured (Transport Layer Security) or password-protected email. If none of these methods can be used, notification by telephone is acceptable with a copy of the CT SAE Report Form sent by overnight mail or courier service.
- Initial notification via telephone does not replace the need for the investigator to complete and sign the CT SAE Report Form pages within the designated reporting time frames.

10.4. Appendix 4: Contraceptive and Barrier Guidance

10.4.1. Male Participant Reproductive Inclusion Criteria

Male participants are eligible to participate if they agree to the following requirements during the intervention period and for at least 21 days after the last dose of study intervention, which corresponds to the time needed to eliminate reproductive safety risk of the study intervention(s):

- Refrain from donating sperm.

  PLUS either:

- Be abstinent from heterosexual or homosexual intercourse as their preferred and usual lifestyle (abstinent on a long-term and persistent basis) and agree to remain abstinent.

  OR

- Must agree to use a male condom when engaging in any activity that allows for passage of ejaculate to another person.

- The male participant should be advised of the benefit for a WOCBP partner using a highly effective method of contraception with a failure rate of <1% per year, as described in Section 10.4.4.

10.4.2. Female Participant Reproductive Inclusion Criteria

The criteria below are part of Inclusion Criterion 1 (Age and Sex; Section 5.1) and specify the reproductive requirements for including female participants. Refer to Section 10.4.4 for a complete list of contraceptive methods permitted in the study.

- A female participant is eligible to participate if she (a) is not pregnant or breastfeeding; and (b) agrees not to donate eggs (ova, oocytes) for the purpose of reproduction for 21 days after the last dose of study intervention; and (c) at least 1 of the following conditions applies:

  - Is not a WOCBP (see definition in Section 10.4.3).

    OR

  - Is a WOCBP and agrees to use a contraceptive method that is highly effective (failure rate of <1% per year) with low user dependency during the intervention period and agrees to use it for at least 21 days after the last dose of study intervention, which corresponds to the time needed to eliminate any reproductive safety risk of the study intervention(s). The investigator should evaluate the effectiveness of the contraceptive method in relationship to the first dose of study intervention.

OR

- Is a WOCBP and agrees to use a highly effective (failure rate of <1% per year) user-dependent method of contraception during the intervention period and for at least 21 days after the last dose of study intervention, which corresponds to the time needed to eliminate any reproductive safety risk of the study intervention(s). In addition to her use of the highly effective method above, she agrees to concurrently use an effective barrier method. The investigator should evaluate the effectiveness of the contraceptive method in relationship to the first dose of study intervention.

The investigator is responsible for review of medical history, menstrual history, and recent sexual activity to decrease the risk for inclusion of a woman with an early undetected pregnancy.

10.4.3. Woman of Childbearing Potential

A woman is considered fertile following menarche and until becoming postmenopausal unless permanently sterile (see below).

If fertility is unclear (eg, amenorrhea or oligomenorrhea) and a menstrual cycle cannot be confirmed before the first dose of study intervention, additional evaluation should be considered.

Women in the following categories are not considered WOCBP:

1. Premenopausal female with 1 of the following:

   - Documented hysterectomy;
   - Documented bilateral salpingectomy;
   - Documented bilateral oophorectomy.

For individuals with permanent infertility due to a medical cause other than the above (eg, mullerian agenesis, androgen insensitivity), investigator discretion should be applied to determining study entry.

Note: Documentation for any of the above categories can come from the site personnel's review of the participant's medical records, medical examination, or medical history interview. The method of documentation should be recorded in the participant's medical record for the study.

2. Postmenopausal female:

- A postmenopausal state is defined as no menses for 12 months without an alternative medical cause. In addition:
- A high FSH level in the postmenopausal range must be used to confirm a postmenopausal state in women under 60 years of age and not using hormonal contraception or HRT.
- A female on HRT and whose menopausal status is in doubt will be required to use one of the highly effective nonestrogen hormonal contraception methods if she wishes to continue her HRT during the study. Otherwise, she must discontinue HRT to allow confirmation of postmenopausal status before study enrollment.

