

Clinical Study Report Synopsis

SYNOPSIS

STUDY TITLE

Pharmacokinetics, pharmacodynamics and safety of ziltivekimab versus placebo in Chinese participants with chronic kidney disease and systemic inflammation

Title on clinicaltrials.gov: A Research Study of How the Medicine Ziltivekimab Works in the Body of Chinese Men and Women With Kidney Disease and Inflammation

STUDY NUMBER

NN6018-4889

REGULATORY AGENCY IDENTIFIER NUMBER

clinicaltrials.gov identifier: NCT05379829 **UTN:** U1111-1266-5585

Paediatric status: Not applicable

STUDY PHASE

Phase 1

NAME OF FINISHED PRODUCT

Ziltivekimab B 15 mg/mL

NAME OF ACTIVE SUBSTANCE

Human monoclonal antibody to interleukin-6

NAME OF SPONSOR/COMPANY

Novo Nordisk A/S, Novo Allé, DK-2880 Bagsvaerd, Denmark.

Novo Nordisk A/S, Clinical Publishing, Transparency and Archiving (2834); email address: clinicaltrials@novonordisk.com.

NUMBER OF STUDY CENTERS AND COUNTRIES

Study participants were screened, randomised, and assigned to treatment at five sites in China.

PUBLICATIONS

No publications were available at the time of this clinical study report synopsis.

STUDY PERIOD

Initiation date: 30 May 2022

Study completion date: 02 September 2024

DATA CUT-OFF DATE

The results presented reflect the data available in the clinical database as of 06 December 2024

BACKGROUND AND RATIONALE

The study was conducted as part of the phase 1 development programme for ziltivekimab to evaluate the pharmacokinetics, pharmacodynamics and safety of ziltivekimab versus placebo in Chinese participants with chronic kidney disease and systemic inflammation.

Advanced chronic kidney disease (CKD) is associated with a persistent inflammatory burden. Systemic inflammation in CKD is associated with all-cause and cardiovascular mortality and are associated with progressive cardio-renal dysfunction. The sub-population of patients with CKD and systemic inflammation is therefore a population at high risk of MACE. Despite currently available treatments targeting other risk factors than residual inflammatory risk, this is a sub-population with high unmet need.

Ziltivekimab is a human monoclonal antibody directed against IL-6 and is being developed to provide the first anti-inflammatory agent that lowers the risk of recurrent cardiovascular events. Ziltivekimab has been designed to enable once-monthly administration by subcutaneous (s.c.) injection. When the current study was designed, three clinical studies had been completed evaluating the effects of ziltivekimab in non-Chinese participants with inflammation at different stages of CKD. Data from the three studies supports that ziltivekimab reduces inflammation as measured by hs-CRP.

All participants were informed of the risks and benefits of the study and provided informed consent before any study activities were performed. Participants were covered by the sponsor's insurance according to local legal requirements.

OBJECTIVES, ENDPOINTS, ESTIMANDS, AND STATISTICAL METHODS

Objectives and endpoints

The primary and secondary objectives of the study are listed in [Table 1](#) together with the endpoints defined to address these objectives. No exploratory endpoints were defined in the protocol.

Table 1 Objectives and Endpoints

Objectives	Endpoints		
Primary	Title	Time frame	Unit
To evaluate the pharmacokinetics of 15 mg ziltivekimab in Chinese participants with CKD and systemic inflammation	<i>Primary:</i>		
	AUC _{τ,MD}	During 3 rd dosing interval (week 8 to week 12)	ng/mL*days
	<i>Supportive secondary:</i>		
	AUC _{τ,SD}	During 1st dosing interval (day 0 to week 4)	ng/mL*days
	C _{max,MD}	After last dose (week 8) to end-of-study (week 20)	ng/mL
	t _½	After last dose (week 8) to end-of-study (week 20)	days
Secondary	Title	Time frame	Unit
To evaluate the effects of ziltivekimab 15 mg on pharmacodynamic marker of inflammation and cardiac risk in Chinese participants with CKD and systemic inflammation	<i>Supportive secondary:</i>		
	Change in hs-CRP	From baseline (week 0) to end-of-treatment (week 12)	mg/L

Abbreviations: AUC_{τ,MD} = area under the ziltivekimab serum concentration-time curve in a 4-week dosing interval i.e., from time 0 to 4 weeks after the 3rd dose (multiple doses [MD]); AUC_{τ,SD} = area under the ziltivekimab serum concentration-time curve in a 4-week dosing interval i.e., from time 0 to 4 weeks after the 1st dose (single dose [SD]); C_{max,MD} = maximum serum concentration of ziltivekimab after 3rd dose; CKD = chronic kidney disease; hs-CRP = high-sensitivity C-reactive protein; t_½ = elimination half-life.

