SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1 NAME OF THE MEDICINAL PRODUCT

Nemluvio 30 mg powder and solvent for solution for injection in pre-filled syringe

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each single-use pre-filled syringe contains 30 mg of nemolizumab per 0.49 ml dose following reconstitution.

Nemolizumab, an interleukin-31 receptor alpha (IL-31RA) antagonist, is a humanized monoclonal modified immunoglobulin G (IgG) antibody targeting IL-31RA. Nemolizumab is produced by recombinant DNA technology in Chinese Hamster Ovary cells.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder and solvent for solution for injection

Powder: lyophilised white powder.

Solvent: A clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Atopic dermatitis (AD)

Nemluvio is indicated for the treatment of moderate-to-severe atopic dermatitis in combination with topical corticosteroids and/or calcineurin inhibitors in adults and adolescents 12 years and older with a body weight of at least 30 kg, who are candidates for systemic therapy.

Prurigo nodularis (PN)

Nemluvio is indicated for the treatment of adults with moderate-to-severe prurigo nodularis who are candidates for systemic therapy.

4.2 Posology and method of administration

Posology

Atopic dermatitis (AD)

The recommended dosage of Nemluvio is:

- An initial dose of 60 mg (two 30 mg injections), followed by 30 mg given every 4 weeks (Q4W)

- After 16 weeks of treatment, for patients who achieve clinical response, the recommended maintenance dose of Nemluvio is 30 mg every 8 weeks (Q8W).

Concomitant Topical Therapies:

Use Nemluvio with topical corticosteroids and/or topical calcineurin inhibitors. When the disease has sufficiently improved, discontinue use of topical therapies.

Consideration should be given to discontinuing treatment with Nemluvio in patients who have shown no response after 16 weeks of treatment.

Prurigo nodularis (PN)

The recommended dose of Nemluvio for patients weighing < 90 kg is an initial dose of 60 mg (two 30 mg injections), followed by 30 mg given every 4 weeks (Q4W).

The recommended dose of Nemluvio for patients weighing ≥ 90 kg is an initial dose of 60 mg dose (two 30 mg injections), followed by 60 mg given every 4 weeks (Q4W).

Consideration should be given to discontinuing treatment in patients who have shown no response after 16 weeks of treatment for prurigo nodularis.

Missed dose

If a dose is missed, administer the dose as soon as possible. Thereafter, resume dosing at the regular scheduled time.

Special populations

Elderly (≥ 65 years)

No dose adjustment is recommended for elderly patients (see section 5.2).

Hepatic and Renal impairment

No dose adjustment is needed in patients with hepatic or renal impairment (see section 5.2).

Body weight

No dose adjustment for body weight is recommended for patients 12 years of age and older with atopic dermatitis (see section 5.2).

For patients with prurigo nodularis and with body weight ≥ 90 kg, the 60 mg dose (two 30 mg injections) is recommended (see section 5.2).

Paediatric population

The safety and efficacy of Nemluvio in children with moderate-to-severe atopic dermatitis younger than 12 years old have not yet been established.

The safety and efficacy of Nemluvio has not been established in patients below the age of 18 years with prurigo nodularis.

Method of administration

Subcutaneous use.

Administer subcutaneous injection into the front upper thighs or abdomen avoiding the 5 cm area around the navel. Injection into the upper arm should only be performed by a caregiver or healthcare professional.

For the initial dose, administer each of the two Nemluvio injections at different injection sites.

For subsequent doses, it is recommended to rotate the injection site with each dose. Nemluvio should not be injected into skin that is tender, inflamed, swollen, damaged or has bruises, scars or open wounds.

Nemluvio is intended for use under the guidance of a healthcare professional. A patient may self-inject Nemluvio or the patient's caregiver may administer Nemluvio if their healthcare professional determines that this is appropriate. Prior to first injection, patients and/or caregivers should be given proper instructions for preparation and administration of Nemluvio according to the instructions for use at the end of the package leaflet.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Hypersensitivity

If a systemic hypersensitivity reaction (immediate or delayed) occurs, administration of Nemluvio should be discontinued and appropriate therapy initiated.

Vaccinations

Consider completing all age-appropriate vaccinations as recommended by current immunization guidelines prior to initiating treatment with Nemluvio. Avoid use of live vaccines in patients treated with Nemluvio. It is unknown if administration of live vaccines during Nemluvio treatment will impact the safety or efficacy of these vaccines. No data are available on the response to non-live vaccines.

Uncontrolled asthma

Patients with uncontrolled asthma were excluded from the trials and no data with Nemluvio are available in this population.