10.4.4. Contraception Methods

Contraceptive use by men or women should be consistent with local availability/regulations regarding the use of contraceptive methods for those participating in clinical trials.

The following contraceptive methods are appropriate for this study:

Highly Effective Methods That Have Low User Dependency

1. Implantable progestogen-only hormone contraception associated with inhibition of ovulation.
2. Intrauterine device.
3. Intrauterine hormone-releasing system.
4. Bilateral tubal occlusion.
5. Vasectomized partner.
    - Vasectomized partner is a highly effective contraceptive method provided that the partner is the sole sexual partner of the WOCBP and the absence of sperm has been confirmed. If not, an additional highly effective method of contraception should be used. The spermatogenesis cycle is approximately 90 days.

Highly Effective Methods That Are User Dependent

6. Combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation:
    - Oral
    - Intravaginal

- Transdermal

7. Progestogen-only hormone contraception associated with inhibition of ovulation:
    - Oral
    - Injectable
8. Sexual abstinence
    - Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study intervention. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the study and the preferred and usual lifestyle of the participant.

10.5. Appendix 5: Genetics

Use/Analysis of DNA

- Genetic variation may impact a participant's response to study intervention, susceptibility to, and severity and progression of disease. Therefore, where local regulations and IRBs/ECs allow, a blood sample will be collected for DNA analysis.
- The results of genetic analyses may be reported in the CSR or in a separate study summary, or may be used for internal decision making without being included in a study report.
- The sponsor or designee will store the DNA samples in a secure storage space with adequate measures to protect confidentiality.
- The samples will be retained as indicated:
  - Samples for specified genetic analysis (see Section 8.6.1 and Section 8.7.1) will not be stored beyond the completion of this study (eg, CSR finalization).
- Samples for genetic research will be labeled with a code. The key between the code and the participant's personally identifying information (eg, name, address) will be held securely at the study site.

10.6. Appendix 6: Liver Safety: Suggested Actions and Follow-Up Assessments

Potential Cases of Drug-Induced Liver Injury

Humans exposed to a drug who show no sign of liver injury (as determined by elevations in transaminases) are termed "tolerators," while those who show transient liver injury but adapt are termed "adaptors." In some participants, transaminase elevations are a harbinger of a more serious potential outcome. These participants fail to adapt and therefore are "susceptible" to progressive and serious liver injury, commonly referred to as DILI. Participants who experience a transaminase elevation above 3 × ULN should be monitored more frequently to determine if they are "adaptors" or are "susceptible."

In the majority of DILI cases, elevations in AST and/or ALT precede T bili elevations (>2 × ULN) by several days or weeks. The increase in T bili typically occurs while AST/ALT is/are still elevated above 3 × ULN (ie, AST/ALT and T bili values will be elevated within the same laboratory sample). In rare instances, by the time T bili elevations are detected, AST/ALT values might have decreased. This occurrence is still regarded as a potential DILI. Therefore, abnormal elevations in either AST OR ALT in addition to T bili that meet the criteria outlined below are considered potential DILI (assessed per Hy's law criteria) cases and should always be considered important medical events, even before all other possible causes of liver injury have been excluded.

The threshold of laboratory abnormalities for a potential DILI case depends on the participant's individual baseline values and underlying conditions. Participants who present with the following laboratory abnormalities should be evaluated further as potential DILI (Hy's law) cases to definitively determine the etiology of the abnormal laboratory values:

- Participants with AST/ALT and T bili baseline values within the normal range who subsequently present with AST OR ALT values ≥3 × ULN AND a T bili value ≥2 × ULN with no evidence of hemolysis and an alkaline phosphatase value <2 × ULN or not available.

- For participants with baseline AST **OR** ALT **OR** T bili values above the ULN, the following threshold values are used in the definition mentioned above, as needed, depending on which values are above the ULN at baseline:

    - Preexisting AST or ALT baseline values above the normal range: AST or ALT values ≥2 times the baseline values AND ≥3 × ULN; or ≥8 × ULN (whichever is smaller).

    - Preexisting values of T bili above the normal range: T bili level increased from baseline value by an amount of ≥1 × ULN **or** if the value reaches ≥3 × ULN (whichever is smaller).

