29 January 2026
EMADOC-1700519818-2608875
Human Medicines Division

# Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

## Nemluvio

Nemolizumab

Procedure no: EMA/PAM/0000308775

## Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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| Status of this report and steps taken for the assessment | | | |
|---|---|---|---|
| **Current step[1]** | **Description** | **Planned date** | **Actual Date** |
| ☐ | CHMP Rapporteur AR | 5 January 2026 | 18 December 2025 |
| ☐ | CHMP comments | 19 January 2026 | n/a |
| ☐ | Updated CHMP Rapporteur AR | 22 January 2026 | n/a |
| ☒ | CHMP outcome | 29 January 2026 | 29 January 2026 |

# Administrative information

| Procedure resources | |
|---|---|
| **Rapporteur** | **Kristina Dunder** |

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# 1. Introduction

On 28 October 2025, the MAH submitted a completed paediatric study for Nemluvio, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

A short critical expert overview has also been provided.

# 2. Scientific discussion

## *2.1. Information on the development program*

The MAH stated that Study RD.06.SPR.118126 (A Multicenter, Open-Label, Single-Group Clinical Trial to Assess the Pharmacokinetics, Safety and Efficacy of nemolizumab (CD14152) in Pediatric Subjects (aged 2 to 11 years) with Moderate-to-Severe Atopic Dermatitis) is part of a paediatric development program agreed with PDCO (EMEA-001624-PIP01-14) since 17 April 2015. The PIP Indication targeted is the treatment of moderate to severe atopic dermatitis not adequately controlled with topical treatments in the subsets of the paediatric population: from 2 years to less than 18 years of age.

Since then, nemolizumab is currently approved in 36 countries including the European Commission Decision for the centralised procedure (EMEA/H/C/006149/0000) that was received on 12 February 2025 (EU/1/24/1901) for both the treatment of adults with moderate-to-severe Prurigo Nodularis (PN) who are candidates for systemic therapy, and the treatment of moderate-to-severe Atopic Dermatitis (AD) in patients aged 12 years and older who are candidates for systemic therapy.

As the paediatric development is still on going in the subset from 2 to 11 years of age, the final paediatric formulation is not yet selected. Nevertheless, this Clinical Study Report (RD.06.SRE.118126) along with a popPK Modeling and Simulation Report will support a future PIP Request for Modification 08 to refine the proposed paediatric development program and the selection of a suitable paediatric formulation.

A line listing of all the concerned studies supporting the 2 to 11 years old paediatric subset is annexed. PIP studies supporting the paediatric subset 12 to 17 years old were omitted from the line listing as this indication was already part of the original marketing authorization.

## *2.2. Information on the pharmaceutical formulation used in the study*

During this PK study, treatments administered were different depending on body weights and type of doses (loading or following doses). The two pharmaceutical forms used were either a lyophilized powder in a single-dose vial or a lyophilized powder and water for solution for injection in a single-dose pre-filled Dual-Chamber Syringe, both for subcutaneous use after reconstitution.

As the paediatric development is still on going in the subset from 2 to 11 years of age, the final paediatric formulation is not yet selected.

## *2.3. Clinical aspects*

### 2.3.1. Introduction

The MAH submitted a final report for:

- Study RD.06.SPR.118126 - A Multicenter, Open-Label, Single-Group Clinical Trial to Assess the Pharmacokinetics, Safety and Efficacy of Nemolizumab (CD14152) in Pediatric Subjects (aged 2 to 11 years) with Moderate-to-Severe Atopic Dermatitis

## 2.3.2. Clinical study

## Study RD.06.SPR.118126 - A Multicenter, Open-Label, Single-Group Clinical Trial to Assess the Pharmacokinetics, Safety and Efficacy of Nemolizumab (CD14152) in Pediatric Subjects (aged 2 to 11 years) with Moderate-to-Severe Atopic Dermatitis

## Description

This Phase 2, multicenter, open-label, single-arm study evaluated the PK, safety, and efficacy of nemolizumab in pediatric subjects (2 to 11 years of age) with moderate-to-severe AD not adequately controlled with topical treatments. The study was performed in the following countries: Hungary (1 center), Poland (6 centers), Spain (2 centers), and United States (8 centers).

Each cohort included a ≥14-day run-in period, a 16-week Treatment Period, a 36-week extension of treatment, and an 8-week Follow-up Period (see Figure 1). Subjects who prematurely discontinued the study before the Week 48 visit were to be followed for 12 weeks after their last dose of study drug.

Subjects meeting the eligibility criteria initiated or continued moisturizer use at screening and were also provided or prescribed background topical therapy for AD (including a medium-potency TCS for the body, and a low-potency TCS or topical calcineurin inhibitor for sensitive areas such as the face, neck, intertriginous areas) for use throughout the study. Use of this authorized background therapy was required for ≥14 days before baseline/Day 1 (i.e., during the run-in period). Subjects who continued to meet the eligibility criteria at the baseline visit were enrolled in the study.

At baseline, eligible subjects entered a 16-week initial Treatment Period with nemolizumab administered subcutaneously every 4 weeks (Q4W) after a loading dose (LD) at baseline/Day 1.