4.5 Interaction with other medicinal products and other forms of interaction

Interactions with cytochrome P450

The effects of nemolizumab on the pharmacokinetics of midazolam (CYP3A4/5 substrate), warfarin (CYP2C9 substrate), omeprazole (CYP2C19 substrate), metoprolol (CYP2D6 substrate), and caffeine (CYP1A2 substrate) were evaluated in a study (SPR.201593) in 14 subjects with moderate to severe AD receiving an initial subcutaneous dose of 60 mg followed by a 30-mg subcutaneous dose every 4 weeks for 12 weeks. No clinically significant changes in the exposure of CYP450 substrates before and after multiple nemolizumab injections were observed, with Cmax and AUC ratios ranging from 88.24 to 107.81%. An effect of nemolizumab on the PK of co-administered medications is not expected.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is a limited amount of data on the use of nemolizumab in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of nemolizumab during pregnancy.

Breast-feeding

No data are present on the excretion of nemolizumab in human milk. In humans, excretion of IgG antibodies in milk occurs during the first few days after birth, which is decreasing to low concentrations soon afterwards. Consequently, transfer of IgG antibodies to the newborns through milk, may happen during the first few days. In this short period, a risk to the breastfed child cannot be excluded. Afterwards, nemolizumab could be used during breast-feeding if clinically needed.

Fertility

Animal studies showed no impairment of fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Nemluvio has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most common adverse reaction in patients with atopic dermatitis is urticaria. The most common adverse reactions in patients with prurigo nodularis are headache, dermatitis atopic, eczema and eczema nummular.

Uncommon cases of hypersensitivity reactions were reported in both indications (see section 4.4).

Tabulated list of adverse reactions

The Nemluvio safety data presented in Table 1 were evaluated in a pool of three randomized, placebo-controlled trials in subjects with atopic dermatitis (1192 patients receiving Nemluvio and 640 patients receiving placebo), and two randomized, placebo-controlled trials in subjects with prurigo nodularis (370 patients receiving Nemluvio and 186 patients receiving placebo).

Listed in Table 1 are adverse reactions observed in clinical trials presented by system organ class and frequency, using the following categories: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1: List of adverse reactions

MedDRA System Organ Class	**Frequency**	**Adverse reactions**
Nervous system disorders	Common	Headache (incl. tension headache)*
Skin and subcutaneous tissue disorders	Common	Urticaria† Dermatitis atopic*, Eczema*, Eczema nummular*
	Uncommon	Angioedema*
General disorders and administration site conditions	Uncommon	Injection site reactions (includes erythema, pruritus, pain†, irritation†, bruising*)
	Rare	Injection site oedema†

†Occurred in atopic dermatitis studies

*Occurred in prurigo nodularis studies

In atopic dermatitis, the safety profile of Nemluvio through Week 52 in the open-label trial (ARCADIA LTE) was generally consistent with the safety profile observed at Week 16.

In prurigo nodularis, the safety profile of Nemluvio through Week 52 in the open-label trial (OLYMPIA LTE) was generally consistent with the safety profile observed at Week 16 and at Week 24.

Description of selected adverse reactions

Hypersensitivity

Type 1 hypersensitivity reactions (Ig-E mediated reactions) were reported in patients treated with Nemluvio in atopic dermatitis and prurigo nodularis. These included mild urticaria and one report of mild facial (peri-ocular) angioedema (0.3%) that did not lead to discontinuation of treatment. There were no reports of anaphylactic shock or serum-sickness.

Injections site reactions

The incidence of injection site reactions during the initial period was low in patients with atopic dermatitis treated either with Nemluvio (1.3% subjects) or placebo (1.1% subjects); during the maintenance period, the incidence remained low with Nemluvio Q4W (0.6%), Nemluvio Q8W (0%) and placebo (0.5%).

In patients with prurigo nodularis, the incidence of injection site reactions was low when treated either with Nemluvio (1.1%) or placebo (1.6%). There were no severe injection site reactions.

For both indications, none of the reactions led to discontinuation of treatment.

Headache

In patients with prurigo nodularis, headache was more frequently reported in Nemluvio-treated patients (7.0%) compared to patients treated with placebo (3.6%). Headache was more frequently observed in female patients in both groups. In the Nemluvio group, headache was mostly mild or moderate in severity and did not lead to discontinuation of treatment.

Eczematous reactions

In patients with prurigo nodularis, eczematous reactions such as dermatitis atopic, eczema nummular or eczema were more frequently reported in Nemluvio-treated patients compared to patients treated with placebo: dermatitis atopic (4.6% subjects versus 0.5% subject respectively), eczema (3.8% subjects versus 2.2% subjects respectively) and eczema nummular (3.5% subjects versus 0% subjects respectively). These eczematous reactions were mild or moderate in severity. Dermatitis atopic led to Nemluvio discontinuation in 2 (0.5%) patients. No event of eczema nummular or eczema led to study discontinuation.

Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity with Nemluvio.

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the trials described below with the incidence of anti-drug antibodies in other trials, including those of nemolizumab.

Anti-Drug-Antibodies (ADA) responses were not generally associated with impact on nemolizumab exposure, safety, or efficacy.

In the Phase 3 Atopic Dermatitis pivotal trials (ARCADIA 1, ARCADIA 2) and ARCADIA LTE trial up to 128 weeks, the incidence of treatment-emergent ADAs was 11.2%; neutralizing antibodies were seen in 0.5% of subjects.

In the Phase 3 Prurigo Nodularis pivotal trials (OLYMPIA 1, OLYMPIA 2) and OLYMPIA LTE trial up to 116 weeks, the incidence of treatment-emergent ADAs was 12.8%; neutralizing antibodies were seen in 3.5% of subjects.

Paediatric population

Atopic dermatitis

Adolescents (12 to 17 years of age)

The safety of Nemluvio was assessed in 176 subjects 12 to 17 years of age with moderate-to-severe atopic dermatitis enrolled in the ARCADIA 1 and ARCADIA 2

trials. The safety profile of Nemluvio in these subjects through Week 16 was similar to the safety profile seen in adults with atopic dermatitis.

The safety profile of Nemluvio in adolescent subjects followed through Week 48 was similar to the safety profile observed at Week 16. The long-term safety profile of Nemluvio in subjects 12 to 17 years of age was consistent with that seen in adults with atopic dermatitis (ARCADIA LTE).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

There is no specific treatment for Nemluvio overdose. In the event of overdosage, monitor the patient for any signs or symptoms of adverse reactions and institute appropriate symptomatic treatment immediately.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other dermatological preparations, agents for dermatitis, excluding corticosteroids, ATC code: D11AH12

Mechanism of action

Nemolizumab is a humanized monoclonal antibody of the IgG2 subclass that inhibits IL-31 signaling by binding selectively to IL-31RA. IL-31 is a neuroimmune cytokine that drives pruritus and inflammation, which are important pathophysiological components of atopic dermatitis and prurigo nodularis. IL-31 has an additional barrier dysfunction effect in atopic dermatitis, and epidermal differentiation and profibrotic effect in prurigo nodularis. Multiple cell types express IL-31RA and are activated by IL-31. Those involved in the pathophysiology of atopic dermatitis and prurigo nodularis include immune cells (e.g. mononuclear phagocytes, granulocytes) and structural cells (e.g. neurons, fibroblasts, keratinocytes). Blocking IL-31RA with nemolizumab ameliorates pruritus and inhibits inflammatory responses in both atopic dermatitis and prurigo nodularis. Additionally, nemolizumab restores barrier integrity in atopic dermatitis and normalizes epidermal differentiation by blocking profibrotic

processes in prurigo nodularis. The mechanism of action of nemolizumab has not been definitively established.

Pharmacodynamic effects

In exploratory biomarker studies conducted in the Phase 3 program, nemolizumab was found to modulate gene expression related to the pathophysiology of atopic dermatitis, with a primary impact on immune system processes, by decreasing the inflammatory and proliferative profile of specific immune cells (T-cells and monocytes/macrophages) without leading to immunosuppression.

In prurigo nodularis, nemolizumab was found to modulate molecular processes related to the pathophysiology of prurigo nodularis, with impact on pruritus, inflammation, epidermal differentiation and fibrosis.

Clinical efficacy and safety in atopic dermatitis

Adults and adolescents with atopic dermatitis

The efficacy and safety of Nemluvio with concomitant topical background therapy was evaluated in two randomized, double-blind, placebo-controlled pivotal studies (ARCADIA 1 and ARCADIA 2) that enrolled a total of 1728 subjects 12 years of age and older with moderate-to-severe atopic dermatitis not adequately controlled by topical treatments. Disease severity was defined by an Investigator's Global Assessment (IGA) score of 3 (moderate) and 4 (severe) in the overall assessment of atopic dermatitis, an Eczema Area and Severity Index (EASI) score of ≥16, a minimum body surface area (BSA) involvement of ≥10%, and a Peak Pruritus Numeric Rating Scale (PP NRS) score of ≥ 4.

Subjects in the studies received initial subcutaneous injections of either Nemluvio 60 mg, followed by 30 mg injections every 4 weeks (Q4W), or matching placebo. Concomitant low and/ or medium potency TCS and/or TCI were administered both in Nemluvio and placebo groups for at least 14 days prior to baseline and continued during the trial. Based on disease activity, these concomitant therapies could be tapered and/or discontinued at investigator discretion.

