TITLE PAGE

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KAN-101-01

A Phase 1 Study of the Safety and Tolerability of Single and Multiple Doses of KAN-101 in Patients with Celiac Disease

Statistical Analysis Plan

Version: 3.0

PPD

Dated: 12-Nov-2021

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SPONSOR SIGNATURE PAGE

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REVISION HISTORY

Version No.	Effective Date	Summary of Change(s)
Final 1.0	[12 Apr 21]	New document
2.0	03 Nov 2021	Minor: few words/sentences were added for below. 1. Covid related data collection: section 3.5.1.1 and 4.8.1. 2. ADA related screening titer information added section 3.5.3. 3. Protocol deviation: section 4.7. 4. Laboratory: section 4.8.2. 5. Part A tables and few Part A and B tables were added for CSR 6. Added condition for analysis if the dose level received is unknown 7. Similar information PK sentences and peptide data were removed as were not applicable Major: 1. CCI
3.0	12 Nov 2021	Minor: 1. PK sections (3.5.2, 4.3.2, 4.4.4, 4.9) were updated to include the necessary PK parameters to be consistent with the shells. 2. Not applicable abbreviations were removed from 'List of Abbreviations'

LIST OF ABBREVIATIONS

List and define all acronyms and abbreviations used in the document here. Abbreviations should be spelled out in full and the abbreviation indicated in parentheses at first appearance in the text. Abbreviations should appear in alphabetical order.

Abbreviation / Acronym	Definition
ADA	Anti-drug anti-body
ADL	Activities of daily living
AE	Adverse event
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
ATAS	All Treated Analysis Set
ATC	Anatomical therapeutic chemical
AUC	Area under the concentration-time curve
$AUC_{0\text{-}inf}$	AUC from time zero extrapolated to infinity
$AUC_{0\text{-}t}$	AUC from time zero to the last quantifiable concentration
$AUC_{0\text{-}\tau\text{-}}$	AUC over the dosing interval
%AUCex	Percentage of $AUC_{0\text{-}inf}$ that is due to extrapolation beyond t_{last}
BDRM	Blinded Data Review Meeting
BLQ	Below the lower limit of quantification
BMI	Body Mass Index
BP	Blood pressure
C_{av}	Average concentration
C_{max}	Maximum observed concentration
C_{min}	Minimum observed concentration in the dosing interval
C_{last}	Last quantifiable concentration at t_{last}
CCI	
CeD	Celiac Disease
CI	Confidence interval
CL	Clearance following IV administration
CRF	Case Report Form

Abbreviation / Acronym	Definition
CS	Clinically significant
CSBM	Complete spontaneous bowel movement
CSP	Clinical Study Protocol
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
CV	Coefficient of Variation
DBL	Database Lock
DGP	Deamidated gliadin peptides
DLT	Dose-limiting toxicity
DN	Dose Normalized
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
CCI	[redacted]
EOS	End-of-Study
ET	Early Termination
FIH	First-In-Human
GC	Gluten challenge
GFD	Gluten-free Diet
GI	Gastrointestinal
GLP	Good Laboratory Practice
HBV	Hepatitis B
HCV	Hepatitis C
HIV	Human immunodeficiency virus
ICF	Informed Consent Form
ICH	International Council for Harmonisation
CCI	[redacted]
IV	Intravenous
MAD	Multiple Ascending Dose
MedDRA	Medical Dictionary for Regulatory Activities

Abbreviation / Acronym	Definition
NA	Not Available
NCS	Not Clinically Significant
NK	Not Known
CCI	
PD	Pharmacodynamic
CCI	
PE	Physical exam
PK	Pharmacokinetic
PKAS	Pharmacokinetic Analysis Set
PLT	Platelet
PO	Protein orally
PT	Preferred term
PTF	Peak Trough Fluctuation
R_{ac}	Accumulation ratio
SAD	Single Ascending Dose
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SBP	Systolic Blood Pressure
SD	Standard Deviation
SE	Standard Error of Mean
SMC	Safety Monitoring Committee
SOC	System Organ Class
SoA	Schedule of Assessments
$t_{½}$	Terminal elimination half-life
t_{last}	Time of last quantifiable concentration
TEAE	Treatment-Emergent Adverse Event
TESAE	Treatment-Emergent Serious Adverse Event
TLF	Tables, Listings and Figures
t_{max}	Time corresponding to occurrence of C_{max}

Abbreviation / Acronym	Definition
TTG	Tissue transglutaminase
V_z	Volume of distribution during terminal phase
WBC	White blood cell
WCBP	Women of child-bearing potential
WHO-DD	World Health Organization - Drug Dictionary
λ_z	Terminal elimination rate constant

1 INTRODUCTION

Study KAN-101-01 is a two-part, multicenter Phase 1, First-In-Human (FIH) study designed to evaluate the initial safety, tolerability, and activity of KAN-101 in patients with celiac disease (CeD) on a gluten-free diet (GFD). The two parts include: Part A – FIH single ascending dose (SAD) and Part B – Randomized, placebo (PBO)-controlled, double-blind, multiple ascending dose (MAD).

The initial starting dose of KAN-101 in KAN-101-01 Protocol version 2.0 was 1.5 mg/kg, a dose level consistent with an expected efficacious dose and supported by findings from the Good Laboratory Practice (GLP) toxicology studies. Due to non-serious adverse events consistent with gluten ingestion in celiac patients observed in only one patient at the 1.5 mg/kg dose level, the protocol was amended to start at the dose of 0.15 mg/kg, 10-fold lower than the dose which induced symptoms.

This Statistical Analysis Plan (SAP) details the statistical methodology to be used in analyzing study data and provides information on Tables, Listings and Figures (TLFs). It describes the study endpoints, variables and populations, derived variables, anticipated data transformations and manipulations, and other details of the analyses not provided in the Clinical Study Protocol (CSP).

The analyses described are based on the clinical study protocol for study number KAN-101-01 Version 7.0 (29 Mar 2021) and Blank CRF Casebook (eCRF) Version 5.0 (23 April 2021). This SAP was developed in accordance with ICH E9 guideline. All decisions regarding statistical analysis, as defined in this SAP document, will be made prior to study database lock (DBL) and describes the statistical analysis as it is foreseen when the study is being planned. The reader of this SAP should also read the clinical protocol, and other relevant documents for details on the planned conduct of this study.

2 STUDY OBJECTIVES

2.1 Primary Objective (Part A and Part B)

- Assess the safety and tolerability of escalating doses of KAN-101 in patients with CeD.

2.2 Secondary Objective (Part A and Part B)

- Assess the pharmacokinetic (PK) of KAN-101 after single and multiple doses of KAN-101 in patients with CeD.

2.3 Exploratory Objectives (Part B only)

CCI

3 INVESTIGATIONAL PLAN

3.1 Overall Study Design and Plan

Study KAN-101-01 is a Phase 1, FIH study designed to evaluate the initial safety, tolerability, and activity of KAN-101 in patients with CeD on a GFD. As this is the first instance of KAN-101 administration to humans, safety, tolerability and PK will be evaluated in an escalating

dose paradigm starting with low doses and escalating to higher doses after careful review of all available data. The study is divided into two parts:

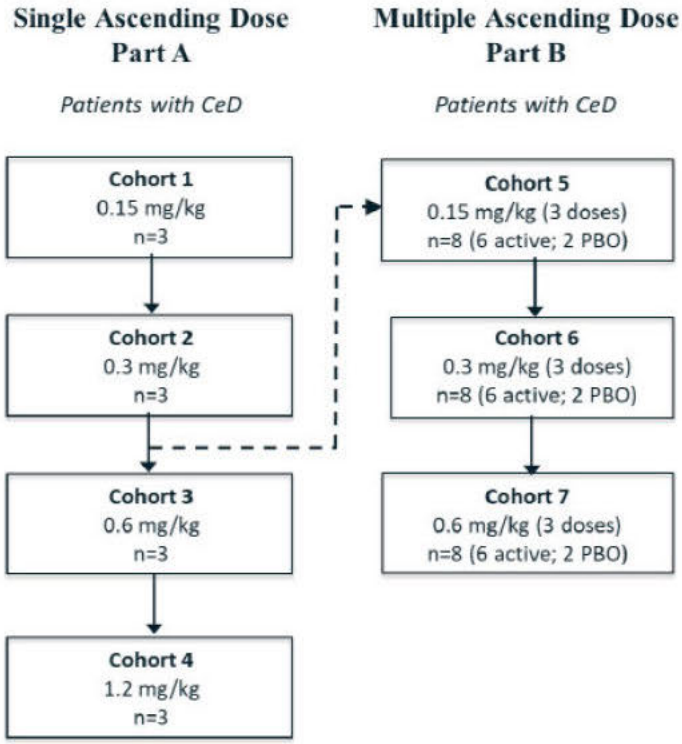
- Part A: Single ascending doses (SAD) in CeD patients (18-70 years).
- Part B: Multiple ascending doses (MAD) in CeD patients (18-70 years).