Three interim analyses (IAs) were planned and performed for this study: IA #1 for Cohort 1, IA #1.1 for Cohort 1.1, and IA #2 for Cohort 2. Each IA was performed after the first 18 subjects in their respective cohort completed the Week 16 visit.

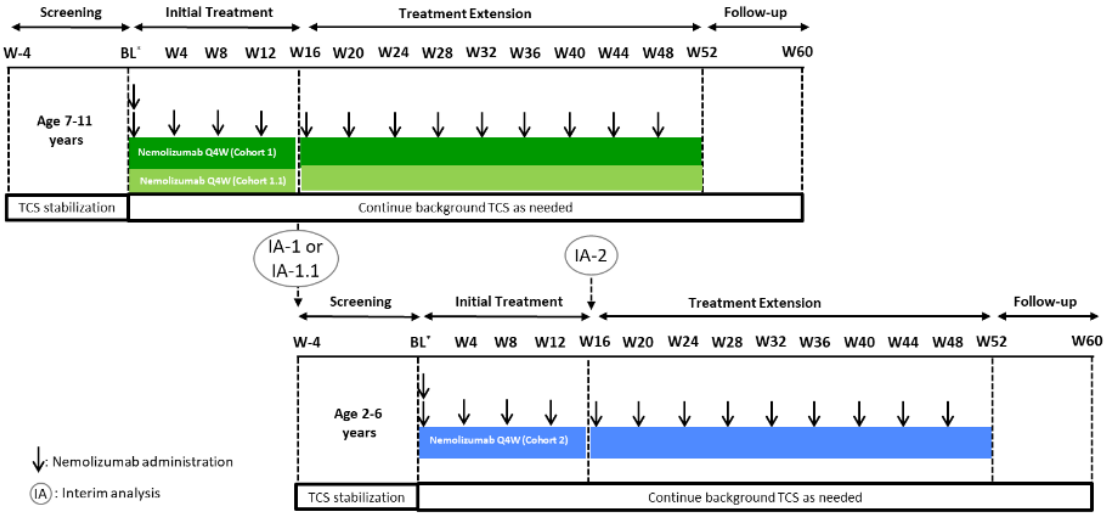
Each IA focused on PK and safety and assessed whether the observed PK and safety data from each cohort were similar to the data obtained in adolescent and adult subjects. During each IA, enrolment continued in each cohort. Each cohort was assessed for:

1. Safety by the Independent Data Monitoring Committee (IDMC) and the Sponsor. The IDMC reviewed and monitored subject safety and provided recommendations based on the safety of the subjects.

2. Drug exposure and dose confirmation by the Sponsor.

This clinical study report presents final results from all cohorts.

**Figure 1: Study design**




BL=baseline; IA=interim analysis; Q4W=every 4 weeks; TCS= topical corticosteroid(s); W=week
* The planned dose for each subject was based on subject body weight. See the table below for the pediatric dose for each cohort.
IA-1, IA-1.1, and IA-2 were initiated after approximately 18 subjects in their respective cohort completed the Week 16 visit.

## Methods

### *Study participants*

The study planned to enroll approximately 105 subjects in 3 cohorts of 35 subjects each as follows:

- Cohort 1: Subjects 7 to 11 years of age
- Cohort 1.1: Subjects 7 to 11 years of age
- Cohort 2: Subjects 2 to 6 years of age

A total of 126 subjects were screened and 109 subjects (36 Cohort 1, 37 Cohort 1.1, and 36 Cohort 2) were enrolled and received at least 1 dose of study drug.

Key inclusion criteria included male or female subjects ≥7 to <12 years of age or ≥2 to <7 years of age with chronic AD documented for at least 1 year (for subjects 7 to 11 years of age) and at least 6 months (for subjects 2 to 6 years of age) before the screening visit. and confirmed according to the American Academy of Dermatology Consensus Criteria, documented history of inadequate response to existing topical medications or use of systemic therapies for disease control, and the following at both screening and baseline: Eczema Area and Severity Index (EASI) score ≥16, Investigator's Global Assessment (IGA) score ≥3, AD involvement ≥10% of body surface area (BSA), Peak Pruritus Numerical Rating Scale (PP NRS) score ≥4.0.

Key exclusion criteria included body weight <10 kg and 1 or more of the following at screening or baseline: documented asthma exacerbation requiring hospitalization in the preceding 12 months; asthma that had not been well controlled; childhood Asthma Control Test (cACT) ≤19 (subjects 7 to 11 years of age with a history of asthma); or peak expiratory flow (PEF) <80% of the predicted value (subjects 7 to 11 years of age).

***Treatments***

The proposed dose for subjects aged 2 to 11 years was initially selected based on a modeling and simulation approach, with the objective of achieving the same systemic exposure observed in adults and 12- to 17-year-old adolescents with 30-mg dosing (with a 60-mg LD).

Patients in cohort 1 received the initially selected dose, see Table 1.

The observed mean steady-state systemic exposure in cohort 1 was approximately 2-fold higher than that observed in adults and 12- to 17-year-old adolescents.