Estimands

Primary estimand

For the primary objective, the aim is to evaluate the total exposure (AUC_{τ,MD}) with ziltivekimab 15 mg if all participants randomised to ziltivekimab 15 mg received all planned doses and only received allowed concomitant medication during the study. The estimand is defined with the five attributes as defined in ICH E9(R1) addendum:

- Treatment condition: The treatment regimen evaluated is ziltivekimab 15 mg added to allowed concomitant medication during the study.
- Population: Defined through the inclusion/exclusion criteria.
- Variable: AUC_{τ,MD} during 3rd dosing interval (week 8 to week 12).
- Remaining intercurrent events: Treatment discontinuation and administration of any of the disallowed medications will be handled by the hypothetical strategy. Death is handled by the while-alive strategy.
- Population-level summary: Geometric mean in participants randomised to ziltivekimab 15 mg.

Secondary estimand

For the secondary objective, the aim is to estimate the treatment effect of ziltivekimab 15 mg vs placebo on change in hs-CRP, if all participants received all doses of the study intervention and only received allowed concomitant medication during the study. The estimand is defined with the five attributes as defined in ICH E9(R1) addendum:

- Treatment condition: The treatment regimen evaluated is ziltivekimab 15 mg vs placebo added to allowed concomitant medication during the study.
- Population: Defined through the inclusion/exclusion criteria.
- Variable: Change in hs-CRP from baseline to end of treatment.
- Remaining intercurrent events: Treatment discontinuation and administration of any of the disallowed medications will be handled by the hypothetical strategy. Death is handled by the while-alive strategy.
- Population-level summary: Difference between ziltivekimab 15 mg and placebo in median change from baseline.

Statistical methods

Analysis sets and observation periods

The following analysis sets were defined in the protocol and the SAP, prior to unblinding

- Full analysis set (FAS) included all randomised participants. Participants were included in the analyses according to the planned intervention.
- Safety analysis set (SAS) included all participants who were exposed to study intervention. Participants were included in the analyses according to the intervention they received.
- Pharmacokinetic (PK) analysis set: All randomised participants who received study intervention and had at least 1 postdose PK blood sample.

Sample size and statistical analyses

Sample size determination

A formal sample size calculation was based on the supportive secondary endpoint, whilst considering that adequate pharmacokinetic data is obtained to achieve the primary objective. A formal power calculation was not performed for the primary endpoint.

In the RESCUE-US study, the median difference in percentage change in hs-CRP between ziltivekimab 15 mg and placebo was -77.7 after aligning for strata. On the log-scale, a standard deviation $SD=0.92$ on the relative change from baseline was observed in each group (data on file). Based on a t-test, assuming a log-normal distribution with $SD=1.0$, it requires 24 participants randomised 1:1 to detect 80% reduction in change from baseline in hs-CRP with 95% power and a 5% significance level. Therefore, the planned sample size of 12 participants per group was considered to provide sufficient power for the secondary objective. Furthermore, pharmacokinetic data from 12 participants was considered adequate to achieve the primary objective.

Statistical analysis

Descriptive statistics for the pharmacokinetic endpoints are presented based on the PK analysis set. The pharmacodynamic endpoint, change in hs-CRP, is presented and analysed as percent change from baseline, and the statistical analysis is based on the FAS.

Primary endpoint analysis: The pharmacokinetic (PK) endpoints was summarised using descriptive statistics.

Secondary endpoint analysis: For the supportive secondary endpoint (change in hs-CRP), the median difference and associated 95% confidence interval between ziltivekimab 15 mg and placebo were analysed by the nonparametric Hodges-Lehmann method stratified for the randomisation stratification variable CKD Stage (3 vs. 4), and the p-value from the Wilcoxon two-sample test were presented.

There were no changes to planned analyses prior to or after unblinding.

METHODOLOGY

This was an interventional, randomised, triple-dose every 4 weeks (Q4W), parallel-group, double-blind, placebo-controlled, multi-centre, 22-week-long study conducted to evaluate the pharmacokinetics, pharmacodynamic and safety of 15 mg ziltivekimab versus placebo in adult Chinese participants with chronic kidney disease and systemic inflammation.