An overview of the 2 parts and proposed dose groups is presented in Figure 1.

All cohorts in of the study will employ sentinel dosing. Part A employs a SAD 3+3 design, in which patients will receive a single IV infusion of KAN-101. Part B employs a randomized, double-blind multiple ascending dose (MAD) design, in which 3 cohorts of patients will be assigned 3:1 to either KAN-101 or matching placebo (PBO). Patients in Part B will receive an IV infusion of KAN-101 or PBO on D1, D4, and D7. To assess the PD effects of KAN-101, on D15 of Part B patients will begin a 3-day, self-administered high-dose (9 g of gluten protein) oral GC. For the GC, patients will self-administer 9 g of gluten protein orally (PO) on D15, D16, and D17, at approximately the same time each day. CCI [redacted]

The Safety Monitoring Committee (SMC) will recommend all dose escalation decisions, and/or any changes to the dosing paradigm based on the review of all accumulated and available data, including safety and PK as per SMC Charter. Individual and cohort stopping rules will be followed as per Protocol section 4.9.

Figure 1: Study Schematic and KAN-101 Treatment Schema



3.2 Sample Size

Under traditional 3+3 design model, Part A may enroll between 12 and 24 patients across 4 dose cohorts (3 or 6 active patients per cohort), depending upon what toxicities are observed. No formal hypothesis testing is planned for Part A. In Part B, the total sample size of 24 patients (n=18 KAN-101; n=6 PBO) across 3 dose cohorts (6 active and 2 PBO patients per cohort) was chosen to allow for a comparison of safety, PK, and PD between KAN-101 and PBO. A sample size of 6 active patients per cohort in Part B allows for an 0.80 power to detect a treatment-related AE occurring at an event rate of 0.25.

Patients in Part A may be replaced if they do not receive the full dose of study drug or do not complete the D8 visit, as long as the discontinuation was not due to a DLT assessed to be related to study drug.

Patients in Part B may be replaced if they do not receive the full 3 doses of study drug or do not complete the D21 visit, as long as the discontinuation was not due to a DLT assessed to be related to study drug.

3.3 Assignment to Cohort

Once a patient has met all entry criteria they will be enrolled in the study. In Part A, patients will be assigned to receive open-label KAN-101 at a dose level based on the next available spot in the cohort(s) currently being enrolled. In Part B, the first 2 eligible patients within each cohort will be randomized in a 1:1 ratio to receive either KAN-101 or PBO. After completion of the sentinel dosing, the remaining 6 patients in each cohort will be randomized 5:1 to receive KAN-101 or PBO.

3.4 Endpoints

3.4.1 Primary Endpoints (Part A and Part B)

Incidence and severity of treatment-emergent adverse events (TEAEs) as assessed by the Common Terminology Criteria for Adverse Events (CTCAE) v5.0 or higher.

3.4.2 Secondary Endpoints (Part A and Part B)

Plasma concentrations and PK parameters of KAN-101.

3.4.3 Exploratory Endpoints (Part B only)

CCI

3.5 Assessments

3.5.1 Safety Assessments

Safety and tolerability of KAN-101 will be assessed by AE and other safety assessments as detailed in Appendix 6.1 Table 8 (Part A) and Table 9 (Part B). All patients in Part A will have

a final Follow-Up at D21 (±1), 20 days after the single administration of KAN-101. All patients in Part B will have a final Follow-Up phone call at D28 (±3), approximately 20 days after the final administration of KAN-101 on D7.

3.5.1.1 Adverse Events (AE)

All AEs from the time of signing of Informed Consent Form (ICF) through the final Follow-Up Visit/phone call will be collected. Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) Version 23.1 (MedDRA Sep 2020) or higher. Ongoing AEs considered at least possibly related to KAN-101 treatment should be followed until resolution, return to baseline, or are considered stable or chronic.

AE:

An AE is defined as any untoward medical occurrence associated with the use of a drug, or with study participation, whether or not consider related to study treatment.

TEAE:

TEAEs are defined as AEs that emerge or worsen in the period from the first dose of study treatment to the final Follow-Up Visit/phone call after the last dose study drug.

The incidence and severity of TEAEs as assessed by the CTCAE v5.0 or higher is considered the primary endpoint. TEAEs that occur before and after gluten challenge will also be examined separately and defined as in section 4.8.1.

DLT:

A dose-limiting toxicity (DLT) for Study KAN-101-01 is defined as any ≥ Grade 3 AE assessed as related to KAN-101 or Grade 2 AE assessed as related to KAN-101 not resolving within 14 days. DLTs do not include those AEs attributable solely to intercurrent illness or other concomitant medications.

AE Severity:

The National Cancer Institute Common Toxicity Criteria Adverse Event (NCI-CTCAE) version 5.0 or higher will be used to grade the severity of all AEs, whether or not they are considered related to KAN-101. Toxicities that are not specified in the NCI-CTCAE will be defined as follows:

- 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 activities of daily living (ADL)
- Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL
- Grade 4: Life-threatening consequences; urgent intervention indicated
- Grade 5: Death related to AE

AE Causality:

Relationship to the study drug for all AEs will be assessed as “drug related” (Possible, Probable, Definite) or “not drug related” (None, Remote).

Impact of COVID-19:

Pandemic related Impact of COVID-19 data will be assessed, detailing the category of impact (example: Missed Visit, Missed Assessment, Early termination, Screen Failure, Adverse Event, Withdrawal of consent, Death, Replacement subject) based on data collection.

3.5.1.2 Other Safety Assessments

Additionally, safety will be also be examined by the following assessments:

- Clinical laboratory evaluations
- Physical examination
- Vital signs
- Prior and concomitant medications and procedures
- Incidental gluten exposure
- Medications for infusion reactions
- Study drug administration

3.5.1.2.1 Clinical Laboratory Evaluation

All statistical analyses of laboratory values will be performed using International System units. The Clinical laboratory parameters and tests to be analyzed locally or centrally by a certified laboratory with corresponding laboratory normal ranges are:

- Serum Chemistry: Blood urea nitrogen, creatinine, glucose, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), bilirubin (total and direct), electrolytes (sodium, chloride, bicarbonate, potassium), amylase, lipase, albumin, magnesium, calcium, and phosphorus
- Hematology: White blood cell (WBC) count, hemoglobin, hematocrit, Platelet (PLT) count, and WBC differential
- Coagulation: Prothrombin time, partial thromboplastin time or activated partial thromboplastin time, and international normalized ratio
- Complete urinalysis with qualitative analysis for protein (dipstick)
- Virus Serology: Human immunodeficiency virus (HIV), hepatitis B (HBV) (HBsAg, anti-HBc and anti-HBs), and hepatitis C (HCV) testing (Screening only)
- Serum pregnancy test will be performed at screening for women of child-bearing potential (WCBP). Serum or urine pregnancy testing for all WCBP will be performed prior to each dose.

The following laboratory tests will be performed centrally at Screening only:

- HLA DQ2.5 and HLA DQ8 testing
- Transglutaminase (tTG) and deaminated gluten peptides (DGP) IgA/IgG

For tTG, a result of <2xULN will be considered negative or weak positive. For DGP, a result of <30 U/mL will be considered negative or weak positive.

For re-screening, the HLA does not need to be repeated and the tTG and DGP antibody tests should only be repeated if >3months have elapsed from end assessment.

Unscheduled assessments should be performed as clinically indicated. For any out-of-range laboratory findings during screening, repeat laboratory testing may be performed at the discretion of the Investigator. Abnormal laboratory findings at screening should be recorded as medical history only if considered clinically significant (CS).

Investigators will assess whether the values outside the clinical reference range are clinically significant and these will be reported as abnormal NCS or abnormal CS.

- Clinically significant abnormal laboratory values will be recorded by the Investigator as AEs.
- The abnormal values will be flagged with 'LOW' for values below the lower limit of the local clinical reference range and 'HIGH' for values above the upper limit of the local clinical reference range and included in the listings.

3.5.1.2.2 Physical Examination

The physical exam (PE) will be conducted at Screening and as clinically indicated, including for early terminated subjects. The PE includes an assessment of general appearance, skin, head, neck, throat, lymph nodes, cardiovascular, neurological, thyroid, musculoskeletal / extremities, respiratory, abdomen, height (screening only) and weight (screening only).

3.5.1.2.3 Vital Signs

Vital signs will include temperature, pulse rate and blood pressure (BP) (sitting for 5 minutes). If vital signs need to be repeated during a single visit, assessments should be conducted approximately 5 minutes apart.