Rises in AST/ALT and T bili separated by more than a few weeks should be assessed individually based on clinical judgment; any case where uncertainty remains as to whether it represents a potential Hy's law case should be reviewed with the sponsor or designee.

The participant should return to the investigator site and be evaluated as soon as possible, preferably within 48 hours from awareness of the abnormal results. This evaluation should include laboratory tests, detailed history, and physical assessment.

In addition to repeating measurements of AST and ALT and T bili for suspected Hy's law cases, additional laboratory tests should include albumin, CK, direct and indirect bilirubin, GGT, PT/INR, eosinophils (%), and alkaline phosphatase. Consideration should also be given to drawing a separate tube of clotted blood and an anticoagulated tube of blood for further testing, as needed, for further contemporaneous analyses at the time of the recognized initial abnormalities to determine etiology. A detailed history, including relevant information, such as review of ethanol, acetaminophen/paracetamol (either by itself or as a coformulated product in prescription or over-the-counter medications), recreational drug, or supplement (herbal) use and consumption, family history, sexual history, travel history, history of contact with a jaundiced person, surgery, blood transfusion, history of liver or allergic disease, and potential occupational exposure to chemicals, should be collected. Further testing for acute hepatitis A, B, C, D, and E infection, total bile acids, liver imaging (eg, biliary tract), and collection of serum samples for acetaminophen/paracetamol drug and/or protein adduct levels may be warranted.

All cases demonstrated on repeat testing as meeting the laboratory criteria of AST/ALT and T bili elevation defined above should be considered potential DILI (Hy's law) cases if no other reason for the LFT abnormalities has yet been found. **Such potential DILI (Hy's law) cases are to be reported as SAEs, irrespective of availability of all the results of the investigations performed to determine etiology of the LFT abnormalities.**

A potential DILI (Hy's law) case becomes a confirmed case only after all results of reasonable investigations have been received and have excluded an alternative etiology.

10.7. Appendix 7: Kidney Safety Monitoring Guidelines

10.7.1. Laboratory Assessment of Change in Kidney Function and Detection of Kidney Injury

Standard kidney safety monitoring requires assessment of baseline and postbaseline Screat measurement to estimate kidney function [Screat-based eGFR] or creatinine clearance [eCrCl]). Baseline and postbaseline Scys makes it feasible to distinguish AKI from other causes of Screat increase. If Screat increase is confirmed after baseline, then reflex measurement of Scys is indicated.

ADULTS: Currently, 2021 CKD-EPI eGFR equations (Screat-only based and combined Screat plus Scys-based) are valid for use in adults only. At baseline Screat and Scys values are needed to calculate 2021 CKD-EPI eGFR by Screat-only based equation (see Table in Section 10.7.2.1) and by combined Screat plus Scys-based equation. When post-baseline Screat increase ≥0.3 mg/dL is confirmed, then reflex Scys measurement is needed to enable post-baseline comparison of eGFR changes (Screat-only based eGFR and combined Screat plus Scys eGFR).

Regardless of whether kidney function monitoring tests are required as a routine safety monitoring procedure in the study, if the investigator or sponsor or sponsor's designee deems it necessary to further assess kidney safety and quantify kidney function, then these test results should be managed and followed per standard of care.