A total of 24 participants with CKD stage 3 or 4 and systemic inflammation were planned to be randomised 1:1 to receive 3 doses Q4W subcutaneously of ziltivekimab 15 mg or placebo.

The study lasted 22 weeks and consisted of a screening period (~2 weeks), a 12-week treatment period, and an 8-week follow-up period after the end-of-treatment visit (Visit 10). An optional pre-screening visit was offered for potential study participants with no recent hs-CRP level, eGFR, HbA_{1c} or tuberculosis status in their medical records.

Study participants were to be randomised and receive the initial dose of study intervention on Day 0 (Visit 2). The subsequent two doses of study intervention were to be administered at weeks 4 and 8, and the follow-up time after last dose was to be 3 months (last month of treatment period + 2 months follow-up after end-of-treatment). The total study duration for an individual participant was estimated to be approximately 6 months.

NUMBER OF PARTICIPANTS (PLANNED AND ANALYSED)

A total of 24 participants with CKD stage 3 or 4 and systemic inflammation were planned to be randomised 1:1 to receive 3 doses every 4 weeks (Q4W) of ziltivekimab 15 mg s.c. or placebo.

A total of 78 participants were screened, of which 46 (59.0%) were screen failures and 8 (10.3%) participants decided to withdraw from the study before randomisation.

A total of 24 participants were randomised in a 1:1 ratio to the two study interventions. All 24 randomised participants were exposed to study intervention. No participants were removed from the FAS, SAS or PK analyses set, consequently, each analyses set contained 24 participants.

In total, 24 (100%) participants completed the study. Of these, 22 (91.7%) participants completed the treatment with study intervention and 2 (8.3%) participants prematurely discontinued treatment with study intervention after the first dose of ziltivekimab 15 mg due to adverse events.

DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION AND EXCLUSION

Key inclusion criteria:

- Estimated glomerular filtration rate (eGFR) ≥ 15 and < 60 mL/min/1.73 m² (using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation).^a
- Serum high-sensitivity C-reactive protein (hs-CRP) ≥ 2 mg/L at screening (visit 1).

^a Laboratory results of eGFR for inclusion can be based on:

- measurements no more than 90 days old at screening, documented in medical records *or*
- measurements obtained at the optional pre-screening visit, documented in medical records *or*
- central laboratory measurement obtained at the screening visit (visit 1).

Key exclusion criteria:

Laboratory values

- Absolute neutrophil count $< 2 \times 10^9$ /L at screening (visit 1).
- Platelet count $< 120 \times 10^9$ /L at screening (visit 1).
- Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) $> 2.5 \times$ upper limit of normal at screening (visit 1).

Medical conditions

- Clinical evidence of, or suspicion of, active infection at the discretion of the investigator.
- History of gastrointestinal perforation. (*Note: History of perforated appendicitis more than 5 years prior to screening (visit 1) is not exclusionary.*)
- History of active diverticulitis in the 5 years prior to randomisation (visit 2).
- History of inflammatory bowel disease that has been clinically active during the 12 months prior to randomisation (visit 2).
- Myocardial infarction, stroke, hospitalisation for unstable angina pectoris, or transient ischaemic attack within 60 days prior to randomisation (visit 2).
- Planned coronary, carotid or peripheral artery revascularisation known on the day of screening (visit 1).
- Major cardiac surgical, non-cardiac surgical, or major endoscopic procedure (thoracoscopic or laparoscopic) within the past 60 days prior to randomisation (visit 2) or any major surgical procedure planned at the time of randomisation (visit 2).

Prior or current medication

- Use of preventive systemic antibiotics, systemic antivirals, or systemic antifungals at screening (visit 1). (*Note: “Systemic” is defined as oral or i.v. administered drugs that are absorbed into the circulation*).
- Use of systemic immunosuppressive drugs (both small molecules and biologics) or disease modifying anti-rheumatic drugs (DMARDs including both biologic DMARDs like anti-TNF-alpha and conventional DMARDs like methotrexate) at screening (visit 1) or anticipated chronic use of such drugs any time during the study. (*Note: Use of otic, ophthalmic, inhaled, and topical corticosteroids or local corticosteroid injections are not exclusionary*).

STUDY INTERVENTIONS, DOSE AND MODE OF ADMINISTRATION

The study interventions administered are described in [Table 2](#).