Any new CS change from baseline should be recorded as an AE.

3.5.1.2.4 ECG

All electrocardiograms (ECGs) will be standard resting 12-lead ECGs performed after the patient has been supine for at least 5 minutes. ECG data will be presented.

3.5.1.2.5 Prior and Concomitant Medications and Procedures

At screening, concomitant medications will be recorded. Assessment of any change in concomitant medications, or procedures since the last visit will occur at all further patient visits through the final Follow-Up Visit. Concomitant medications will be coded using the World Health Organization Drug Dictionary drug (WHO Drug Global Sep 2019) and will be presented by WHO-DD Anatomical Therapeutic Chemical (ATC) therapeutic Level 4 classification and preferred term (PT). Below rules will be applied to decide if the medications and procedures are prior, concomitant or both.

- Medications that start and stop prior to the first dose of study medication will be classified as prior only.
- If a medication starts before the date of first dose of study medication and stops on or after the date of first dose of study medication, then the medication will be classified as both prior and concomitant.
- Medications will be classified as concomitant only if they have a start date on or after the first dose of study medication.
- If medication start and/or stop dates are missing or partial, the dates will be imputed (section 4.4.3.2).
    - Medications will be assumed to be concomitant only, unless there is clear evidence (through comparison of partial dates) to suggest that the medication started prior to the single dose of study medication.

- If there is clear evidence to suggest that the medication started prior to the single dose of study medication, the medication will be assumed to be both prior and concomitant, unless there is clear evidence to suggest that the medication stopped prior to the single dose of study medication.
- If there is clear evidence to suggest that the medication stopped prior to the single dose of study medication, the medication will be assumed to be prior only.

3.5.1.2.6 Incidental Gluten Exposure

Assessment (date and source) of any incidental gluten exposure will be captured at all study visits.

3.5.1.2.7 Medications for Infusion Reactions

Details of medications to treat infusion reactions will be collected at all study visits.

3.5.1.2.8 Study Drug Administration

Weight of the IV bag/line, dates and times will be captured for each infusion of the study drug. Study drug infusion details will also include whether the infusion was interrupted or re-started along with the reasons for the interruption (for more administration instructions refer KAN-101-01 Pharmacy Manual).

3.5.2 Pharmacokinetic Assessments

For the secondary endpoint, blood samples will be collected for measurement of KAN-101, as specified in Appendix 6.1 Table 8 (Part A) and Table 9 (Part B). The timing of sampling may be altered based on the emerging PK data, and appropriately documented in database. PK concentrations data along with dosing data will be used to determine the PK parameters.

PK parameters will be calculated relative to start of the infusion (approximate duration 30 minutes), hence nominal time will be calculated in hours relative to start of infusion (in ADPC) for PK parameter summarization and determination of deviations from actual time of sample collection, e.g. end of infusion sample, 0 (+2) min, will be considered 0.5 h sample, 7 (±2) min will be considered 0.62 h sample etc.

For Part A, PK parameters as outlined in Table 1 will be determined for KAN-101 following single dose administration.

For Part B, PK parameters as outlined in Table 2 will be determined for KAN-101 following multiple dose administration.

For non-compartmental analysis, actual sampling times relative to dosing rather than nominal times will be used in the calculation of all derived pharmacokinetic parameters, except when parameters are calculated for safety/dose escalation meetings when nominal times may be used to calculate PK parameters.

Table 1: Pharmacokinetic Parameters after Single Dose Administration (Part A) and after First Dose Administration (Part B)

Parameter	Definition	Method of Determination
C_{max}	Maximum observed plasma concentration	Obtained directly from the concentration-time data

Parameter	Definition	Method of Determination
DNC_{max}	Dose-normalized C_{max}	Obtained by dividing C_{max} by total dose administered in mg (scheduled dose will be used e.g. if dose level is 0.3 mg/kg and is subject weight is 50 kg, then dose administered will be 15 mg, DNC_{max} will be C_{max} divided by 15.
t_{max}	Time to first occurrence of C_{max}	Obtained directly from the concentration-time data
λ_z	Terminal elimination rate constant	Terminal phase rate constant calculated by linear regression of the log-linear concentration-time curve. Only those data points judged to describe the terminal log-linear decline will be used in the regression. • A minimum number of three data points in the terminal phase will be used in calculating λ_z with the line of regression starting at any post-C_{max} data point (C_{max} should not be part of the regression slope) and including C_{last}, t_{last}. • The adjusted correlation coefficient (R^2 adjusted) in general should be greater than 0.90. Any value less than 0.90 may be used at the PK Scientist's best knowledge and judgment. • An appropriate number of decimal places should be used for λ_z to enable the reported value of $t_{½}$ to be calculated.
$t_{1/2}$	Terminal elimination half-life	$Log_e(2)/ \lambda_z$
AUC_{0-t}	AUC from time zero to the last quantifiable concentration	The linear-log trapezoidal method will be employed to calculate AUCs. The linear method will be used for all incremental trapezoids arising from increasing concentrations and the logarithmic trapezoidal method will be used for those arising from decreasing concentrations. $AUC_{0-t} = \int_0^t \mathbf{C(t)dt}$.
$DNAUC_{0-t}$	Dose normalized AUC_{0-t}	Obtained by dividing AUC_{0-t} by total dose administered in mg (scheduled dose will be used e.g. if dose level is 0.3 mg/kg and is subject weight is 50 kg, then dose administered will be 15 mg, $DNAUC_{0-t}$ will be AUC_{0-t} divided by 15.
AUC_{0-inf}	AUC from time zero extrapolated to infinity	$AUC_{0-inf} = \int_0^t \mathbf{C(t)dt} + \int_t^\infty \mathbf{C(t)dt} = AUC_{0-t} + C_{last}/\lambda_z$, where C_{last} is last observed quantifiable concentration.
$DNAUC_{0-inf}$	Dose normalized AUC_{0-inf}	Obtained by dividing AUC_{0-inf} by total dose administered in mg (scheduled dose will be used e.g. if dose level is 0.3 mg/kg and is subject weight is 50 kg, then dose administered will be 15 mg, $DNAUC_{0-inf}$ will be AUC_{0-inf} divided by 15.
$\%AUC_{ex}$	Percentage of $AUC_{(0-inf)}$ obtained by extrapolation	$(1 - [AUC_{0-t}/AUC_{0-inf}]) \times 100$

Parameter	Definition	Method of Determination
CL	Clearance following intravenous administration	dose/$AUC_{0\text{-}inf}$
V_z	Volume of distribution during terminal phase	$CL/F/\lambda_z$

Table 2: Pharmacokinetic Parameters on Day 7 after Multiple Dose Administration (Part B)

Parameter	Definition	Method of Determination
C_{max}	Maximum observed concentration	Obtained directly from the concentration-time data
DNC_{max}	Dose normalized C_{max}	Obtained by dividing C_{max} by total dose administered in mg (scheduled dose will be used e.g. if dose level is 0.3 mg/kg and is subject weight is 50 kg, then dose administered will be 15 mg, DNC_{max} will be C_{max} divided by 15.
C_{min}	Minimum observed concentration	Obtained directly from the concentration-time data
t_{max}	Time corresponding to occurrence of C_{max}	Obtained directly from the concentration-time data
λz	Terminal elimination rate constant	Terminal phase rate constant calculated by linear regression of the log-linear concentration-time curve. Only those data points judged to describe the terminal log-linear decline will be used in the regression. A minimum number of three data points in the terminal phase will be used in calculating λz with the line of regression starting at any post- C_{max} data point (C_{max} should not be part of the regression slope) and include C_{last}, t_{last}. The adjusted correlation coefficient (R^2 adj) in general should be greater than 0.90. Any value less than 0.90 may be used at the PK Scientist's best knowledge and judgment. An appropriate number of decimal places should be used for λz to enable the reported value of t½ to be calculated.
t½	Terminal elimination half-life	Loge(2)/ λz
$AUC_{0\text{-}t}$	AUC from time zero to the last quantifiable concentration	The linear-log trapezoidal method will be employed to calculate AUCs. The linear method will be used for all incremental trapezoids arising from increasing concentrations and the logarithmic trapezoidal method will be used for those arising from decreasing concentrations. $AUC_{0\text{-}t} = \int_0^t \mathbf{C(t)dt}$.