10.7.2. Age-Specific Kidney Function Calculation Recommendations

10.7.2.1. Adults (18 Years and Above)—2021 CKD-EPI Equations

2021 CKD-EPI Screat Only	**Screat** *(mg/dL)*	**Scys** *(mg/L)*	**Recommended eGFR Equation**
Female	if ≤0.7	NA	$eGFR = 143 \times (Screat/0.7)^{-0.241} \times (0.9938)^{Age}$
Female	if >0.7	NA	$eGFR = 143 \times (Screat/0.7)^{-1.200} \times (0.9938)^{Age}$
Male	if ≤0.9	NA	$eGFR = 142 \times (Screat/0.9)^{-0.302} \times (0.9938)^{Age}$
Male	if >0.9	NA	$eGFR = 142 \times (Screat/0.9)^{-1.200} \times (0.9938)^{Age}$
2021 CKD-EPI Screat-Scys Combined	**Screat** *(mg/dL)*	**Scys** *(mg/L)*	**Recommended eGFR Equation**
Female	if ≤0.7	if ≤0.8	$eGFR = 130 \times (Screat/0.7)^{-0.219} \times (Scys/0.8)^{-0.323} \times (0.9961)^{Age}$
Female	if ≤0.7	if >0.8	$eGFR = 130 \times (Screat/0.7)^{-0.219} \times (Scys/0.8)^{-0.778} \times (0.9961)^{Age}$
Female	if >0.7	if ≤0.8	$eGFR = 130 \times (Screat/0.7)^{-0.544} \times (Scys/0.8)^{-0.323} \times (0.9961)^{Age}$
Female	if > 0.7	if > 0.8	$eGFR = 130 \times (Screat/0.7)^{-0.544} \times (Scys/0.8)^{-0.778} \times (0.9961)^{Age}$
Male	if ≤0.9	if ≤0.8	$eGFR = 135 \times (Screat/0.9)^{-0.144} \times (Scys/0.8)^{-0.323} \times (0.9961)^{Age}$
Male	if ≤0.9	if >0.8	$eGFR = 135 \times (Screat/0.9)^{-0.144} \times (Scys/0.8)^{-0.778} \times (0.9961)^{Age}$
Male	if >0.9	if ≤0.8	$eGFR = 135 \times (Screat/0.9)^{-0.544} \times (Scys/0.8)^{-0.323} \times (0.9961)^{Age}$
Male	if >0.9	if >0.8	$eGFR = 135 \times (Screat/0.9)^{-0.544} \times (Scys/0.8)^{-0.778} \times (0.9961)^{Age}$

(Inker et al, 2021)

10.7.3. Kidney Function Calculation Tools

The sponsor has provided the following resources to investigational sites when required to calculate age-specific kidney function at Screening, Baseline, and post-Baseline visits. Site calculations of kidney function can be performed manually, using the age appropriate formulae (see Section 10.7.2) and can use recommended online kidney function calculators to reduce the likelihood of a calculation error.

The United States National Kidney Foundation Online Calculators.

- Adults (18 years and above) - 2021 CKD-EPI Creatinine Online Calculator (eGFR): https://www.kidney.org/professionals/KDOQI/gfr_calculator

Investigational sites are responsible to ensure that the accurate age-specific equation is selected and that the correct units are used for serum creatinine (mg/dL only), serum cystatin C (mg/L only), total body weight (kg only), and age (years). Investigators are expected to (i) review and confirm correctness of the kidney function calculation results and (ii) evaluate the calculated value within the context of historical information available to them in the participant's medical record. Investigators are responsible for the clinical oversight of the participant eligibility process, kidney function calculation, and dose selection and adjustments per study protocol. Investigators are encouraged to direct questions or uncertainties regarding kidney function and dosing to the sponsor or sponsor's designee, if needed.

10.7.4. Adverse Event Grading for Kidney Safety Laboratory Abnormalities

AE grading for decline in kidney function (ie, eGFR or eCrCl) will be according to KDIGO criteria for adult participants.

KDIGO criteria grade (G)	**Study Population**	**G1**	**G2**	**G3**	**G4**	**G5**
Decreased Kidney Function due to either Acute or Chronic Kidney Injury	Adult participants eGFR (mL/min/1.73m²)	≥90	≥60 to 89	30 to 59	15 to 29	<15

10.8. Appendix 8: ECG Findings of Potential Clinical Concern

ECG Findings That May Qualify as AEs
• Marked sinus bradycardia (rate <40 bpm) lasting minutes. • New PR interval prolongation >280 ms. • New prolongation of QTcF to >480 ms (absolute) • New prolongation of QTcF by >60 ms from baseline. • New-onset atrial flutter or fibrillation, with controlled ventricular response rate: ie, rate <120 bpm. • New-onset type I second-degree (Wenckebach) AV block of >30 seconds' duration. • Frequent PVCs, triplets, or short intervals (<30 seconds) of consecutive ventricular complexes.
ECG Findings That May Qualify as SAEs