Patients in cohort 1.1 and cohort 2 received a reduced dose (for subjects with bw ≥10 kg; 5-mg Q4W with a 10-mg LD, bw ≥20 kg; 10-mg Q4W with a 20-mg LD and bw ≥30 kg; 15-mg Q4W with a 30-mg LD), see Table 1.

**Table 1: Doses in study Study RD.06.SPR.118126.**

| Body weight[a] | Q4W – dose | | | Baseline – loading dose | | |
|---|---|---|---|---|---|---|
| | Dose | Formulation presentation | # of injections | Loading dose | Formulation presentation | # of injections |
| **Cohort 1** | | | | | | |
| ≥10 kg and <20 kg | 10 mg | 10 mg vial | 1 | 20 mg | 20 mg vial | 1 |
| ≥20 kg and <30 kg | 20 mg | 20 mg vial | 1 | 40 mg | 20 mg vial | 2 |
| ≥30 kg | 30 mg | 30 mg DCS | 1 | 60 mg | 30 mg DCS | 2 |
| **Cohort 1.1 and Cohort 2** | | | | | | |
| ≥10 kg and <20 kg | 5 mg | 10 mg vial[b] | 1 | 10 mg | 10 mg vial | 1 |
| ≥20 kg and <30 kg | 10 mg | 10 mg vial | 1 | 20 mg | 20 mg vial | 1 |
| ≥30 kg | 15 mg | 20 mg vial[c] | 1 | 30 mg | 30 mg DCS | 1 |

DCS=dual-chamber syringe; Q4W=every 4 weeks
a Body weight at baseline, Week 16, and Week 32
b Subjects were to receive a 5-mg dose from the 10-mg vial.
c Subjects were to receive a 15-mg dose from the 20-mg vial.

***Objective(s)***

The primary objective was to assess the pharmacokinetics (PK), safety, and tolerability of nemolizumab administered concomitantly with topical corticosteroids (TCS) in pediatric subjects with moderate-to-severe atopic dermatitis (AD) not adequately controlled with topical treatments.

The secondary objective was to assess the efficacy of nemolizumab and to further characterize the relationship between nemolizumab concentrations and clinical efficacy endpoints.

***Outcomes/endpoints***

***Primary endpoints***

Pharmacokinetics

- The primary endpoints for PK were nemolizumab serum concentrations at Weeks 4, 8, 12, 16, 32, and 52 and nemolizumab serum PK parameters extrapolated with a population PK (popPK) analysis.

Safety

- The primary endpoints for safety were the incidence of adverse events (AEs), including treatment-emergent AEs (TEAEs), AEs of special interests (AESIs), AEs leading to discontinuation, and serious AEs (SAEs), through the study. Safety assessments (vital signs, physical examinations, electrocardiogram recording, AEs, respiratory examination and assessments, and clinical laboratory results [routine hematology and biochemistry]) were performed throughout the study.

***Secondary endpoints***

Efficacy

- Absolute and percent change in EASI score (EASI-50, EASI-75, and EASI-90) from baseline at each visit up to Week 16 and up to Week 52.
- IGA success rate (defined as an IGA of 0 [clear] or 1 [almost clear] and a ≥2-point improvement from baseline) at each visit up to Week 16 and up to Week 52.
- Change in BSA involvement of AD, reported as a percentage of all major body sections combined, from baseline at each visit up to Week 16 and up to Week 52.
- Percent change in SCORing Atopic Dermatitis (SCORAD) score from baseline at each visit up to Week 16 and up to Week 52.
- Absolute and percent change in weekly average of PP NRS score from baseline at each visit up to Week 16 and up to Week 52.
- Absolute and percent change in weekly average of Average Pruritus Numeric Rating Scale (AP NRS) score from baseline at each visit up to Week 16 and up to Week 52.
- Absolute and percent change in weekly Sleep Disturbance Numeric Rating Scale (SD NRS) score from baseline at each visit up to Week 16 and up to Week 52.
- Change in Children's Dermatology Life Quality Index (cDLQI) for subjects ≥4 years of age from baseline up to Week 16 and up to Week 52.
- Change in Infants' Dermatology Quality of Life Index (IDQOL) for subjects <4 years of age from baseline up to Week 16 and up to Week 52.
- Change in Patient-Oriented Eczema Measure (POEM) from baseline up to Week 16 and up to Week 52.

PK/pharmacodynamic (PD)

- Relationship between nemolizumab concentrations and clinical efficacy endpoints (PP NRS, EASI, and IGA).

Immunogenicity

- Anti-drug antibody (ADA) assessments (screening, confirmatory, neutralizing antibodies) at baseline, Weeks 16, 52, and unscheduled visits that were conducted for safety reasons.

***Sample size***

The study planned to enroll approximately 105 subjects in 3 cohorts of 35 subjects each: Cohort 1 (subjects 7 to 11 years of age), Cohort 1.1 (subjects 7 to 11 years of age), and Cohort 2 (subjects 2 to 6 years of age). A total of 126 subjects were screened and 109 subjects (36 Cohort 1, 37 Cohort 1.1, and 36 Cohort 2) were enrolled and received at least 1 dose of study drug.