Parameter	Definition	Method of Determination
$DNAUC_{0-t}$	Dose normalized AUC_{0-t}	Obtained by dividing AUC_{0-t} by total dose administered in mg (scheduled dose will be used e.g. if dose level is 0.3 mg/kg and is subject weight is 50 kg, then dose administered will be 15 mg, $DNAUC_{0-t}$ will be AUC_{0-t} divided by 15.
AUC_{0-inf}	AUC from time zero extrapolated to infinity	$AUC_{0-inf} = \int_0^t C(t)dt + \int_t^\infty C(t)dt = AUC_{0-t} + C_{last}/\lambda_z$, where C_{last} is last observed quantifiable concentration.
$DNAUC_{0-inf}$	Dose normalized AUC_{0-inf}	Obtained by dividing AUC_{0-inf} by total dose administered in mg (scheduled dose will be used e.g. if dose level is 0.3 mg/kg and is subject weight is 50 kg, then dose administered will be 15 mg, $DNAUC_{0-inf}$ will be AUC_{0-inf} divided by 15.
$\%AUC_{ex}$	Percentage of $AUC_{(0-inf)}$ obtained by extrapolation	(1－[AUC0-t/AUC0-inf])×100
$AUC_{0-\tau}$	AUC over the dosing interval	Linear-log trapezoidal method; all incremental trapezoids arising from increasing concentrations and the logarithmic trapezoidal method will be used for those arising from decreasing concentrations.
$DNAUC_{0-\tau}$	Dose normalized AUC_0-τ	Obtained by dividing AUC_0-τ by total dose administered in mg (scheduled dose will be used e.g. if dose level is 0.3 mg/kg and is subject weight is 50 kg, then dose administered will be 15 mg, $DNAUC_{0-\tau}$ will be $AUC_{0-\tau}$ divided by 15.
CL	Clearance following intravenous administration	dose/AUC_0-τ
V_z	Volume of distribution during terminal phase	CL/F/λz
C_{av}	Average concentration	$AUC_{0-\tau/\tau}$
PTF	Peak trough fluctuation	(Mean C_{max}) / (Mean C_{min})
Rac	Accumulation ratio	Calculated from $AUC_{0-}\tau$ and $AUC_{0-}\tau$ after first dose of the multiple dosing regimen
L	Linearity index	Calculated from $AUC_{0-}\tau$ and AUC_{0-inf} after first dose of the multiple dosing regimen

Day 7 parameters will be calculated relative to that day's dosing. The value of τ will be 72 hours since dosing in Part B is 3 days apart. All above parameters will be calculated but only relevant parameters will be reported in tables, figures and listings, as per the PK scientist's evaluation of the parameters.

Following single or multiple dose administration, other PK parameters, e.g. t_{last} and partial area under the curve may be derived, if needed, but may not be reported.

3.5.3 Immunogenicity Assessments

Anti-drug antibody (ADA) sampling will be performed at the time points shown in Appendix 6.1 Table 8 (Part A) and Table 9 (Part B). ADA-positive or ADA-negative will be determined for each time point. If the first test comes back positive then the reactivity to the CCI

CCI will be assessed separately. Titers will be determined for ADA positive sample if the quantity is sufficient for the determination. If Screening tier is Negative then ADA response is Negative at the corresponding visit. If Screening tier is Positive then ADA response is Confirmatory Tier response (Positive, Negative or QNS (quantity not sufficient) at the corresponding visit.

3.5.4 Pharmacodynamic Assessments

CCI

3.5.5 Other Assessments

3.5.5.1 Informed Consent

An ICF must be signed by prospective patients prior to initiating any study-specific procedures.

3.5.5.2 Inclusion and Exclusion Criteria

Inclusion and exclusion criteria will be reviewed for each potential patient. Eligibility will be documented in the eCRF (for more information refer Protocol section 5).

3.5.5.3 Demographics, Celiac Disease History and Medical History

Complete medical history will be obtained, including demographics, symptoms at diagnosis, disease history, and length of time on a GFD.

3.5.5.4 C

CCI

[redacted]

3.5.5.5 GC (Part B only) Administration

Dates and times will be captured for GC administration on D15, D16, and D17. Patient compliance will be recorded by the study Investigator.

4 STATISTICAL METHODS

The following treatment groups will be considered for reporting for each part, except for PK reporting:

<u>Part A (SAD)</u>

- KAN-101 0.15 mg/kg
- KAN-101 0.30 mg/kg
- KAN-101 0.60 mg/kg
- KAN-101 1.20 mg/kg
- KAN-101 1.5 mg/kg
- Pooled KAN-101

<u>Part B (MAD)</u>

- Pooled Placebo
- KAN-101 0.15 mg/kg
- KAN-101 0.30 mg/kg
- KAN-101 0.60 mg/kg
- Pooled KAN-101

All summary tables will be presented for Part A and Part B separately (unless otherwise specified). Also, summary tables will be presented for Part A and Part B combined for the same dose level treatment group for the following:

- PK data: PK concentrations and parameters for Day 1 in 0.15, 0.30, and 0.60 mg/kg dose levels will be summarized using descriptive statistics
- Disposition, analysis population, demographics, baseline celiac disease, ADA, and Treatment-Emergent Serious Adverse Events (TESAEs).

Listings will be presented for subjects from Part A and Part B to display the collected data of clinical and statistical importance. All by-subject listings will include part, treatment group,

center, and subject ID for enrolled subjects. All TLFs will be analyzed by dose level received and not by cohort number.

The principal of 'As Treated' (as dose level received) will be applied to the subject treatment data. If there are randomization or cohort assignment errors they will still be analyzed in the treatment group of the dose level they received. If the actual dose level received is unknown then the subject will be analyzed under the planned dose level, however for PK TFLs, the concentrations and parameters from such subject/s will be listed and flagged in the Listings, but excluded from summary tables and statistical analysis, since these are not pharmacokinetically meaningful if the dose is unknown.

4.1 Data Quality Assurance

All TLFs data to be included in the report will be independently checked for consistency, integrity and in accordance with standard Parexel procedures. Datasets will be prepared using headings from Clinical Data Interchange Consortium (CDISC) Study Data Tabulation Model (SDTM) implementation for human clinical trials and Analysis Dataset Model.

4.2 Changes in the SAP Compared to the Study Protocol

No changes.

4.3 General Presentation Considerations and Descriptive Statistics

No formal statistical hypotheses or inferential statistics will be performed in this study. For Part A and Part B, summary statistics and listings will be provided by dose.

All by-visit summaries will be based on the nominal day/time per Appendix 6.1 Table 8 (Part A) and Table 9 (Part B) as recorded on the eCRF.

Study day will be calculated relative to the date of first dose, 'Study Day' = Assessment Date – First Dose Date + 1.

4.3.1 Non-PK Tables, Listings and Figures

- 'Baseline' is defined as the last available pre-treatment assessment, including any unscheduled assessment. Every effort will be made to ensure that accurate baseline information is collected. Subjects will not be excluded from any of the analysis populations due to missing baseline. However, if a subject is missing baseline information, they will have a missing change from baseline result.
- Continuous data will be summarized in terms of the number of observations (n), mean (arithmetic), standard deviation (SD), median, and range (minimum and maximum), unless otherwise stated.
- The minimum and maximum will be reported to the same number of decimal places as the raw data recorded in the database. The mean and median will be reported to one more decimal place than the raw data recorded in the database. The SD will be reported to two more decimal places than the raw data recorded in the database. In general, the maximum number of decimal places reported shall be four for any summary statistic.
- Categorical data will be summarized in terms of the number of subjects providing data at the relevant time point (n), frequency counts and percentages.

- Percentages will be rounded to the nearest one decimal place. Percentages will not be presented for zero counts. Percentages will generally be calculated using the number of subjects in a group (n) as the denominator, otherwise the method will be noted in a footnote.
- Unscheduled and early termination visits may not be summarized in the tables but will be presented in the listings.

4.3.2 PK Tables, Listings and Figures

The following rules will be followed with regards to the number of decimal places and presentation of data in the tables and listings for PK concentration data:

- Source data shall be used in all derived PK concentrations without prior rounding.
- The mean, SD, geometric mean and median will be tabulated to same significant digit compared to the source data, but with a maximum of four significant digits.
- Minimum and maximum values will be tabulated to the same precision as the source data, but with a maximum of four significant digits.
- Geometric coefficient of variation (geometric CV%) and arithmetic coefficient of variation (CV%) will be presented to one decimal place.

The following rules will be followed with regards to the number of decimal places and presentation of data in the tables and listings for PK parameters:

- Individual PK parameters will be presented to three significant digits, with the exception of t_{max}, which will be presented to three decimal places.
- Parameters derived directly from source data (e.g. C_{max}) shall be reported with the same precision as the source data (if this is not four significant digits).
- The mean, geometric mean, median and SD values will be reported to three significant digits, all other descriptive statistics will also be reported to three significant digits except for CV% and geometric CV% which will be presented to one decimal place.
- For t_{max}, the minimum and maximum will be presented to three decimals places and all other descriptive statistics will be presented to three decimal places.
- Estimates and confidence intervals in the form of percentages will be presented to two decimal places.