• QTcF prolongation >500 ms.
• Absolute value of QTcF >450 ms AND QTcF change from baseline >60 ms.
• New ST-T changes suggestive of myocardial ischemia.
• New-onset LBBB (QRS complex >120 ms).
• New-onset right bundle branch block (QRS complex >120 ms).
• Symptomatic bradycardia.
• Asystole:
  • In awake, symptom-free participants in sinus rhythm, with documented asystolic pauses ≥3 seconds or any escape rate <40 bpm, or with an escape rhythm that is below the AV node;
  • In awake, symptom-free participants with atrial fibrillation and bradycardia with 1 or more asystolic pauses of at least 5 seconds or longer;
  • Atrial flutter or fibrillation, with rapid ventricular response rate: rapid = rate >120 bpm.

- Sustained supraventricular tachycardia (rate >120 bpm) ("sustained" = short duration with relevant symptoms or lasting >1 minute).
- Ventricular rhythms >30 second duration, including idioventricular rhythm (HR <40 bpm), accelerated idioventricular rhythm (HR 40 bpm to <100 bpm), and monomorphic/polymorphic ventricular tachycardia (HR >100 bpm [such as torsades de pointes]).
- Type II second-degree (Mobitz II) AV block.
- Complete (third -degree) heart block.

ECG Findings That Qualify as SAEs

- Change in pattern suggestive of new myocardial infarction.
- Sustained ventricular tachyarrhythmias (>30 second duration).
- Second- or third-degree AV block requiring pacemaker placement.
- Asystolic pauses requiring pacemaker placement.
- Atrial flutter or fibrillation with rapid ventricular response requiring cardioversion.
- Ventricular fibrillation/flutter.
- At the discretion of the investigator, any arrhythmia classified as an adverse experience.

The major events of potential clinical concern listed above are recommended as "alerts" or notifications from the core ECG laboratory to the investigator and the sponsor study team, and not to be considered as all-inclusive of what to be reported as AEs/SAEs.

10.9. Appendix 9: Infusion-Related Reactions

Participants will be monitored in the clinic for 4 hours following IV study drug administration for IRR. IRR may include, but are not limited to: erythema, induration, ecchymosis, pain, and pruritus.

If an IRR occurs during study intervention administration, the following treatment recommendations are provided and may be modified per local treatment standards and guidelines as appropriate:

- **Grade 1 (mild):** Infusion rate modification not indicated. Administer symptomatic treatment (eg, antihistamines, antipyretics, antiemetics) as needed. Closely monitor participant until resolution. Prophylaxis with diphenhydramine 50 mg (or equivalent) and/or acetaminophen/paracetamol 325 to 1000 mg is recommended at least 30 minutes prior to future study intervention infusions.

- **Grade 2 (moderate):** Slow infusion rate to ≤50% of the original infusion rate and treat symptoms with appropriate medical therapy, including but not limited to antihistamines, antipyretics, and analgesics. Increase monitoring of vital signs as medically indicated until participant is deemed stable. Prophylaxis with diphenhydramine 50 mg (or equivalent) and/or acetaminophen/paracetamol 325 to 1000 mg is recommended at least 30 minutes prior to future study intervention infusions.

- **Grade 3 (severe):** Stop infusion and institute appropriate symptom-directed therapy, including but not limited to antihistamines, antipyretics, corticosteroids, bronchodilators, and O_2. Increase monitoring of vital signs as medically indicated until participant is deemed stable.

    - If the reaction has not resolved within 6 hours of study drug preparation, the remainder of the infusion will not be administered and study intervention will be permanently discontinued.

    - Following the completion or termination of a restarted infusion due to an IRR:

        - All participants must be monitored until resolution of symptoms or for at least 2 hours in the absence of additional symptoms.

        - Prophylaxis with diphenhydramine 50 mg (or equivalent) and/or acetaminophen/paracetamol 325 to 1000 mg is recommended at least 30 minutes prior to future study intervention infusions.