Table 2 Study interventions administered

Study intervention name	Ziltivekimab B 15 mg/mL	Placebo Ziltivekimab B
Intervention type	IMP, test product	IMP, reference therapy
Pharmaceutical form	Solution for injection	
Medical device	See row 'Packaging and labelling'	
Route of administration	Subcutaneous (s.c.)	
IMP strength	15 mg/mL	0 mg (volume equivalent to 15 mg/mL ziltivekimab).
Dose and dose frequency	Single dose of 15 mg administered three times Q4W (weeks 0, 4 and 8)	Single dose of 0 mg administered three times Q4W (weeks 0, 4 and 8)
Dosing instructions and administration	• All baseline assessments had to be finalized prior to administration of the first study intervention dose. • Only participants randomised to treatment could receive study intervention. • All dosing was to be administered on site by delegated site staff. • Injections were to be performed s.c. in a lifted skinfold in the abdomen, thigh, or upper arm. • The date, time and site of injection (abdomen, thigh, or upper arm) of each dose administered were to be recorded in the eCRF.	
Sourcing	Manufactured and supplied by Novo Nordisk A/S	
Packaging and labelling	• Labelled and packaged by Novo Nordisk A/S. • Labelled in accordance with EU CTR Annex VI, local regulations and study requirements. • IMPs were provided in single-use pre-filled DV3430-C1 manual syringes^a (device constituent of non-approved drug-device combination product^b).	
Storage conditions	Not in use: • Store in refrigerator (2°C-8°C) in original packaging • Protect from light • Do not freeze In use (if removed from refrigerator): • Store at 8°C-25°C • Use within 1 week • For single use • Protect from light • Do not refrigerate	
Abbreviations: IMP = investigational medicinal product		
^a The pre-filled DV3430-C1 manual syringe was a non-investigational medical device.		
^b The drug-device combination product is currently not approved.		

DURATION OF STUDY INTERVENTION

The total study duration for an individual participant was approximately 6 months.

SUMMARY OF RESULTS AND CONCLUSIONS

Demographic and other baseline characteristics

The demographic and baseline characteristics are presented in [Table 3](#) (categorical variables) and [Table 4](#) (continuous variables) and summarised below.

The demographic and baseline characteristics were comparable between the two study intervention groups at baseline. Of the 24 participants exposed to study intervention, [REDACTED] were females

and [REDACTED] were males. All participants [REDACTED] were [REDACTED]. Participants had a mean age of 56.2 years and a mean body weight of 74.57 kg. The mean BMI was 26.8 kg/m² and most participants had BMI between 25 and 29 (11 participants) or below 25 (8 participants).

Of the 24 participants, 14 (58.3%) participants had CKD Stage 3, and 10 (41.7%) participants had CKD Stage 4. The mean eGFR was 36.92 mL/min/1.73m². The mean HbA_{1c} was 6.42%. The median hs-CRP level was 4.3 mg/L and the median IL-6 level was 4.0 pg/mL.

Table 3 Baseline characteristics and demographics – categorical variables – full analysis set

	Zilti 15 mg		Placebo		Total	
	N	(%)	N	(%)	N	(%)
Number of participants	12		12		24	
Sex						
Female						
Male						
Race						
White						
Black or African American						
Asian						
American Indian or Alaska Native						
Native Hawaiian or Other Pacific Islander						
Other						
Ethnicity						
Hispanic or Latino						
Not Hispanic or Latino						
CKD stage						
CKD stage 3	7	(58.3)	7	(58.3)	14	(58.3)
CKD stage 4	5	(41.7)	5	(41.7)	10	(41.7)
BMI category						
< 25	4	(33.3)	4	(33.3)	8	(33.3)
25 <= to < 30	6	(50.0)	5	(41.7)	11	(45.8)
>= 30	2	(16.7)	3	(25.0)	5	(20.8)

N: Number of participants, SD: Standard deviation.

CKD: Chronic Kidney Disease. CKD stages are determined per randomisation strata using the estimated glomerular filtration rate (eGFR).