4.4 Analysis and Data Handling Conventions

4.4.1 Multi-center Studies

The term ‘Center’ will be used to define each investigator site. The data from all study centers (approximately 5 to 12 US sites) will be pooled together for analyses and summary statistics.

4.4.2 Adjustments for Covariates

No adjustments for covariates are planned for the study.

4.4.3 Handling of Dropouts or Missing Data

All missing or partial data will be presented in the patient data listing, as they are recorded on the eCRF. Patients lost to follow-up or withdrawn will be included in statistical analyses up to the point of their last evaluation.

4.4.3.1 Missing Start and Stop Dates/Time for Adverse Events

Due diligence will be done to obtain accurate AE information. If all planned methods to obtain accurate time AE information have failed, missing and partial AE onset and end dates will be imputed. Imputed dates will be flagged in the individual supportive subject listings. Unless otherwise specified, the following conventions will be used:

Missing and Partial AE onset dates:

- If onset date is completely missing, then onset date is set to date of first dose.
- If onset year is present and

  - month and day are missing:
    - If onset year = year of first dose, then set onset date to date of first dose.
    - If onset year < year of first dose, then set onset month and day to December 31st.
    - If onset year > year of first dose, then set onset month and day to January 1st.

  - month is missing:
    - If onset year = year of first dose, then set onset date to date of first dose.
    - If onset year < year of first dose, then set onset month to December.
    - If onset year > year of first dose, then set onset month to January.

- If onset month and year are present and day is missing:

  - If onset year = year of first dose and
    - onset month = month of first dose then set onset date to date of first dose.
    - onset month < month of first dose then set onset date to last day of month.
    - onset month > month of first dose then set onset date to 1st day of month.

  - If onset year < year of first dose, then set onset date to last day of month.

  - If onset year > year of first dose, then set onset date to 1st day of month.

- For all other cases, set onset date to date of first dose.

Missing and Partial AE end dates:

- If end date is completely missing, end date is not imputed and the AE is flagged as "ongoing".
- If year is present and

  - month and day are missing:
    - If year = year of last dose, then set end date to the date of last dose.
    - If year < year of last dose, then set end month and day to December 31st.
    - If year > year of last dose, then set end month and day to January 1st.

  - month is missing:
    - If year = year of last dose, then set end date to date of last dose.
    - If year < year of last dose, then set end month to December.
    - If year > year of last dose, then set end month to January.

- If month and year are present and day is missing:

  - If year = year of last dose and

    - month = month of last dose then set day to day of last dose.
    - month < month of last dose then set day to last day of month.
    - month > month of last dose then set day to 1st day of month.

  - If year < year of last dose, then set end date to last day of the month.

  - If year > year of last dose, then set end date to 1st day of month.

- For all other cases, set end date to date of last dose.
- Screen failures are collected in EDC and will be a part of SDTM. Screen failure data are not analyzed and will not be included in the ADaM except for demographics (ADSL) and inclusion/exclusion criteria (ADIE).

Any AEs with incomplete start and end dates/times will be treated as follows:

- Adverse events with unknown start and/or end times (but where the date is known) will be imputed with a time of 00:00 h for the tabulations but will be shown as NK: NK in the listings (where NK = Not Known).

4.4.3.2 Missing Start and Stop Dates for Prior and Concomitant Medication

For the purpose of inclusion in prior and/or concomitant medication tables, incomplete medication starts and stop dates will be imputed as follows:

- If year and month are present and day is missing, then set day to first day of month for start date and set day to last day of month for end date.
- If year and day are present and month is missing, then set month to January for start date, and set month to December for end date.
- If year is present and month and day are missing, then set month and day to January 1 for start date and set month and day to December 31 for end date.
- Completely missing date will not be imputed.

The partial dates will be provided as such in the subject data listings (with the imputed dates).

When imputing a start date, the programmer will ensure that the new imputed date is sensible i.e. it is before the end date of prior and concomitant medications.

4.4.3.3 [redacted]

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4.4.4 Concentrations Below the Limit of Quantification (BLQ)

For PK data, all concentrations that are BLQ will be labeled as "BLQ" in the concentration data listings (Footnote describing the BLQ value will be added to the listing).

For summary: For concentration summary tables and mean concentration time plots, all BLQs will be considered zero, and the number of BLQs and non-BLQs at each scheduled time point will be reported.

For individual data: For non-compartmental PK analysis, all below the limit of quantification (BLQ) values pre-dose to the first dose, and prior to the first quantifiable concentration will be substituted by zeros. BLQ values between non-BLQ concentrations will be considered missing before the calculation of the PK variables. Terminal BLQ values will be considered missing.

4.4.5 Adjustment for Multiplicity

No formal multiple statistical analyses are planned. Hence no adjustments for multiplicity are required.

4.4.6 Interim Analyses

No formal interim analyses are planned.

4.4.7 Unblinding

Part A is open-label.

Part B is double-blinded, such that study personnel (e.g., Investigators, site coordinators) and patients are blinded to treatment assignments and will remain blinded throughout the study.

Unblinded personnel include those involved in drug preparation and allocation (e.g., data systems support and pharmacists), and the study pharmacokineticist to allow for expedited review of PK data prior to SMC review.

The data for dose escalation in Part B will be presented and reviewed by the SMC in a blinded fashion. If required SMC will be unblinded as per SMC Charter and Blinded Maintenance Plan for Part B.

After completion of SMC review and once all patients in the cohort have completed the study, the sponsor study team members involved in biomarker data analysis may be unblinded to complete pharmacodynamic assessments as per Protocol section 4.4.

4.4.8 Final Analysis

The final analysis of the study data will be conducted once the last remaining patient has completed the study or is withdrawn from the study prior to completion, all data have been entered into the database, all data issues resolved, the protocol deviations have been addressed, and the database has been locked and released.

4.5 Software

All report outputs (tables, figures and listings) will be produced using SAS® version 9.4 or a later version in a secure and validated environment [1].

Non-compartmental PK analyses will be produced using Phoenix® WinNonLin (WNL) version [8.0] or a later version in a secure and validated environment [1].

All report outputs will be provided to the Sponsor in RTF and PDF format. Outputs will be printed in 8pt font size and Courier New font type.

4.6 Analysis Sets

Data for all subjects will be assessed to determine if subjects meet the criteria for inclusion in each analysis population in Table 3. These analysis sets will be used to present the TLFs.

Table 3: Analysis Sets

Population	Description
All Treated Analysis Set (ATAS)	All patients who received any amount of study drug with treatment group based on the dose level received.
Pharmacokinetic Analysis Set (PKAS)	All patients who received at least one dose of KAN-101 and have at least one drug concentration value.
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The screened subjects are subjects who signed the ICF (including Screening failures). Enrolled subjects are the subjects who were enrolled in Part A or randomized for Part B and were not screen failures. PKAS and CCI are subsets of ATAS. PK analysis will be done on the PKAS CCI

For Part A and Part B (separately and combined), summary tables will be provided by treatment group for analysis population shown in Table 3 on enrolled subjects.

A by-subject listing will be provided by study part and treatment group for analysis population on enrolled subjects, unless otherwise specified in the table shells document.

4.7 Protocol Deviations

Protocol deviations are documented when the study protocol is not followed. Deviations from the protocol including violations of inclusion/exclusion criteria will be assessed as 'minor' or 'major.' Major protocol deviations are defined as those deviations from the protocol that are likely to have an impact on the subject's right, safety, well-being, and/or the validity of the data for analysis. Minor deviations include all deviations from the protocol excluding those considered as major. Suggested Major/Minor protocol deviations are defined in study specific Protocol Deviation Specification.

All protocol deviations will be discussed during the Blinded Data Review Meeting (BDRM) per the applicable SOP between Parexel and Sponsor. An assessment will be made to determine whether any deviation warrants exclusion of a subject from descriptive statistical analyses. Decisions made regarding the exclusion of subjects and/or subject data from analyses will be documented in BDRM minutes and approved by the Sponsor (for more information on BDRM refer section 4.7.1).

A by-subject listing will be provided by study part and treatment group for protocol deviations along with COVID-19 protocol deviations on enrolled subjects.

4.7.1 Blinded Data Review Meeting (BDRM)

A BDRM will be held after the last subject data is entered into the clinical database (DB) and prior to DBL. The primary purposes of the BDRM are to:

- Confirm that the database is ready to be hard locked.

- Agree on the assignment of each subject to the appropriate analysis sets of the study, if applicable.
- Identify any major/minor protocol deviation to finalize the analyses set.