        - The next infusion should initiate at a rate of 2 hours per dose, or 25% of the rate at which the reaction occurred. If no IRRs are observed within the first 30 minutes, the infusion rate may increase to 30-minutes-per dose rate as outlined in Section 6.1.1.

- In cases where infusion has started but cannot be completed with 6 hours of study drug preparation, the remainder of the infusion will not be administered and study intervention will be permanently discontinued.

- If second occurrence of Grade 3 or greater IRR, permanently discontinue study intervention.

- **Grade 4 (life-threatening):** Stop infusion and immediately institute appropriate symptom directed therapy and supportive measures as necessary, including but not limited to, corticosteroids, bronchodilators, O_2/respiratory support, and vasopressors. Hospitalization and/or intensive care unit admission may be indicated.

  - Permanently discontinue study intervention.

10.10. Appendix 10: Common Terminology Criteria For Adverse Events

CTCAE Terms

AEs are defined in Appendix 3. An AE is a term that is a unique representation of a specific event used for medical documentation and scientific analyses. Each CTCAE term as a MedDRA Lowest Level Term. The latest available version of CTCAE will be used (NCI NIH, 2022).

Definitions

A brief definition is provided to clarify the meaning of each AE term.

Grades

Grade refers to the severity of the AE and are specified in Appendix 3. Further details are provided below. CTCAE v6.0 grades for GI disorders frequently observed in the FIH study KAN-101-01 are provided in Table 4.

The CTCAE displays Grades 1 through Grade 5 with unique clinical descriptions of severity for each AE based on this general guideline:

- **Grade 1:** Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
- **Grade 2:** Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL*
- **Grade 3:** Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting selfcare ADL**
- **Grade 4:** Life-threatening consequences; urgent intervention indicated
- **Grade 5:** Death related to AE

A semi-colon indicates 'or' within the description of the grade.

A single dash (-) indicates a grade is not available.

Not all grades are appropriate for all AEs. Therefore, some AEs are listed with fewer than 5 options for Grade selection. Grade 5 (Death) is not appropriate for some AEs and is therefore not an opinion.

Table 4. CTCAE v6.0 or Higher Grades for GI Disorders Observed in KAN-101-01 (FIH Study)

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Nausea	Loss of appetite without alteration in eating habits	Oral intake decreased without significant weight loss, dehydration or malnutrition	Inadequate oral caloric or fluid intake; tube feeding, TPN, or hospitalization indicated	-	-
Abdominal pain	Mild pain	Moderate pain, limiting instrumental ADL	Severe pain; limiting selfcare ADL	-	-
Vomiting	Intervention not indicated	Outpatient IV hydration; medical intervention indicated	Tube feeding, TPN, or hospitalization indicated	Life-threatening consequences	Death
Constipation	Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema	Persistent symptoms with regular use of laxatives or enemas; limiting instrumental ADL	Obstipation with manual evacuation indicated; limiting selfcare ADL	Life-threatening consequences; urgent intervention indicated	Death
Diarrhea	Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4 - 6 stools per day over baseline; moderate increase in ostomy output compared to baseline; limiting instrumental ADL	Increase of >=7 stools per day over baseline; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting selfcare ADL	Life-threatening consequences; urgent intervention indicated	Death
Dyspepsia	Mild symptoms; intervention not indicated	Moderate symptoms; medical intervention indicated	Severe symptoms; operative intervention indicated	-	-
Flatulence	Mild symptoms; intervention not indicated	Moderate symptoms; psychosocial sequelae	-	-	-

CTCAE: Common Terminology Criteria for Adverse Events; FIH: First- in- Human, ADL: Activities of daily living.

Activities of Daily Living

* Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.