After 16 weeks, subjects achieving either EASI-75 or IGA success continued into the trial maintenance period for another 32 weeks to evaluate the maintenance of response achieved at Week 16. Nemluvio responders were re-randomized to either Nemluvio 30 mg every 4 weeks, Nemluvio 30 mg every 8 weeks or placebo every 4 weeks (all groups continued background TCS/TCI). Subjects randomized to placebo in the initial treatment period who achieved the same clinical response at Week 16 continued to receive placebo every 4 weeks. Non-responders at Week 16, subjects who lost clinical response during the maintenance period and subjects who completed maintenance period had the opportunity to enrol into the open-label trial (ARCADIA LTE) and receive treatment with Nemluvio 30 mg every 4 weeks up to 200 weeks.

Endpoints

Both ARCADIA 1 and ARCADIA 2 assessed the primary endpoints of:

- Proportion of subjects with an IGA success (defined as an IGA of 0 [clear] or 1 [almost clear] and a ≥2-point reduction from baseline) at Week 16
- Proportion of subjects with EASI-75 (≥75% improvement in EASI from baseline) at Week 16

Key secondary endpoints included PP NRS improvement ≥4 from baseline at Weeks 1, 2, 4 and 16, PP NRS <2 at Week 4 and Week 16, Sleep Disturbance Numeric Rating Scale (SD NRS) improvement ≥4 from baseline at Week 16, subjects with both EASI-75 and PP NRS improvement ≥4 from baseline at Week 16, and subjects with both IGA success and PP NRS improvement ≥4 from baseline at Week 16. Other secondary endpoints included change from baseline to week 16 in PP NRS, SD NRS, AD-associated pain frequency and intensity and Dermatology Life Quality Index (DLQI).

Baseline characteristics

In these studies, at baseline, 51.0% of subjects were male, 79.9% were White, and 15.4% of subjects were 12-17 years of age. 70% of subjects had a baseline IGA score of 3 (moderate AD), and 30% of subjects had a baseline IGA score of 4 (severe AD). The mean baseline EASI score was 27.5, the baseline weekly average PP NRS was 7.1 (severe itch), baseline weekly average SD NRS was 5.8 and the mean baseline DLQI was 15.0. Overall, 63.3% of patients received other previous systemic treatments for atopic dermatitis.

Clinical Response

ARCADIA 1 and ARCADIA 2 – Adults and Adolescents - induction period, week 0 to week 16

Nemluvio was statistically significantly superior to placebo with respect to skin-related co-primary endpoints IGA success and EASI-75 over 16 weeks (Table 2).

Table 2 – Efficacy Results of Nemluvio (30 mg Q4W) with concomitant TCS/TCI in ARCADIA 1 and ARCADIA 2 at Week 16

	ARCADIA 1		**ARCADIA 2**	
	Nemluvio + TCS/ TCI	**Placebo + TCS/ TCI**	**Nemluvio + TCS/ TCI**	**Placebo + TCS/ TCI**
Number of subjects randomized (Baseline PP NRS ≥4)	620	321	522	265
% of subjects with IGA 0 or 1[a]	35.6	24.6	37.7	26.0
Strata-adjusted proportion	11.5[#] (5.5, 17.5)		12.2[#] (5.6, 18.8)	

difference (95%CI)				
% of subjects with EASI-75[a]	43.5	29.0	42.1	30.2
Strata-adjusted proportion difference (95%CI)	14.9* (8.7, 21.1)		12.5# (5.6, 19.3)	
Number of subjects with severe pruritus (Baseline PP NRS≥7)	406	210	316	164
% of subjects with IGA 0 or 1[a]	35.5	21.4	36.7	22.0
Strata-adjusted proportion difference (95%CI)	14.3# (7.1, 21.5)		14.9# (6.7, 23.1)	
% of subjects with EASI-75[a]	41.6	23.8	41.1	25.0
Strata-adjusted proportion difference (95%CI)	18.1* (10.7, 25.5)		16.3# (7.8, 24.8)	

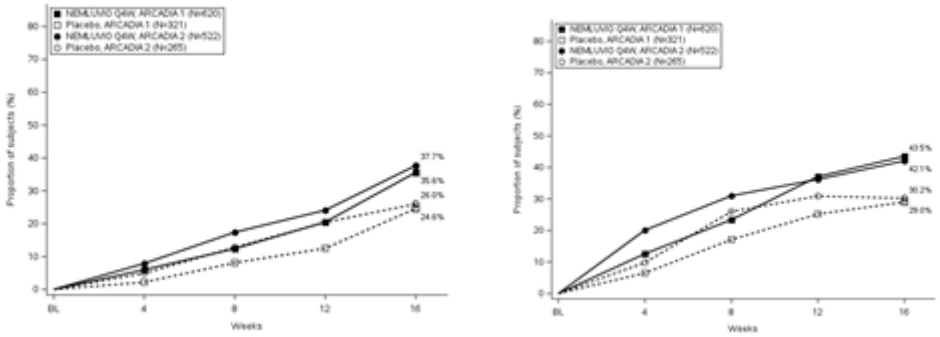
[a] Subjects who received rescue treatment or with missing data were considered as non-responders