Results and decisions made during the meeting will be summarized in BDRM minutes which will be signed off by Parexel representatives and the Sponsor.

The PKAS is decided at the PK data review meeting if needed, which occurs after the unblinded PK concentration data is received. For final analysis, the PK TLFs will be generated on the PK dataset created after data unblinding for Part B.

Parexel Protocol Deviation tool will be used to document the deviations.

4.8 Safety Evaluation

All safety summaries and analyses will be on ATAS.

4.8.1 Adverse Events

For Part A (SAD) and Part B (MAD) separately, the following AE summaries will be provided for the number of subjects reporting at least one AE by treatment group using the ATAS:

- An overall summary of TEAE will include the number of subjects with any TEAEs, drug-related TEAEs, ≥ Grade 3 TEAEs, TESAEs, TEAEs leading to discontinuation (treatment and study);
- Before and after GC, overall summary of TEAE will include the number of subjects with any TEAEs, drug-related TEAEs, ≥ Grade 3 TEAEs, treatment-emergent serious AEs (TESAEs), TEAEs leading to discontinuation (treatment and study); (this table is for Part B only);
- A summary of the number and percentage of subjects reporting a TEAE by system organ class (SOC) and PT;
- A summary of the number and percentage of subjects reporting a TEAE by causality, SOC and PT;
- A summary of the number and percentage of subjects reporting a TEAE by severity, SOC and PT.

AE summaries will be ordered in terms of decreasing frequency for SOC, and PT within SOC, in the Total group, and then alphabetically for SOC, and PT within SOC.

For each subject and each AE, the worst severity recorded will be attributed and used in the by-severity summaries. Similarly, the worst causality (most related to treatment) will be attributed and used in the by-causality summaries.

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A summary of TESAE will be presented for Part A and B combined.

For Part A and Part B, by-subject listings of AEs will be presented by study part and treatment group for the following listings:

- All DLT events
- All TEAEs
- All SAEs
- All TESAEs
- TEAEs Leading to Study Discontinuation
- TEAEs Leading to Permanent Discontinuation of Study Drug

The following information will be included in the listings: verbatim (reported term), PT, SOC, AE onset date (and time), AE end date (and time), AE duration, relationship to study drug, AE outcome, severity and SAE indicator flag. If available, confirmed and suspected SARS-CoV-2 infections and/or COVID-19 cases will be recorded in the AE eCRF and data will be presented.

Pandemic related Impact of COVID-19 will be presented in listing, detailing the category of impact (example: Missed Visit, Missed Assessment, Early termination, Screen Failure, Adverse Event, Withdrawal of consent, Death, Replacement subject) based on data availability.

4.8.2 Clinical Laboratory Evaluation

For Part A (SAD) and Part B (MAD) separately, the following clinical laboratory summaries will be provided for serum chemistry, hematology, coagulation and urinalysis (specific gravity and pH only).

- Continuous descriptive statistics of observed values and change from baseline by study visit;
- Summary tables by reference range indicator;
- Shift summary tables by reference range indicator

Unscheduled and early termination visits may not be summarized in the tables but will be presented in the listings.

The following by-subject laboratory listings (values and change from baseline if applicable) will be provided by study part and treatment group using the enrolled subjects:

- Serum Chemistry
- Hematology
- Coagulation
- Urinalysis
- Virus Serology (screening only)
- Serum and Urine Pregnancy test
- HLA DQ2.5 and HLA DQ8 testing (screening only)

- Transglutaminase and deaminated gluten peptides IgA/IgG (screening only)
- Lab abnormality experiencing ≥ Grade 3 in Severity.

Toxicity, in reflection of safety laboratory results will be graded locally according to NCI-CTCAE v5.0 or higher and included in listings. If any laboratory value falls above or below the upper or lower level of quantification, the value of the upper or lower level of quantification will be used.

Protocol doesn't require Urine micro analysis under the microscope for urinalysis, leukocyte count, erythrocyte count, epithelial cell count and bacterial count. So, these parameters will be shown in the listings only.

There are tests with multiple standard units. "Standard-Unit" per test/subject will be taken into consideration in deriving the baseline. Post-baseline records will not have a 'Change' value if the unit doesn't match with baseline record unit for that subject and test.

4.8.3 Physical Examination, Vital Signs and ECG

For Part A (SAD) and Part B (MAD) separately, categorical and continuous descriptive statistics of observed values and change from baseline will be presented for:

- Each vital sign measurement by scheduled study visit and change from baseline.
- Each physical examination measurement by scheduled study visit(Normal, Abnormal, Not done).
- Each ECG measurement by scheduled study visit (Normal, Abnormal Non-Clinically Significant (ANCS), Abnormal Clinically Significant (ACS))

The following by-subject listings will be provided by study part and treatment group on enrolled subjects:

- Vital Signs (values and change from baseline)
- Physical Examination (screening and as clinically indicated)
- ECG

4.8.4 Prior and Concomitant Medications and Procedures

All prior and concomitant medications including dose, form, route of administration, frequency and indication will be provided in a by-subject listing for each study part and treatment group for prior and concomitant medications by ATC Levels and PT on enrolled subjects.

For Part A (SAD) and Part B (MAD) separately, summary tables will be provided by treatment group for prior and concomitant medications by ATC Levels and PT on ATAS.

4.8.5 Incidental Gluten Exposure

A by-subject listing will be provided by study part and treatment group for any incidental gluten exposure (Yes/No) on enrolled subjects. Number of times the subjects is exposed to gluten within the study period will be calculated.

4.8.6 Medications for Infusion Reactions

A by-subject listing will be provided by study part and treatment group for any medications to treat infusion reactions by ATC levels and PT on enrolled subjects.

4.8.7 Study Drug Administration and Compliance

A by-subject listing for study drug administration and compliance will be provided by study part and treatment group on enrolled subjects.

4.8.8 Gluten Challenge Compliance

Patient compliance with GC will be listed as well as number of GC completed (Part B only).

For Part B (MAD), by-subject listings for the GC compliance will be provided on enrolled subjects.

4.9 Pharmacokinetics

All pharmacokinetic summaries and analyses will be on PKAS.

4.9.1 Pharmacokinetic Concentrations

Plasma concentrations for KAN-101 will be summarized by treatment group, day of dose, and nominal protocol timepoint for PKAS in Part A (SAD) and Part B (MAD) separately, Additionally, PK concentrations for Day 1 in 0.15, 0.30, and 0.60 mg/kg dose levels in Part A and B will be combined to summarize by treatment group, day of dose, and nominal protocol timepoint using descriptive statistics.

A by-subject listing for plasma concentration data for KAN-101-01, will be listed by study part, treatment group, subject, day and time of sampling for PKAS. Listings will include nominal and protocol time, actual sampling time relative to start and end of infusion, actual infusion duration, scheduled infusion duration (30 minutes) and difference between scheduled and actual infusion duration.

Following will be presented for Part A and Part B:

- Linear mean (+/- SD) plasma concentration-time profiles for KAN-101 by Day of dose (all doses on one plot)
- Semilogarithmic mean (+/- SD) plasma concentration-time profiles for KAN-101by Day of dose (all doses on one plot)
- Linear individual concentration-time combined profiles for KAN-101 by Day of dose (all subjects on same dose on one plot)
- Semilogarithmic individual concentration-time combined profiles for KAN-101 by Day of dose (all subjects on same dose on one plot)
- Linear individual concentration-time profiles for KAN-101 (separate plot for each subject)
- Semilogarithmic individual concentration-time profiles for KAN-101 (separate plot for each subject)

4.9.2 Pharmacokinetic Parameters

PK parameters for KAN-101 will be summarized by study part, treatment group and day of dose For Part A and Part B separately, using the PKAS.

Additionally, Part A and B parameters will be pooled for the first (Day 1) dose for doses common in Parts A and B for summary tables and plots.

- Descriptive statistics for calculated PK parameters will include n, arithmetic mean, SD, %CV, geometric mean, geometric CV% (calculated as: geometric CV% =SQRT(es²-1)*100; where s is the standard deviation of the log-transformed values), median, minimum and maximum values.
- For t_{max}, only median, minimum and maximum values will be presented.
- λz or $Lambda_z$ dependent PK parameters, i.e. λ_z, $AUC_{0\text{-}inf}$, CL, V_z will not be summarized if r^2adj is <0.90 , and/or span of the terminal phase is <1.3 times the half-life and/or the %extrapolation to calculate $AUC_{0\text{-}inf}$ is >30%, unless otherwise determined by the PK scientist. Such parameters will be flagged in parameters listing, and if flagged parameters are not used for calculation of descriptive summaries, it will be footnoted in the PK parameters listing.