CKD Stage 3: 30 <= eGFR < 60 mL/min/1.73m², CKD Stage 4: 15 <= eGFR < 30 mL/min/1.73m².
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Table 4 Baseline characteristics and demographics – continuous variables – full analysis set

	Zilti 15 mg	Placebo	Total
Number of participants	12	12	24
Age (years)			
N	12	12	24
Mean (SD)	56.3 (16.5)	56.2 (10.1)	56.2 (13.4)
Median	■	■	■
Min ; Max	■	■	■
BMI (kg/m ²)			
N	12	12	24
Mean (SD)	27.1 (3.2)	26.6 (4.2)	26.8 (3.6)
Median	27	26	26
Min ; Max	23 ; 33	20 ; 34	20 ; 34
hs-CRP (mg/L)			
N	12	12	24
Mean (SD)	6.86 (6.92)	4.94 (3.08)	5.90 (5.33)
Geom. Mean (CV)	4.25 (143.15)	3.94 (93.56)	4.09 (114.28)
Median	3.2	5.1	4.3
eGFR (mL/min/1.73 m ²)			
N	12	12	24
Mean (SD)	36.83 (16.18)	37.00 (14.25)	36.92 (14.91)
Geom. Mean (CV)	33.48 (49.75)	34.46 (41.73)	33.97 (44.78)
Median	31.0	38.5	35.5
Interleukin 6 (pg/mL)			
N	12	12	24
Mean (SD)	5.60 (4.95)	5.34 (2.85)	5.47 (3.95)
Geom. Mean (CV)	4.13 (93.75)	4.67 (59.57)	4.39 (75.47)
Median	3.7	4.2	4.0
HbA1c (%)			
N	12	12	24
Mean (SD)	6.08 (0.96)	6.76 (1.13)	6.42 (1.08)
Geom. Mean (CV)	6.02 (15.13)	6.67 (16.49)	6.34 (16.37)
Median	6.0	6.6	6.3
Height (m)			
N	12	12	24
Mean (SD)	1.67 (0.09)	1.65 (0.09)	1.66 (0.09)
Median	■	■	■
Min ; Max	■	■	■
Body Weight (kg)			
N	12	12	24
Mean (SD)	76.01 (13.65)	73.13 (16.70)	74.57 (14.99)
Median	■	■	■
Min ; Max	■	■	■

N: Number of participants, SD: Standard deviation, BMI: Body mass index.

Baseline information is defined as the measurement at the latest assessment before dosing. BMI is calculated based on baseline measurements of body weight and height.

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Pharmacokinetic and pharmacodynamic evaluation

Primary objective

The evaluation of the pharmacokinetics of ziltivekimab 15 mg in Chinese participants with CKD and systemic inflammation was addressed by the following endpoints and results:

- **AUC_{τ,MD} during 3rd dosing interval (week 8 to week 12) – Primary endpoint**
 - The geometric mean exposure from week 8 to end-of-treatment (week 12) was 43,972 day*ng/mL (with a CV of 31.6%)
- **AUC_{τ,SD} during 1st dosing interval (day 0 to week 4) – Supportive secondary endpoint**
 - The geometric mean exposure during 1st dosing interval was 17,148 day*ng/mL (with a CV of 31.2%)
- **C_{max,MD} after last dose (week 8) to end-of-study (week 20) – Supportive secondary endpoint**
 - The median C_{max} after last dose to end-of-study was 1,785 ng/mL (948; 3,080)_{min; max}
- **t_½ after last dose (week 8) to end-of-study (week 20) – Supportive secondary endpoint**
 - The median t_½ after last dose to the end-of-study was 53.38 days (46.62; 110.41)_{min; max}

Secondary objective

The evaluation of the effects of ziltivekimab 15 mg on pharmacodynamic marker of inflammation and cardiac risk in Chinese participants with CKD and systemic inflammation was addressed by the following endpoint and results:

- **Change in hs-CRP from baseline (week 0) to end-of-treatment (week 12) - Supportive secondary endpoint**
 - The median change in hs-CRP levels from baseline to end-of-treatment for ziltivekimab was -91.82% (-95.37; -89.81)_{Q1; Q3} and for placebo 18.19% (20.61; 172.08)_{Q1; Q3}.
 - The median of differences in the hs-CRP change from baseline to end-of-treatment between ziltivekimab and placebo was -105.30 (-290.64; 69.57)_{95%CI}, p-value < 0.0001.

Ziltivekimab 15 mg reduced hs-CRP levels by 91.82% from baseline to end-of treatment. The difference in the hs-CRP level change from baseline to end-of-treatment between ziltivekimab and placebo was statistically significant (p-value < 0.0001).

Safety results

Ziltivekimab treatment was generally well-tolerated and no new safety concerns were identified in the study. No deaths were reported in the study, and no participants withdrew from the study due to an AE. The safety evaluation is summarised as follows:

Adverse events

- A total of 63 AEs were reported in 20 (83.3%) participants:
 - Ziltivekimab: 36 AEs in 11 (91.7%) participants
 - Placebo: 27 AEs in 9 (75.0%) participants
- Most AEs were judged as unlikely (52 AEs in 18 [75.0%] participants) related to study intervention by the investigators. Eight (8) AEs in 6 (25.0%) participants were judged as possibly related to study intervention and 3 AEs in 2 (8.3%) participants as probably related to study intervention by the investigators.