*p-value <0.0001, #p-value <0.001
Strata adjusted p-value is based on the CMH test stratified by PP NRS (≥7, <7) and IGA score (3= moderate, 4=severe) at baseline

Figure 1a. and Figure 1b. represent the proportion of subjects with IGA success and EASI-75 from baseline to Week 16 in ARCADIA 1 and ARCADIA 2.

Figure 1 – Proportion of subjects with IGA success and EASI-75 from baseline to Week 16 in ARCADIA 1 and ARCADIA 2

Figure 1a. IGA Success **Figure 1b. EASI-75**



Significant improvement in pruritus for patients treated with Nemluvio in ARCADIA 1 and ARCADIA 2 compared to placebo based on PP NRS improvements ≥4 and PP NRS percent change from baseline was observed starting at Week 1 and was maintained up to Week 16 (Table 3, Figure 2 and Figure 3).

Table 3 – Efficacy results on Itch for Nemluvio with concomitant TCS/TCI in ARCADIA 1 and ARCADIA 2 up to Week 16

	ARCADIA 1		**ARCADIA 2**	
	Nemluvio + TCS/TCI	**Placebo + TCS/TCI**	**Nemluvio + TCS/ TCI**	**Placebo + TCS/ TCI**

Number of subjects randomized (Baseline PP NRS ≥4)[a]	620	321	522	265
% of subjects with PP NRS improvement ≥4[a]				
At Week 1	4.7	1.2	6.7	0.4
Strata-adjusted proportion difference (95%CI)	3.4[§] (1.4, 5.5)		6.4* (4.1, 8.7)	
At Week 2	17.7	3.1	16.9	1.9
Strata-adjusted proportion difference (95%CI)	14.6* (11.1, 18.2)		15.1* (11.5, 18.7)	
At Week 4	27.4	6.5	26.1	5.3
Strata-adjusted proportion difference (95%CI)	20.9* (16.5, 25.4)		20.9* (16.3, 25.5)	
At Week 16	42.7	17.8	41.0	18.1
Strata-adjusted proportion difference (95%CI)	24.9* (19.2, 30.7)		23.2* (17.0, 29.4)	
% of subjects with PP NRS <2[a]				
At Week 4	16.0	3.7	15.9	2.6
Strata-adjusted proportion difference (95%CI)	12.2* (8.7, 15.8)		13.2* (9.5, 16.8)	
At Week 16	30.6	11.2	28.4	11.3
Strata-adjusted proportion difference (95%CI)	19.5* (14.5, 24.4)		17.1* (11.7, 22.5)	
LS Mean change from baseline (%)[b]				
At Week 16	-56.1	-30.6	-55.6	-30.3
LS mean difference (95%CI)	-25.5[^] (-30.3, -20.6)		-25.2[^] (-30.3, 20.2)	
Number of subjects with severe pruritus (Baseline PP NRS≥7)	406	210	316	164
% of subjects with PP NRS improvement ≥4[a]				
At Week 1	6.2	1.9	8.5	0.6
Strata-adjusted proportion difference (95%CI)	4.3[§] (1.3, 7.3)		8.0[#] (4.7, 11.3)	
At Week 2	20.7	3.8	19.3	3.0
Strata-adjusted proportion difference (95%CI)	16.9* (12.2, 21.6)		16.3* (11.2, 21.4)	
At Week 4	28.3	7.1	30.4	7.9
Strata-adjusted proportion difference (95%CI)	21.2* (15.6, 26.8)		22.5* (15.9, 29.0)	
At Week 16	46.1	18.6	48.4	21.3
Strata-adjusted proportion difference (95%CI)	27.5* (20.4, 34.7)		27.1* (18.7, 35.4)	
% of subjects with PP NRS <2[a]				
At Week 4	12.6	2.9	11.1	1.2
Strata-adjusted proportion difference (95%CI)	9.7* (5.8, 13.6)		9.9[#] (6.1, 13.8)	
At Week 16	27.8	7.6	26.9	8.5
Strata-adjusted proportion difference (95%CI)	20.3* (14.6, 25.9)		18.4* (11.9, 24.9)	
LS Mean change from baseline (%)				