***Randomisation and blinding (masking)***

***Statistical Methods***

Subject disposition, demographic and baseline characteristics, and medical history were summarized by descriptive statistics for the intent-to-treat (ITT) set, which consisted of all enrolled subjects.

*Pharmacokinetic*

Pharmacokinetic analysis was performed on the PK set, including all subjects who received at least 1 dose of study drug and had at least 1 measurable post-baseline concentration. Trough nemolizumab concentrations were summarized using descriptive statistics (number of observations [n], arithmetic mean, standard deviation, coefficient of variation%, 95% confidence interval of arithmetic mean, geometric mean, minimum, first quartile, median, third quartile, maximum, and number of samples below the limit of quantification) by cohort, body weight (where applicable), and timepoint. Weight categories from Week 4 to Week 16 were based on body weight at baseline. Weight categories for Week 32 and Week 52 were based on body weight at Week 16 and Week 32, respectively. Serum concentrations below the limit of quantification were treated as missing for calculation of concentration descriptive statistics.

Pharmacokinetic parameters were derived using a non-linear mixed effect modeling approach. A pre-specified popPK model based on information from previous studies in adults and adolescents was used to derive empirical Bayesian estimates in the pediatric population based on their baseline characteristics, dosing history, and measured concentrations. The adequacy of the model to properly describe the pediatric data was based on the model diagnostic tools and described in a separate modeling and simulation plan.

## Results

***Baseline Demographics***

A total of 109 subjects were enrolled and received at least 1 dose of study drug. Of the 109 enrolled subjects, 6 (5.5%) subjects early terminated. The most common reason for ET was subject/caregiver request (11.1%, 0%, and 0% in Cohort 1, Cohort 1.1, and Cohort 2, respectively).

The majority of subjects were White and not Hispanic or Latino. Based on study design, the mean age of subjects in Cohort 1 and Cohort 1.1 was higher (8.9 and 8.6 years, respectively) than subjects in Cohort 2 (3.8 years). Consequently, mean height and mean body weight were higher in Cohort 1 and Cohort 1.1 than in Cohort 2. Other demographic and baseline characteristics were generally similar among cohorts.

***Efficacy results***

In each cohort, clinically meaningful mean reductions and mean percent reductions in EASI total score were observed as early as Week 4 and increased over time.

The proportion of all subjects with EASI-75 (defined as a ≥75% improvement in EASI from baseline) was 45.0% at Week 4 and increased to 88.0% at Week 52. A similar pattern was observed at Week 4 and Week 52 in Cohort 1 (27.8% and 93.8%, respectively), Cohort 1.1 (48.6% and 82.9%, respectively), and Cohort 2 (58.3% and 87.9%, respectively).

The proportion of all subjects with EASI-90 (defined as a ≥90% improvement in EASI from baseline) was 23.9% at Week 4 and increased to 67.0% at Week 52. A similar pattern was observed at Week 4 and Week 52 in Cohort 1 (8.3% and 68.8%, respectively), Cohort 1.1 (35.1% and 57.1%, respectively), and Cohort 2 (27.8% and 75.8%, respectively).

The proportion of all subjects with IGA success (defined as an IGA of 0 [clear] or 1 [almost clear] and a ≥2-grade improvement from baseline) was 24.8% at Week 4 and increased to 60.0% at Week 52, with a similar pattern observed at Week 4 and Week 52 in Cohort 1 (13.9% and 46.9%, respectively), Cohort 1.1 (32.4% and 60.0%, respectively), and Cohort 2 (27.8% and 72.7%, respectively).

The mean weekly average PP NRS at baseline was 7.39 overall, and 7.33, 7.34, and 7.49 in Cohort 1, Cohort 1.1, and Cohort 2, respectively, with a mean change from baseline of -5.54, -4.66, -5.62, and -6.32, respectively, at Week 52. The mean percent reduction in weekly average PP NRS overall, and in Cohort 1, Cohort 1.1, and Cohort 2 was -75.49%, -65.73%, -75.85%, and -84.82%, respectively, at Week 52.

The proportion of all subjects with an improvement of ≥4 points from baseline in weekly average PP NRS was 9.3% at Week 1 and increased to 78.0% at Week 52. A similar pattern was observed at Week 1 and Week 52 in Cohort 1 (0% and 65.4%, respectively), Cohort 1.1 (8.3% and 80.0%, respectively), and Cohort 2 (76.5% and 88.5%, respectively).

The mean weekly average AP NRS at baseline was 6.78 overall, and 6.61, 6.63, and 7.10 in Cohort 1, Cohort 1.1, and Cohort 2, respectively, with a mean change from baseline of -5.20, -4.53, -5.19, and -5.89, respectively, at Week 52. The mean percent reduction in weekly average AP NRS overall, and in Cohort 1, Cohort 1.1, and Cohort 2 was -78.39%, -71.11%, -78.63%, and -85.40%, respectively, at Week 52.

The mean weekly average SD NRS at baseline was 6.51 overall, and 5.97, 6.42, and 7.14 in Cohort 1, Cohort 1.1, and Cohort 2, respectively, with a mean change from baseline of -5.04, -4.25, -5.02, and -5.87, respectively, at Week 52. The mean percent reduction in weekly average SD NRS overall, and in Cohort 1, Cohort 1.1, and Cohort 2 was -79.08 %, -75.37%, -77.67%, and -84.52%, respectively, at Week 52.