A by-subject listings for PK parameters and dose-normalized PK parameters for KAN-101-01 will be listed by study part and treatment group, subject and day of dose using the PKAS.

4.9.2.1 Assessment of Dose Proportionality

No formal dose proportionality assessment will be performed. Informal assessment of dose proportionality will be done using Box plots for C_{max} and AUCs and corresponding dose-normalized parameters by Part A, Part B, and combined parts A and B for the common doses.

4.10 Immunogenicity

For Part A (SAD) and Part B (MAD) (separately and combined), immunogenicity summaries will be provided by treatment group on ATAS. Subjects with any ADA positive samples, screening (ADA status) and confirmatory assay (titer and ADA status) results will be included. The results for 3-Tiers will be displayed. If the sample is ADA-positive then the reactivity to the CCI will be included.

A by-subject listing of immunogenicity will be provided by study part and treatment group on enrolled subjects.

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4.12 Disposition of Subjects and Screen Failures

A clear accounting of the disposition of all subjects who enter the study will be provided, from screening to end of study participation. Number and percentage of subjects screened, enrolled/randomized, subjects completed treatment, subjects discontinued from the study and discontinuation reasons (including reasons for early withdrawal).

For Part A and Part B (separately and combined), summary tables will be provided by treatment group for subject disposition on enrolled subjects.

Listing will consist of ICF date, enrollment details (last contact date, reason of screened failure), randomization codes, visit dates, and withdrawal details (including reason for discontinuation and duration of treatment prior to discontinuation).

A by-subject listing will be provided by study part and treatment group for study treatment / randomization codes, study drug completion status, study completion status and subject disposition will be on enrolled subjects. Screen failures, and subjects who did not meet study eligibility criteria listings will be on listing of screened subjects.

4.13 Demographics and Baseline Celiac Disease Characteristics

For summary table, continuous and categorical demographic characteristics (age, sex, race, ethnicity; height and weight at Screening; and body mass index (BMI) derived) will be provided.

For Part A and Part B (separately and combined), summary tables will be provided by treatment group for demographics on ATAS.

The summary table will contain continuous and categorical celiac disease specific baseline characteristics (example years since first CeD diagnosis, number of years on GFD) will be provided by treatment group.

For Part A and Part B (separately and combined), summary tables will be provided by treatment group for baseline celiac disease characteristics on ATAS.

A by-subject listing will be provided by study part and treatment group for demographics and baseline celiac disease characteristics on enrolled subjects.

4.14 Medical History

All medical history will be coded using Version 23.1 or higher of the Medical Dictionary for Regulatory Activities (MedDRA).

For Part A (SAD) and Part B (MAD) separately, summary tables will be provided by treatment group for Medical History on ATAS.

Listings will include start and stop dates.

A by-subject listing will be provided by study part and treatment group for medical history on enrolled subjects.

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5 REFERENCES

[1] SAS® Version 9.4 of the SAS System for Personal Computers. Copyright © 2002-2003. SAS Institute Inc. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA.

[2] Phoenix®WinNonlin® Professional Software Version 8.0. https://www.certara.com

6 APPENDICES

6.1 Schedule of Assessments

Table 8: Schedule of Assessments Part A (SAD)

Assessment	Screening	Study Period				Early Term.
Study Day	**-28**	**1**	**4 (±1)**	**8**	**D21 (±1)**	
Screening Assessments						
Informed Consent	X					
Medical History & Demographics	X					
Disease History	X					
Inclusion/Exclusion	X					
ECG	X	X[2]		X		
HIV, HBV, HCV testing	X					
HLA Genotype and CeD Serology[1]	X					
Clinical Procedures						
Physical Examination	X[3]					X
Pregnancy Test[4]	X	X[5]				
Vital Signs[6]	X	X[5]		X		
Con Meds/Procedures, Incidental Gluten Exposure	X	X	X	X	X	X
Safety Assessments						
Adverse Events	X	X[7]	X	X	X	X
Lab Tests (Safety)	X	X[5]	X	X		X
Study Drug Administration						
KAN-101 Administration		X				
Additional Blood Samples						
PK Blood Sample		X[8]				
ADA Serum Sample		X[5]			X	X

1. All patients will be assessed via central laboratory for HLA genotype and CeD serology (eg, tTG-IgA and DGP-IgG) at screening to confirm eligibility. For rescreening, HLA does not need to be repeated and CeD serology only needs to be repeated if >3months have elapsed from last assessment.
2. ECG performed pre dose (at least 5 min before infusion), 20(±5) min after start of infusion, and 1 hour (±10 min) post infusion.
3. Includes weight and height at screening only.
4. Pregnancy test at screening must be serum; serum or urine tests are acceptable on D1 prior to dosing. Pregnancy test must be negative before study drug is administered.
5. Samples/Measurements taken pre-dose (at least 5 min prior to infusion).

Assessment	Screening	Study Period				Early Term.
Study Day	**-28**	**1**	**4 (±1)**	**8**	**D21 (±1)**	
6. Vital signs (pulse rate, temperature, diastolic and systolic BP). 7. On D1 patients will be observed in the clinic/hospital unit for 10 h after initiation of IV infusion and followed up with by phone approximately 24 hours after dosing. 8. PK samples to be taken pre-dose (at least 5 min prior to infusion) and the following timepoints after the end of infusion: 0 (+2) min, 7 (±2) min, 15 (±2) min, 30 (±5) min, 1 h (±5) min), 2 h (±5 min), 3 h (±5 min), 4 h (±5 min), 6 h (±5 min).						
Abbreviations: ADA = anti-drug antibodies; BP = blood pressure; CeD = celiac disease; Con Meds = concomitant medications; ECG = electrocardiogram; Early Term. = early termination; HBV = hepatitis B; HCV = hepatitis C; HIV = human immunodeficiency virus; HLA = Human Leukocyte Antigen; PK = pharmacokinetics; SAD = single ascending dose.						

Table 9: Schedule of Assessments Part B (MAD)

Assessments	Screening	Treatment Period			PD Assessment		Follow-up[1]	Early Term.
Study Day	**-28**	**1**	**4**	**7**	**15**	**21**	**28 (±3)**	
Screening Assessments								
Informed Consent	X							
Medical History & Demographics	X							
Disease History	X							
Inclusion/Exclusion	X							
ECG	X	X[2]		X[2]	X[15]			
HIV, HBV, HCV testing	X							
HLA Genotype and CeD Serology[3]	X							
Clinical Procedures								
Physical Exam	X[4]							X
Pregnancy Test[5]	X	X[6]	X[6]	X[6]				
Vital Signs[7]	X	X[6]			X			
Con Meds/Procedures, Incidental Gluten Exposure	X	X	X	X	X	X	X	X
3-Day GC					X[8]			
CCI [redacted]								
Safety Assessments								
Adverse Events	X	X[10]	X[10]	X[10]	X	X	X	X
Lab Tests (Safety)	X	X[6]	X[6]	X[6]	X			X
Study Drug Administration								
KAN-101/PBO Administration		X	X	X				
Additional Blood Samples								
PK Blood Sample		X[11]	X[6]	X[12]	X[15]			
ADA Sample		X[6]				X		X
CCI [redacted]								

Assessments	Screening	Treatment Period			PD Assessment		Follow-up[1]	Early Term.
Study Day	**-28**	**1**	**4**	**7**	**15**	**21**	**28 (±3)**	
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1. Phone call.
2. ECG performed pre dose (at least 5 min before infusion), 20(±5) min after start of infusion, and 1 hour (±10 min) post infusion.
3. All patients will be assessed via central laboratory for HLA genotype and CeD serology (eg, tTG-IgA and DGP IgG) at screening to confirm eligibility. For rescreening, HLA does not need to be repeated and CeD serology only needs to be repeated if >3months have elapsed from last assessment.
4. Includes weight and height at screening only.
5. Pregnancy test at screening must be serum; serum or urine tests are acceptable predose on D1, D4, and D7. Pregnancy test must be negative before each dose of study drug is administered.
6. Samples/Measurements taken pre-dose (at least 5 min prior to infusion).
7. Vital signs (pulse rate, temperature, diastolic and systolic BP).
8. The GC will consist of patients self-administering 9 g of gluten protein PO for each of 3 days (D15 to D17), with the first administration in the clinic on D15. GC should be administered at approximately the same time each day.
9. CCI
10. On D1 patients will be observed in-clinic for 10 h from the start of IV infusion and followed up with by phone approximately 24 hours after dosing; on D4 and D7 (dosing days) patients will be observed for 4 h in clinic from the start of IV infusion.
11. PK samples to be taken at pre-dose (at least 5 min prior to infusion) and the following timepoints after the end of infusion: 0 (+2) min, 7 (±2) min, 15 (±2) min, 30 (±5) min, 1 h (±5 min), 2 h (±5 min), 3 h (±5 min), 4 h (±5 min), 6 h (±5 min).
12. PK samples to be taken at pre-dose (at least 5 min prior to infusion) and the following timepoints after the end of infusion :0 (+2) min, 7 (±2) min, 15 (±2) min, 30 (±5) min, 1 h (±5 min), 2 h (±5 min), and 4 h (±5 min).
13. CCI
14. CCI
15. Collected prior to oral gluten challenge.