At Week 16	-55.5	-27.9	-57.0	-30.2
LS mean difference (95%CI)	-27.7^ (-33.5, -21.8)		-26.8^ (-33.0, -20.6)	

[a] Subjects who received rescue treatment or with missing data were considered as non-responders

[b] Not adjusted for multiplicity

*p-value <0.0001, #p-value <0.001, §p-value <0.05

^nominal p-value <0.0001
Strata adjusted p-value is based on the CMH test stratified by PP NRS (≥7, <7) and IGA score (3= moderate, 4=severe) at baseline

Figure 2 –Proportion of subject with PP NRS improvement of ≥4 from baseline up to Week 16 in ARCADIA 1 and ARCADIA 2

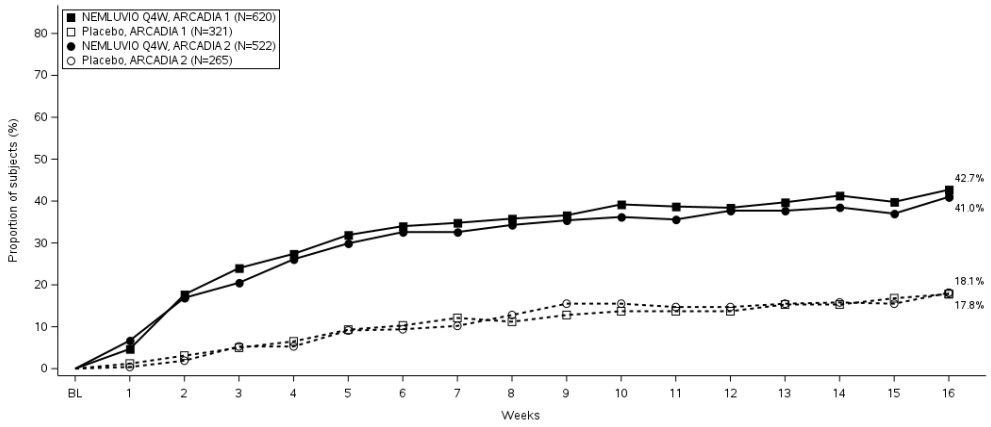
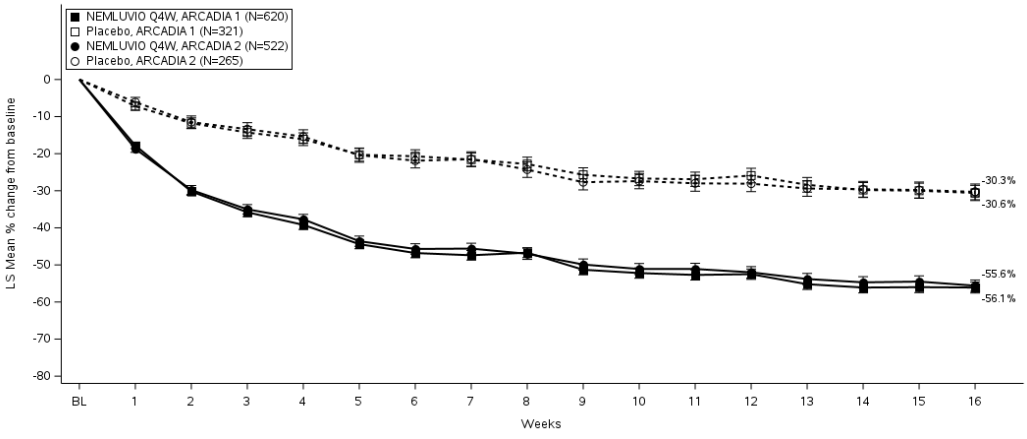


Figure 3 – Mean percent change from baseline in PP NRS up to Week 16 in ARCADIA 1 and ARCADIA 2



The SD NRS is a daily scale used by the subjects to report the degree of their sleep loss related to atopic dermatitis. A significant improvement in sleep disturbance was observed at Week 16 when compared to placebo (Table 4).

Table 4 – Efficacy on Sleep Disturbance for Nemluvio with concomitant TCS/TCI in ARCADIA 1 and ARCADIA 2 at Week 16