** Selfcare ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bed ridden.

10.11. Appendix 11: ASA Physical Status Classification System

ASA Physical Status Classification	Definition	Adult Examples, including, but not Limited to:
ASA I	A normal healthy patient	Healthy, non-smoking, no or minimal alcohol use
ASA II	A patient with mild systemic disease	Mild diseases only without substantive functional limitations. Current smoker, social alcohol drinker, pregnancy, obesity (30<BMI<40), well-controlled DM/HTN, mild lung disease
ASA III	A patient with severe systemic disease	Substantive functional limitations; One or more moderate to severe diseases. Poorly controlled DM or HTN, COPD, morbid obesity (BMI ≥40), active hepatitis, alcohol dependence or abuse, implanted pacemaker, moderate reduction of ejection fraction, ESRD undergoing regularly scheduled dialysis, history (>3 months) of MI, CVA, TIA, or CAD/stents
ASA IV	A patient with severe systemic disease that is a constant threat to life	Recent (<3 months) MI, CVA, TIA or CAD/stents, ongoing cardiac ischemia or severe valve dysfunction, severe reduction of ejection fraction, shock, sepsis, DIC, ARD or ESRD not undergoing regularly scheduled dialysis
ASA V	A moribund patient who is not expected to survive without the operation	Ruptured abdominal/thoracic aneurysm, massive trauma, intracranial bleed with mass effect, ischemic bowel in the face of significant cardiac pathology or multiple organs/system dysfunction
ASA VI	A declared brain-dead patient whose organs are being removed for donor purposes	

ARD-Acute Respiratory Distress; ASA-American Society of Anesthesiologists; BMI-Body Mass Index; CAD-Coronary Artery Disease; COPD-Chronic Obstructive Pulmonary Disease; CVA-Cerebrovascular Accident; DIC-Disseminated Intravascular Coagulation; DM-Diabetes Mellitus; ESRD-End-Stage Renal Disease; HTN-Hypertension; MI-Myocardial Infarction; TIA-Transient Ischemic Attack

American Society of Anesthesiologists. (2020)

10.12. Appendix 12: Abbreviations

The following is a list of abbreviations that may be used in the protocol.

Abbreviation	Term
Abs	absolute
ADA	anti-drug antibodies
ADL	activity/activities of daily living
AE	adverse event
AKI	acute kidney injury
ALP	alkaline phosphatase
ALT	alanine aminotransferase
ANC	absolute neutrophil count
ANCOVA	analysis of covariance
ANOVA	analysis of covariance
aPTT	activated partial thromboplastin time
ARD	Acute respiratory distress
ASA	American Society of Anesthesiologists
AST	aspartate aminotransferase
AUC	area under the curve
AUC_{inf}	area under the plasma-concentration time curve from time 0 extrapolated to infinite time
AUC_{last}	area under the plasma concentration-time profile from time 0 to the time of the last quantifiable concentration (C_{last})
AV	atrioventricular
AxMP	auxiliary medicinal product
β-hCG	β-human chorionic gonadotropin
BL	baseline
BMI	Body mass index
BP	blood pressure
bpm	beats per minute
CDSD	Celiac Disease Symptom Diary
CAD	coronary artery disease
CeD	celiac disease
CFR	Code of Federal Regulations
CI	confidence interval
CIOMS	Council for International Organizations of Medical Sciences
CK	creatine kinase
CKD-EPI	chronic kidney disease epidemiology
C_{max}	maximum plasma concentration
CO_2	carbon dioxide (bicarbonate)
COPD	chronic obstructive pulmonary disease
COVID-19	coronavirus disease 2019
C_{last}	last quantifiable concentration
CM	concomitant medications
CRF	case report form
CRO	contract research organization
CSR	Clinical Study Report
CT	clinical trial
CTCAE	Common Terminology Criteria for Adverse Events
CTIS	Clinical Trial Information System
CV	Cardiovascular; Coefficient of variation