The percentage of subjects using a rescue therapy at any visit during the Treatment Period was 7.3% overall, and 13.9%, 2.7%, and 5.6% in Cohort 1, Cohort 1.1, and Cohort 2, respectively.

By Week 52, the mean percent reduction in SCORAD in all subjects was -75.26%; similar mean percent reductions were observed in Cohort 1 (-72.03%), Cohort 1.1 (-74.60%), and Cohort 2 (-79.09%).

The mean cDLQI total score in all subjects was 15.12 at baseline. Mean reductions in cDLQI total score increased over time, with a mean change of -11.55 at Week 52. A similar pattern was observed in Cohort 1, Cohort 1.1, and Cohort 2, with mean reductions of -10.72, -11.97, and -12.00, respectively, at Week 52. The mean IDQOL total score at baseline was 19.07 in Cohort 2; mean reductions in IDQOL total score generally increased over time, with a mean change of -13.27 at Week 52.

In each cohort, nemolizumab was effective in reducing the POEM total score compared with baseline at Week 52.

In summary, the treatment effect of nemolizumab in pediatric subjects with moderate-to-severe AD not adequately controlled with topical treatments increased over time in this study in all cohorts.

***Pharmacokinetic results***

The proposed dose for subjects aged 2 to 11 years was initially selected based on a modeling and simulation approach, with the objective of achieving the same systemic exposure observed in adults and 12- to 17-year-old adolescents with 30-mg dosing (with a 60-mg LD). Adults and adolescents enrolled in the phase 3 studies were used as the reference to match nemolizumab exposure levels in children aged 2 to 11 years. In pivotal Phase 3 studies median steady-state observed concentration at week 16 ranged from 2.42 µg/mL (P5-P95: 0.78 -5.12) in adults to 3.06 µg/mL (P5-P95: 0.50-6.59) in adolescents.

The observed mean steady-state systemic exposure in Cohort 1 was approximately 2-fold higher than that observed in adults and adolescents 12 to 17 years of age, see Table 2. The observed mean steady-state systemic exposure in Cohort 1.1 and Cohort 2, with lower doses, was approximately 2-fold lower than that observed in Cohort 1. Overall, results of Cohort 1.1 and Cohort 2 in 2- to 11-year-old children showed that a body weight dose adjustment for subjects weighing ≥10 kg (i.e., 5 mg with a 10-mg LD), for subjects weighing ≥20 kg (i.e., 10 mg with a 20-mg LD), and for subjects weighing ≥30 kg (i.e., 15 mg with a 30-mg LD) provides comparable systemic exposure as the dose level in adults and adolescents (i.e., 30-mg dose with a 60-mg LD).

In all 3 cohorts, the consistency of trough concentration measured across sampling times and the accumulation ratios below 1 confirmed steady-state condition was reached at Week 4 after the LD.

**Table 2: Observed Ctrough serum nemolizumab concentrations in µg/mL (mean±SD) (PK set)**

| | Cohort 1 (7-11 yo) (N=36) | | Cohort 1.1 (7-11 yo) (N=37) | | Cohort 2 (2-6 yo) (N=36) | | |
|---|---|---|---|---|---|---|---|
| **Dose** | **20 mg (40-mg LD)** | **30 mg (60-mg LD)** | **10 mg (20-mg LD)** | **15 mg (30-mg LD)** | **5 mg (10-mg LD)** | **10 mg (20-mg LD)** | **15 mg (30-mg LD)** |
| **Weight range** | **≥20 kg and <30 kg** | **≥30 kg** | **≥20 kg and <30 kg** | **≥30 kg** | **≥10 kg and <20 kg** | **≥20 kg and <30 kg** | **≥30 kg** |
| Week 4 | 5.29±1.81 (n=17) | 6.53±2.46 (n=19) | 2.45±0.72 (n=16) | 3.24±0.87 (n=21) | 2.56±0.81 (n=23) | 4.15±1.31 (n=10) | 4.43 (n=1) |
| Week 8 | 4.84±2.11 (n=17) | 5.43±2.21 (n=19) | 2.46±0.96 (n=16) | 3.06±0.95 (n=21) | 2.11±0.94 (n=24) | 3.52±1.60 (n=10) | 3.62 (n=1) |
| Week 12 | 4.44±1.67 (n=17) | 5.01±1.66 (n=18) | 2.10±0.77 (n=16) | 2.88±1.34 (n=21) | 2.09±1.29 (n=20) | 3.26±1.50 (n=9) | 3.63 (n=1) |
| Week 16 | 4.15±1.37 (n=16) | 5.03±1.80 (n=19) | 1.64±0.60 (n=14) | 2.44±1.11 (n=20) | 2.12±1.45 (n=23) | 2.94±1.51 (n=10) | 4.48 (n=1) |
| Week 32 | 4.32±1.99 (n=15) | 4.44±2.23 (n=19) | 2.21±0.71 (n=14) | 3.14±1.26 (n=20) | 2.26±1.46 (n=21) | 3.05±1.44 (n=10) | 2.89-4.93[a] (n=2) |
| Week 52 | 3.24±1.07 (n=12) | 5.14±2.85 (n=19) | 1.67±0.64 (n=13) | 2.60±0.93 (n=22) | 2.17±1.46 (n=18) | 3.08±1.30 (n=13) | 4.58-4.69 (n=2) |