Abbreviations: ADA = anti-drug antibodies; BP = blood pressure; CCI CeD = celiac disease; Con Meds = concomitant medications; Early Term = early termination; ECG = electrocardiogram; CCI GC = gluten challenge; HBV = hepatitis B; HCV = hepatitis C; HIV = human immunodeficiency virus; HLA = Human Leukocyte Antigen; IV = intravenous; MAD = multiple ascending dose; CCI PBO = placebo; PD = pharmacodynamics; PK = pharmacokinetics; CCI

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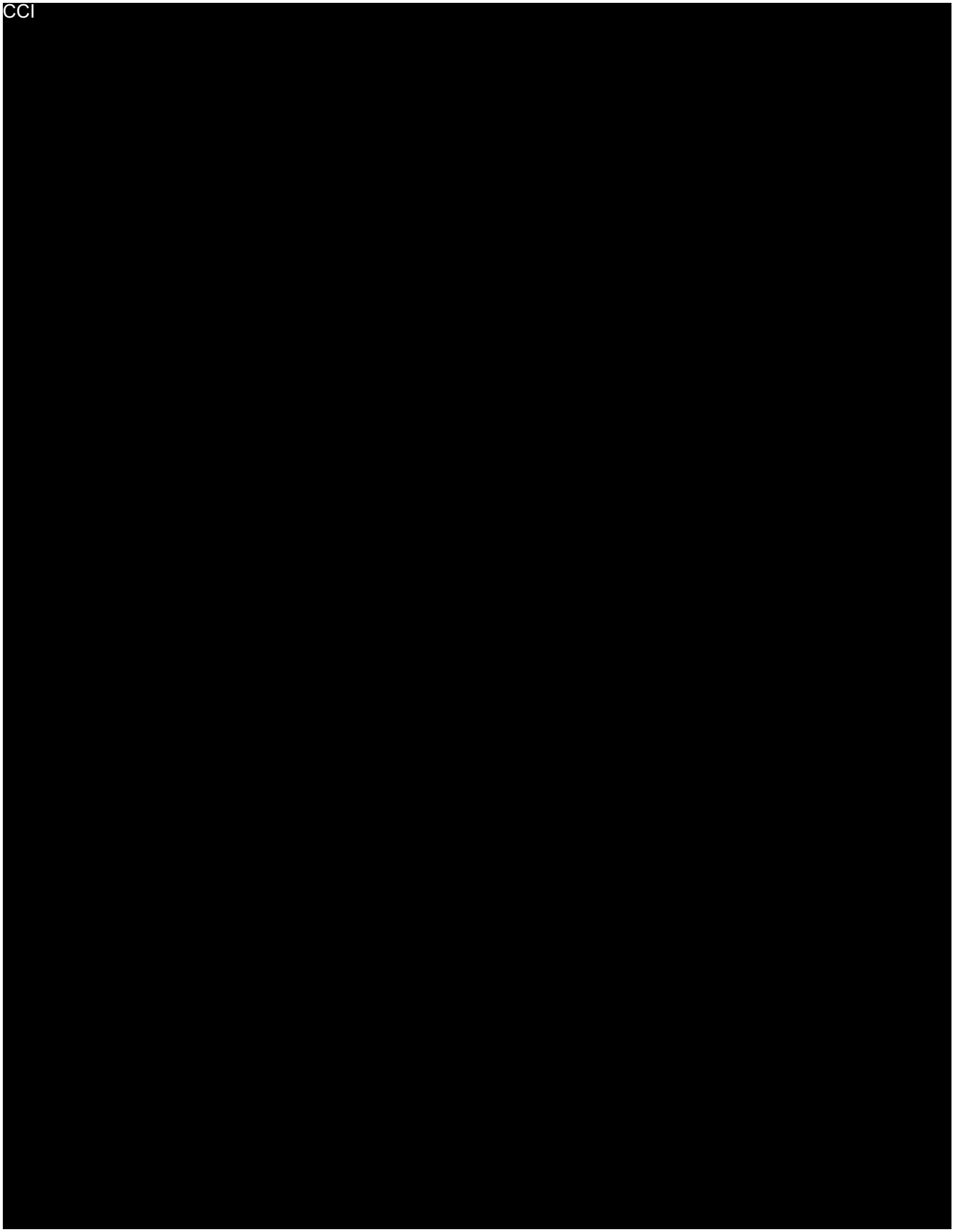

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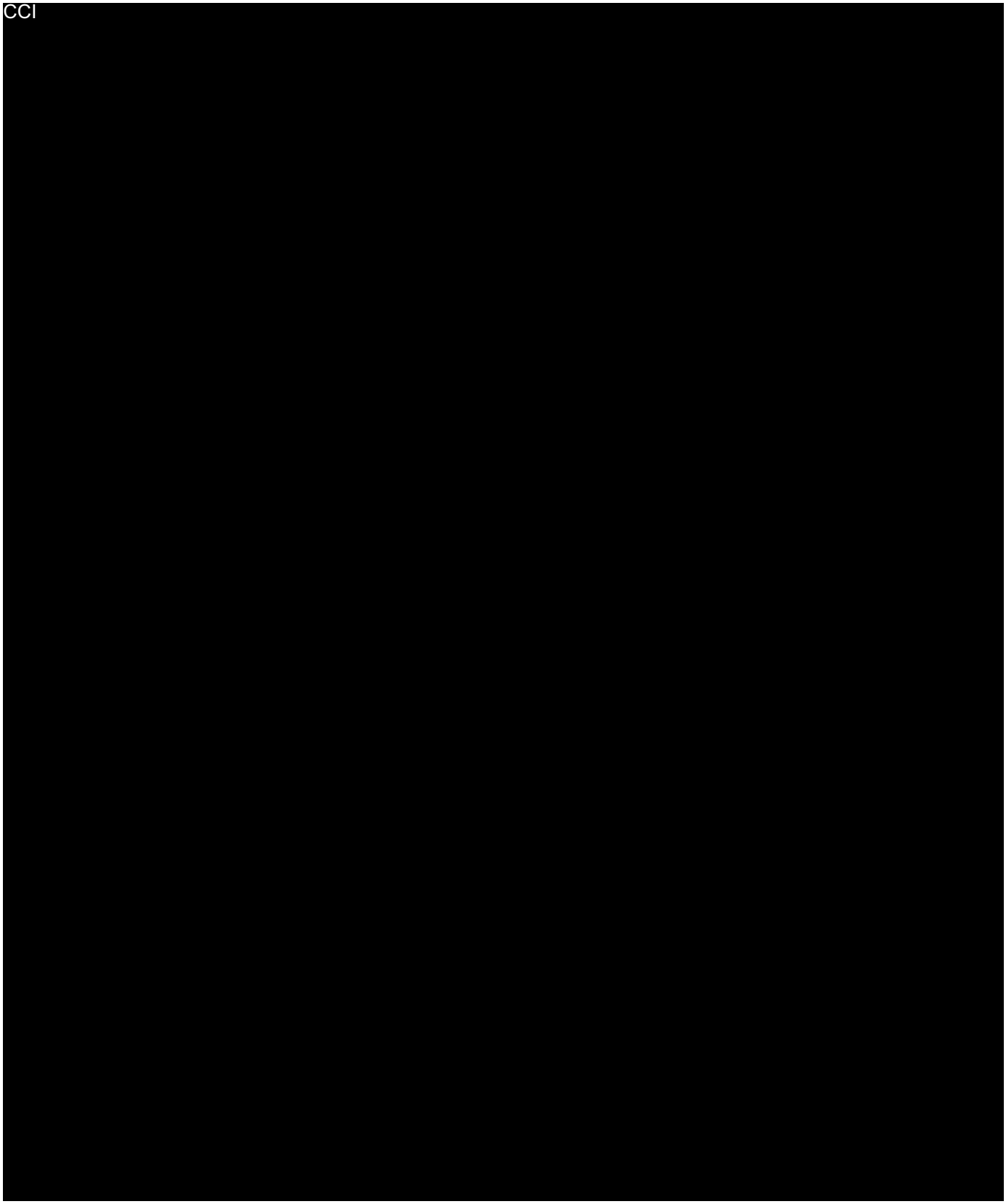

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PPD