	ARCADIA 1		ARCADIA 2	
	Nemluvio + TCS/TCI	**Placebo + TCS/TCI**	**Nemluvio + TCS/ TCI**	**Placebo + TCS/ TCI**
Number of subjects randomized(Baseline PP NRS ≥4)[a]	620	321	522	265
% of subjects with SD NRS improvement ≥4[a]	37.9	19.9	33.5	16.2
Strata-adjusted proportion difference (95%CI)	17.9* (12.1, 23.7)		17.5* (11.6, 23.4)	
LS Mean change from baseline (%)[b]	-64.6	-38.1	-59.7	-35.4
LS mean difference (95%CI)	-26.4^ (-32.6, -20.3)		-24.3^ (-32.1, -16.4)	
Number of subjects with severe pruritus (Baseline PP NRS≥7)	406	210	316	164
% of subjects with SD NRS improvement ≥4[a]	42.1	22.4	42.7	20.7
Strata-adjusted proportion difference (95%CI)	19.7* (12.3, 27.1)		21.9* (13.7, 30.2)	
LS Mean change from baseline (%)[b]	-62.6	-37.0	-60.7	-42.0
LS mean difference (95%CI)	-25.6^ (-33.5, -17.6)		-18.6^ (-26.7, -10.5)	

[a] Subjects who received rescue treatment or with missing data were considered as non-responders

[b] Not adjusted for multiplicity

*p-value <0.0001

^nominal p-value <0.0001
Strata adjusted p-value is based on the CMH test stratified by PP NRS (≥7, <7) and IGA score (3= moderate, 4=severe) at baseline

ARCADIA 1 and ARCADIA 2 – Adults and Adolescents – maintenance period, week 16 to week 48

The clinical response in Nemluvio responders (IGA 0/1 or EASI-75 at Week 16) was evaluated between Week 16 and Week 48 in ARCADIA 1 and ARCADIA 2 studies. For the maintenance treatment period, 507 Nemluvio responders were re-randomized to Nemluvio 30 mg Q4W, Nemluvio 30 mg Q8W or placebo Q4W (Nemluvio withdrawal) with concomitant TCS/TCI. The pooled efficacy results for this period in the pivotal studies (ARCADIA 1 and ARCADIA 2) with Nemluvio at Week 48 are presented in Table 5.

Table 5 –Maintenance Period Pooled Efficacy Results for Nemluvio with concomitant TCS/TCI in ARCADIA 1 and ARCADIA 2 at Week 48

	Nemluvio + TCS/TCI Q4W N=169	**Nemluvio + TCS/TCI Q8W N=169**	**Placebo + TCS/TCI Q4W (Nemluvio withdrawal) N=169**
% of subjects with IGA 0 or 1[a,b]			
Week 16	84.0	84.0	77.5

(maintenance baseline)			
Week 48	61.5	60.4	49.7
Strata-adjusted proportion difference (95%CI)	11.8* (1.3, 22.3)	10.7* (0.3, 21.0)	
% of subjects with EASI-75[a,b]			
Week 16 (maintenance/baseline)	96.4	96.4	92.9
Week 48	76.3	75.7	63.9
Strata-adjusted proportion difference (95%CI)	12.4* (2.7, 22.0)	11.8* (2.1, 21.5)	

[a] Subjects who received rescue treatment or with missing data were considered as non-responders

[b] Not adjusted for multiplicity

*nominal p-value <0.05
Strata adjusted p-value is based on the CMH test stratified by PP NRS (≥7, <7) and IGA score (3= moderate, 4=severe) at baseline

Treatment effects in subgroups (weight, age, gender race, and prior treatment, including immunosuppressants) in ARCADIA 1 and ARCADIA 2 were generally consistent with the results in the overall study population.

Other patient-reported outcomes

In both studies (ARACADIA 1 and ARCADIA 2), Nemluvio significantly improved patient-reported symptoms and the impact of atopic dermatitis on health-related quality of life as measured by DLQI total score, at week 8 and week 16 compared to placebo (Table 6).

Table 6 –Efficacy results on DLQI for Nemluvio with concomitant TCS/TCI in ARCADIA 1 and ARCADIA 2 up to week 16

	ARCADIA 1		**ARCADIA 2**	
	Nemluvio + TCS/TCI N=620	**Placebo + TCS/TCI N=321**	**Nemluvio + TCS/ TCI N=522**	**Placebo + TCS/ TCI N=265**
LS Mean change in DLQI from baseline[a,b]				
At Week 8	-6.9	-4.7	-6.1	-4.6
LS mean difference (95%CI)	-2.3* (-3.3, -1.2)		-1.6[#] (-2.6, -0.6)	
At Week 16	-7.8	-5.3	-7.0	-4.5
LS mean difference (95%CI)	-2.5* (-3.6, -1.4)		-2.4* (-3.6, -1.3)	

[a] If a subject received any rescue therapy, the data after receipt of rescue therapy is considered treatment failure and the data set to the worst possible value. Subjects with missing results are considered as non-responders. ANCOVA MI-MAR model is used for the change from Baseline as the dependent variable including treatment group and the randomization stratification variables (IGA severity [3=moderate, 4=severe] and

PP NRS [>=7, <7] for full population; IGA severity only for Baseline PP NRS >=7 population) as factors and the Baseline DLQI as a covariate.
[b] Not adjusted for multiplicity

*nominal p-value <0.0001, [#]nominal p-value =0.0022 Strata adjusted p-value using the randomized stratification variables

In assessments of other patient reported outcomes, improvements in signs and symptoms related to pain frequency and intensity were observed at Week 16 when compared to placebo.