$C_{trough}$=trough concentration; LD=loading dose; PK=pharmacokinetic; SD=standard deviation
Mean±SD $C_{trough}$ are presented in µg/mL by dividing the $C_{trough}$ concentration in listing (unit: ng/mL) by 1000.
a) n=2, individual values presented

***Immunogenicity results***

Treatment-emergent ADAs with low titers (9.9 - 40) were observed only in Cohort 1 in 4 pediatric subjects out of 36. None of these subjects had Nabs.

***Safety results***

No clinically meaningful differences in the safety results were observed overall or among cohorts.

Among the 109 subjects 2 to 11 years of age, 94 (86.2%) experienced at least 1 TEAE during the Treatment Period (up to Week 52)/ET. Of these subjects, the majority experienced TEAEs that were considered mild or moderate in severity. The most common TEAEs experienced during the Treatment Period (up to Week 52)/ET were upper respiratory tract infection, nasopharyngitis, and bronchitis. Twelve (11.0%) subjects experienced at least 1 TEAE during the Follow-up Period; the only TEAEs experienced by >1 subject during the Follow-up Period were nasopharyngitis and upper respiratory tract infection.

Study drug-related TEAEs were experienced by 22 (20.2%) subjects; study drug-related TEAEs experienced by >1 subject during the Treatment Period (up to Week 52)/ET were upper respiratory tract infection, bronchitis, herpes virus infection, and impetigo. No subject experienced a study drug-related TEAE during the Follow-up Period.

No subject experienced a TEAE leading to death, a treatment-emergent SAE, or a TEAE leading to treatment discontinuation. One subject in Cohort 1 experienced a TEAE (lower respiratory tract infection) that led to study discontinuation; the event was considered not related to study drug or protocol procedure, mild in severity, and resolved.

No subject experienced an injection-related reaction, an AESI of peripheral edema: limbs, bilateral, or had alanine aminotransferase or aspartate aminotransferase >3×upper limit of normal in combination with elevated bilirubin >2×upper limit of normal during the study. No subject experienced an AESI during the Follow-up Period.

Among all subjects, 3 (2.8%) experienced an AESI of infection; 2 (1.8%) experienced an AESI of COVID-19, and 1 (0.9%) each experienced an AESI of asymptomatic COVID-19 and impetigo. All AESIs of infection were non-serious, considered mild or moderate in severity, and resolved; only 1 event (impetigo) was considered study drug-related.

One (0.9%) subject experienced an AESI of facial edema (lip swelling), which was considered mild in severity, not related to study drug or protocol procedure, and resolved the same day.

Three (2.8%) subjects experienced an AESI with a PT of asthma and 1 (0.9%) subject experienced an AESI with a PT of peak expiratory flow rate decreased; each event was non-serious, considered mild or moderate in severity, not related to study drug or protocol procedure, and resolved.

Five (4.6%) subjects had TEAEs adjudicated by the IAC during the Treatment Period (up to Week 52)/ET; no subject experienced confirmed new onset asthma. Three (2.8%) subjects experienced confirmed worsening of (pre-existing) asthma (all 3 subjects reported the PT of asthma); each event was non-serious, considered mild in severity (as adjudicated by the IAC), not related to study drug or protocol procedure, and resolved.

No notable trends over time were observed for laboratory parameters, vital signs, electrocardiograms, physical examinations, PEF assessments, or the cACT.

A summary of study drug-related TEAEs during the Treatment Period is presented by cohort in Table 3. Study drug-related TEAEs experienced by >1 subject during the Treatment Period (up to Week 52)/ET in subjects 2 to 11 years of age were upper respiratory tract infection (6 [5.5%] subjects) and bronchitis, herpes virus infection, and impetigo (2 [1.8%] subjects each).

**Table 3: Treatment-related TEAEs during the initial treatment period (up to week 16)/ET and during the treatment period (up to week 52)/ET (safety set)**