Abbreviation	Term
CVA	Cerebrovascular attack
D	day
DCT	data collection tool
DGP	deamidated gliadin peptide(s)
DIC	Disseminated Intravascular Coagulation;
DILI	drug-induced liver injury
DM	Diabetes mellitus
DNA	deoxyribonucleic acid
DSMB	Data Safety Monitoring Board
DU	dispensable unit
EAE	experimental autoimmune encephalomyelitis
EC	ethics committee
ECC	emergency contact card
ECG	electrocardiogram or electrocardiography
eCrCl	estimated creatinine clearance
eCRF	electronic case report form
EDB	exposure during breastfeeding
EDP	exposure during pregnancy
EFD	embryonic fetal development
EGD	esophagogastroduodenoscopy
eGFR	estimated glomerular filtration rate
eSAE	electronic serious adverse event
ESRD	End-stage renal disease
ET	early termination
et al	and others
EU	European Union
EudraCT	European Union Drug Regulating Authorities Clinical Trials (European Clinical Trials Database)
FAS	full analysis set
FIH	First-in-human
FSH	follicle-stimulating hormone
FU	follow-up
GC	gluten challenge
GCP	Good Clinical Practice
GFD	gluten-free diet
GGT	gamma-glutamyl transferase
GI	gastrointestinal
GM	geometric mean
GP	gliadin peptide
HBcAb	hepatitis B core antibody
HBsAb	hepatitis B surface antibody
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCV	hepatitis C virus
HCVAb	hepatitis C virus antibody
HIV	human immunodeficiency virus
HLA	human leukocyte antigen
HLA-DQ2.5	human leukocyte antigen loci encoded by HLA-DQA1*05 and HLA-DQB1*02 (homozygotes or heterozygotes) genotype
HLA-DQ8	human leukocyte antigen serotype with the HLA-DQ serotype group

Abbreviation	Term
HLA-DQA1 and HLA-DQB1	human leukocyte antigen loci
HR	heart rate
HRT	hormone replacement therapy
HTN	hypertension
IA	interim analysis
IB	Investigator's Brochure
IBS	Irritable Bowel Syndrome
ICD	Informed Consent Document
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ID	Identification
IEL	intraepithelial lymphocytes
IgA	immunoglobulin A
IgG	immunoglobulin G
IL-2	interleukin-2
IMP	investigational medicinal product
IND	Investigational New Drug
INR	international normalized ratio
IPAL	Investigational Product Accountability Log
IPM	Investigational product manual
IRB	Institutional Review Board
IRR	infusion-related reaction
IRT	Interactive Response Technology
IV	intravenous(ly)
KDIGO	Kidney Disease: Improving Global Outcomes
K_{el}	elimination rate constant
LBBB	left bundle branch block
LFT	liver function test
LSM	least-squares mean
MAD	multiple ascending dose
MedDRA	Medical Dictionary for Regulatory Activities
MHC	major histocompatibility complex
MI	Myocardial infarction
MQI	medically qualified individual
MTD	maximum tolerated dose
NA	Not Applicable
NCI	National Cancer Institute
NIMP	noninvestigational medicinal product
NOAEL	no observed adverse effect level
n	number
O_2	diatomic oxygen
OTC	over the counter
PBO	placebo
PGIC	Patient Global Impression of Change
PGIS	Patient Global Impression of Severity
PI	Primary Investigator
PK	pharmacokinetic(s)
PO	by mouth; oral(ly)
PP	per protocol
PPS	per protocol set

Abbreviation	Term
PR	pulse rate
PRO	patient reported outcomes
PSSA	Pfizer SAE submission assistant
PT	prothrombin time
PVC	premature ventricular contractions
QTc	corrected QT interval
QTcF	QTc corrected using Fridericia's formula
qual	qualitative
RBC	red blood cell
RNA	ribonucleic acid
RSI	reference safety information
SAD	single ascending dose
SAE	serious adverse event
SAP	Statistical Analysis Plan
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
Scr.	screening
Screat	serum creatinine
Scys	serum cystatin C
SoA	schedule of activities
SOC	standard of care
SOP	standard operating procedure
SRSD	Single Reference Safety Document
SUSAR	Suspected Unexpected Serious Adverse Reactions
$t_{½}$	terminal phase half-life
TBD	to be determined
T bili	total bilirubin
TEAE	treatment-emergent adverse events
TIA	Transient ischemic attack
T_{max}	time to reach C_{max}
TPN	total parenteral nutrition
tTG	transglutaminase
ULN	upper limit of normal
US	United States
UTI	urinary tract infection
V	visit
Vh:Cd	villous height:crypt depth ratio
WBC	white blood cell
WOCBP	woman/women of childbearing potential

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