- Most AEs were mild in severity (52 AEs in 19 [79.2%] participants). Ten (10) AEs in 8 (33.3%) participants were moderate in severity and 1 AE in 1 (4.2%) participant were severe in severity.
- Two (2) serious AEs (SAEs) were reported in 2 (16.7%) participants in the ziltivekimab group. Both were judged by the investigators to be unlikely related to study intervention.
- Most AEs were recovered/resolved (44 AEs in 17 [70.8%] participants) by the end of the study.
- Three (3) AEs with PTs 'Thrombocytopenia', 'Urticaria' and 'Asthma' reported in 2 participants in the ziltivekimab group led to permanent discontinuation of study intervention. All three AEs were judged by the investigator to be probably related to study intervention.
- The most frequently reported AEs were within the SOC 'Infections and infestations' (13 AEs in 7 [29.2%] participants) and 'Metabolism and nutrition disorders' (12 AEs in 8 [33.3%] participants). Within the SOC 'Infections and infestations' the most frequently reported AE by PT was 'Upper respiratory tract infection' (4 AEs in 3 [12.5%] participants). Within the SOC 'Metabolism and nutrition disorders' the most frequently reported AEs by PTs were 'Hyperkalaemia' (6 AEs in 4 [16.7%] participants).

Adverse events requiring additional data collection

- Of the 19 reported AEs requiring additional data collection, most (13 AEs) were infections (ziltivekimab 7 AEs in 5 participants, placebo 6 AEs in 3 participants).
- Two (2) hepatic events, 2 hypersensitivity events, and 1 thrombocytopenia event were reported in 4 participants in the ziltivekimab group.
- One (1) hypersensitivity event was reported in 1 participant in the placebo group.
- No AEs in the categories 'Neoplasms (malignant and non-malignant)', 'Injection site reaction' or 'Medication error, misuse and abuse' were reported.

Clinical laboratory evaluation

- No clinically significant mean changes were observed for either of the two study intervention groups in the haematology, biochemistry, lipids and urinalysis laboratory parameters assessed in this study.
- A total of 15 clinically significant individual laboratory abnormalities with related AEs was identified in 9 participants (ziltivekimab 5, placebo 4).
- No participants had sustained (at least 2 consecutive visits) thrombocytopenia of any grade.
- One (1) participant (placebo group) had sustained (at least 2 consecutive visits) neutropenia grade 1 (neutrophil count $<2 - 1.5 \times 10^9/L$).
- One (1) participant (ziltivekimab group) tested positive for anti-ziltivekimab antibodies at the end-of-treatment, follow-up, and end-of-study visits.

Vital signs, physical findings and other observations related to safety

- No notable or clinically significant changes in vital signs were observed.
- One (1) AE within the SOC 'Skin and subcutaneous tissue disorders' was reported in the placebo group.
- Three (3) AEs related to ECG findings were reported in 3 participants in the ziltivekimab group.
- No pregnancies and no technical complaints were reported in the study.

CONCLUSIONS

- The $AUC_{\tau, MD}$ (week 8 to week 12) and $AUC_{\tau, SD}$ (week 0 to week 4) of 43,972 ng/mL*days (CV of 31.6%) and 17,148 ng/mL*days (CV of 31.2%), respectively, were consistent with three monthly dosing events and a median half-life of 53 days. Maximal ziltivekimab concentrations of 1,785 ng/mL were observed on study day 71, which was 15 days after the last dose.
- Ziltivekimab 15 mg reduced hs-CRP levels by 91.82% from baseline to end-of treatment. The difference in the hs-CRP level change from baseline to end-of-treatment between ziltivekimab and placebo was statistically significant (p-value < 0.0001).
- Ziltivekimab 15 mg was well-tolerated and no new safety concerns were identified.

DATE AND VERSION OF THIS REPORT

12 February 2025, version 1.0

COMPLIANCE STATEMENT

The study was conducted in accordance with the Declaration of Helsinki (2013) and ICH Good Clinical Practice (GCP) Guideline (2016), including archiving of essential documents. The study was conducted in accordance with FDA 21 CFR 312.120 (updated 2023).

The submitted information, reflecting the data available at the data cut-off date for this report, is confirmed to be accurate.