| | Initial Treatment Period (up to Week 16)/ET | | | | | Treatment Period (up to Week 52)/ET | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| System organ class<br>Preferred term | Cohort 1 (7-11 yo) N=36 n (%) | Cohort 1.1 (7-11 yo) N=37 n (%) | Cohort 2 (2-6 yo) N=36 n (%) | Overall (7-11 yo) N=73 n (%) | Overall (2-11 yo) N=109 n (%) | Cohort 1 (7-11 yo) N=36 n (%) | Cohort 1.1 (7-11 yo) N=37 n (%) | Cohort 2 (2-6 yo) N=36 n (%) | Overall (7-11 yo) N=73 n (%) | Overall (2-11 yo) N=109 n (%) |
| Subjects with at least 1 treatment-related TEAE | 3 (8.3) | 3 (8.1) | 6 (16.7) | 6 (8.2) | 12 (11.0) | 7 (19.4) | 8 (21.6) | 7 (19.4) | 15 (20.5) | 22 (20.2) |
| Infections and infestations | 2 (5.6) | 2 (5.4) | 4 (11.1) | 4 (5.5) | 8 (7.3) | 6 (16.7) | 6 (16.2) | 4 (11.1) | 12 (16.4) | 16 (14.7) |
| Bronchitis | 0 | 0 | 1 (2.8) | 0 | 1 (0.9) | 1 (2.8) | 0 | 1 (2.8) | 1 (1.4) | 2 (1.8) |
| Herpes simplex | 1 (2.8) | 0 | 0 | 1 (1.4) | 1 (0.9) | 1 (2.8) | 0 | 0 | 1 (1.4) | 1 (0.9) |
| Herpes virus infection | 0 | 0 | 1 (2.8) | 0 | 1 (0.9) | 1 (2.8) | 0 | 1 (2.8) | 1 (1.4) | 2 (1.8) |
| Herpes zoster | 0 | 1 (2.7) | 0 | 1 (1.4) | 1 (0.9) | 0 | 1 (2.7) | 0 | 1 (1.4) | 1 (0.9) |
| Impetigo | 0 | 1 (2.7) | 0 | 1 (1.4) | 1 (0.9) | 1 (2.8) | 1 (2.7) | 0 | 2 (2.7) | 2 (1.8) |
| Laryngitis | 0 | 0 | 0 | 0 | 0 | 1 (2.8) | 0 | 0 | 1 (1.4) | 1 (0.9) |
| Nasopharyngitis | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.7) | 0 | 1 (1.4) | 1 (0.9) |
| Oral herpes | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.7) | 0 | 1 (1.4) | 1 (0.9) |
| Otitis media | 0 | 0 | 1 (2.8) | 0 | 1 (0.9) | 0 | 0 | 1 (2.8) | 0 | 1 (0.9) |
| Upper respiratory tract infection | 0 | 0 | 2 (5.6) | 0 | 2 (1.8) | 2 (5.6) | 2 (5.4) | 2 (5.6) | 4 (5.5) | 6 (5.5) |
| Urinary tract infection | 1 (2.8) | 0 | 0 | 1 (1.4) | 1 (0.9) | 1 (2.8) | 0 | 0 | 1 (1.4) | 1 (0.9) |
| Blood and lymphatic system disorders | 0 | 0 | 1 (2.8) | 0 | 1 (0.9) | 1 (2.8) | 0 | 1 (2.8) | 1 (1.4) | 2 (1.8) |
| Eosinophilia | 0 | 0 | 1 (2.8) | 0 | 1 (0.9) | 0 | 0 | 1 (2.8) | 0 | 1 (0.9) |
| Leukopenia | 0 | 0 | 0 | 0 | 0 | 1 (2.8) | 0 | 0 | 1 (1.4) | 1 (0.9) |
| Gastrointestinal disorders | 0 | 1 (2.7) | 0 | 1 (1.4) | 1 (0.9) | 0 | 1 (2.7) | 0 | 1 (1.4) | 1 (0.9) |
| Vomiting | 0 | 1 (2.7) | 0 | 1 (1.4) | 1 (0.9) | 0 | 1 (2.7) | 0 | 1 (1.4) | 1 (0.9) |
| General disorders and administration site conditions | 1 (2.8) | 0 | 0 | 1 (1.4) | 1 (0.9) | 1 (2.8) | 0 | 0 | 1 (1.4) | 1 (0.9) |
| Injection site erythema | 1 (2.8) | 0 | 0 | 1 (1.4) | 1 (0.9) | 1 (2.8) | 0 | 0 | 1 (1.4) | 1 (0.9) |
| Reproductive system and breast disorders | 0 | 0 | 1 (2.8) | 0 | 1 (0.9) | 0 | 0 | 1 (2.8) | 0 | 1 (0.9) |
| Breast hyperplasia | 0 | 0 | 1 (2.8) | 0 | 1 (0.9) | 0 | 0 | 1 (2.8) | 0 | 1 (0.9) |
| Respiratory, thoracic and mediastinal disorders | 0 | 0 | 1 (2.8) | 0 | 1 (0.9) | 0 | 0 | 1 (2.8) | 0 | 1 (0.9) |
| Oropharyngeal pain | 0 | 0 | 1 (2.8) | 0 | 1 (0.9) | 0 | 0 | 1 (2.8) | 0 | 1 (0.9) |
| Eye disorders | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.7) | 1 (2.8) | 1 (1.4) | 2 (1.8) |
| Astigmatism | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.7) | 0 | 1 (1.4) | 1 (0.9) |
| Hypermetropia | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.8) | 0 | 1 (0.9) |
| Myopia | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.7) | 0 | 1 (1.4) | 1 (0.9) |
| Investigations | 0 | 0 | 0 | 0 | 0 | 1 (2.8) | 0 | 0 | 1 (1.4) | 1 (0.9) |
| Electrocardiogram QT prolonged | 0 | 0 | 0 | 0 | 0 | 1 (2.8) | 0 | 0 | 1 (1.4) | 1 (0.9) |
| Skin and subcutaneous tissue disorders | 0 | 0 | 0 | 0 | 0 | 1 (2.8) | 0 | 0 | 1 (1.4) | 1 (0.9) |
| Pityriasis | 0 | 0 | 0 | 0 | 0 | 1 (2.8) | 0 | 0 | 1 (1.4) | 1 (0.9) |

ET=early termination; N=number of subjects in the population; n=number of subjects who experienced the event; TEAE=treatment-emergent adverse event; ; yo=years of age

Note: Percentages were calculated using N of each column as the denominator. At each level of subject summarization, a subject was counted once if the subject reported 1 or more events. Initial treatment period Week 16/ET was defined as the period from Day 1 (baseline) up to Week 16 visit date or, for early terminated subjects, until 28 days after last dosing date or ET date, whichever occurred first. Treatment period Week 52/ET was defined as the period from Day 1 (baseline) up to Week 52 visit date or, for early terminated subjects, until 28 days after last dosing date or ET date, whichever occurred first. Adverse events were coded using the Medical Dictionary for Regulatory Activities Version 25.0.

## The MAH´s conclusions

The proposed dose for subjects aged 2 to 11 years was initially selected based on a modeling and simulation approach, with the objective of achieving the same systemic exposure observed in adults and 12- to 17-year-old adolescents with 30-mg dosing (with a 60-mg LD).

The observed mean steady-state systemic exposure in Cohort 1 was approximately 2-fold higher than that observed in adults and 12- to 17-year-old adolescents. After dose reduction, results of Cohort 1.1 and Cohort 2 in 2- to 11-year-old children showed that a body weight dose adjustment for subjects weighing ≥10 kg (i.e., 5-mg with a 10-mg LD), for subjects weighing ≥20 kg (i.e., 10-mg with a 20-mg LD) and for subjects weighing ≥30 kg (i.e., 15-mg with a 30-mg LD) provide comparable systemic exposure as the dose level in adults and adolescents (i.e., 30-mg dose with a 60-mg LD).

Nemolizumab was safe and well tolerated for all subjects 2 to 11 years of age with moderate-to-severe AD, with no new safety signals identified.

Clinically meaningful improvements in itch and skin lesions over time were observed in all cohorts. All pruritus endpoints showed consistent improvements from baseline early in the Treatment Period that generally increased through Week 52.

### 2.3.3. Discussion on clinical aspects

The observed mean steady-state systemic exposure in Cohort 1 was approximately 2-fold higher than that observed in adults and adolescents 12 to 17 years of age. After dose reduction, administered doses in Cohort 1.1 and Cohort 2 provides comparable systemic exposure as the dose level in adults and adolescents (i.e., 30-mg dose with a 60-mg LD).

The population PK and PK/PD analyses has not been assessed within this procedure, and full assessments will be performed in a future Type II variation.

Efficacy was analysed as secondary endpoints and will not be further commented on in this report.

No new safety signals were observed, the safety results were consistent with currently documented safety profile of the product.

## 3. CHMP overall conclusion and recommendation

The final results of study RD.06.SRE.118126, assessing the pharmacokinetics, safety and efficacy of nemolizumab in subjects 2 to 11 years with moderate-to-severe atopic dermatitis, have been reported. The assessment of the benefit-risk profile of nemolizumab is not affected by this study. The MAH has not suggested any update to the Summary of Product Characteristics based on the performed study, which is supported by the CHMP.

☒ **Fulfilled:**

No regulatory action required.

# Annex. Line listing of all the studies included in the development program

The studies should be listed by chronological date of completion:

## Non clinical studies

Product Name: Active substance:

| Study title | Study number | Date of completion | Date of submission of final study report |
|---|---|---|---|
| | | | |
| | | | |
| | | | |

## Clinical studies

Product Name: **Nemluvio** Active substance: **nemolizumab**

| Study title | Study number | Date of completion | Date of submission of final study report |
|---|---|---|---|
| A Multicenter, Open-Label, Single-Group Clinical Trial to Assess the Pharmacokinetics, Safety and Efficacy of Nemolizumab (CD14152) in Pediatric Subjects (aged 2 to 11 years) with Moderate-to-Severe Atopic Dermatitis | RD.06.SPR.118126<br><br>Study 12 in the agreed PIP | Date of last subject completed the study: 28 Apr 2025 | 28 Oct 2025 |
| Double-blind, randomised, placebo-controlled trial to evaluate efficacy and safety of nemolizumab in children from 2 years to less than 12 years with moderate to severe atopic dermatitis | RD.06.SPR.204784<br><br>Study 13 in the agreed PIP | Not yet started<br><br>Further to the PK Study 118126 completion and with the addition of a new PK/PD Modeling and Simulation Report, the Applicant is planning to submit a Request for Modification (RfM08) to the agreed PIP to modify the objectives of PIP Studies 13 and 14. | Not Applicable |
| Open-label, long-term, extension trial to evaluate safety and activity of nemolizumab in children from 2 years to less than 12 years with moderate to severe atopic dermatitis | RD.06.SPR.205513<br><br>Study 14 in the agreed PIP | | Not Applicable |