Adolescents with atopic dermatitis (12 to 17 years of age)

The efficacy results of the ARCADIA 1, ARCADIA 2 studies at Week 16 for paediatric patients 12 to 17 years of age are presented in Table 7 and Table 8, respectively. The results in the paediatric patient population were generally consistent with the results in the adult patient population.

Table 7 – Efficacy Results for Nemluvio (30 mg Q4W) with concomitant TCS/TCI in ARCADIA 1 and ARCADIA 2 at Week 16 in paediatric patients 12 to 17 years of age

	ARCADIA 1 AND ARCADIA 2	
	Nemluvio + TCS/TCI	**Placebo + TCS/TCI**
Number of subjects randomized (Baseline PP NRS ≥4)	176	90
% of subjects with IGA 0 or 1 [a,b]	48.9	34.4
Strata-adjusted proportion difference (95%CI)	12.7* (0.3, 25.1)	
% of subjects with EASI-75 [a,b]	53.4	43.3
Strata-adjusted proportion difference (95%CI)	8.6[§] (-4.1, 21.3)	
Number of subjects with severe pruritus (Baseline PP NRS≥7)	120	61
% of subjects with IGA 0 or 1 [a,b]	54.2	32.8
Strata-adjusted proportion difference (95%CI)	18.9* (4.3, 33.5)	
% of subjects with EASI-75 [a,b]	57.5	42.6
Strata-adjusted proportion difference (95%CI)	12.7[#] (-2.5, 27.9)	

[a] Subjects who received rescue treatment or with missing data were considered as non-responders

[b] Not adjusted for multiplicity

*nominal p-value <0.05, [#]nominal p-value =0.1025, [§]nominal p-value =0.1824

Strata adjusted p-value is based on the CMH test stratified by PP NRS (≥7, <7) and IGA score (3= moderate, 4=severe) at baseline

Table 8 – Efficacy results on Itch and Sleep Disturbance for Nemluvio (30mg Q4W) with concomitant TCS/TCI in ARCADIA 1 and ARCADIA 2 at Week 16 for paediatric patients 12 to 17 years of age

	ARCADIA 1 and ARCADIA 2

	Nemluvio + TCS/TCI	Placebo + TCS/TCI
Number of subjects randomized (Baseline PP NRS ≥4)	176	90
% of subjects with PP-NRS improvement ≥4 [a,b]	40.9	17.8
Strata-adjusted proportion difference (95%CI)	21.7[#] (11.2, 32.3)	
% of subjects with PP NRS <2 [a,b]	30.1	6.7
Strata-adjusted proportion difference (95%CI)	22.8* (14.3, 31.3)	
% of subjects with SD NRS improvement ≥4 [a,b]	31.8	20.0
Strata-adjusted proportion difference (95%CI)	10.9[§] (0.2, 21.6)	
Number of subjects with severe pruritus (Baseline PP NRS≥7)	120	61
% of subjects with PP-NRS improvement ≥4 [a,b]	48.3	21.3
Strata-adjusted proportion difference (95%CI)	25.4[#] (11.8, 39.1)	
% of subjects with PP NRS <2 [a,b]	30.0	4.9
Strata-adjusted proportion difference (95%CI)	24.6[#] (14.7, 34.5)	
% of subjects with SD NRS improvement ≥4 [a,b]	35.8	21.3
Strata-adjusted proportion difference (95%CI)	13.7[∞] (0.2, 27.2)	

[a] Subjects who received rescue treatment or with missing data were considered as non-responders

[b] Not adjusted for multiplicity

*nominal p-value <0.0001, [#]nominal p-value <0.001, [§]nominal p-value =0.0591, [∞]nominal p-value =0.0606

Strata adjusted p-value is based on the CMH test stratified by PP NRS (≥7, <7) and IGA score (3= moderate, 4=severe) at baseline

Clinical efficacy and safety in adults with prurigo nodularis

The efficacy and safety of Nemluvio as monotherapy was evaluated in two randomized, double-blind, placebo-controlled pivotal studies (OLYMPIA 1 and OLYMPIA 2) that enrolled a total of 560 subjects 18 years of age and older with prurigo nodularis. Disease severity was defined using an Investigator's Global Assessment (IGA) in the overall assessment of prurigo nodularis nodules on a severity scale of 0 to 4. Subjects enrolled in these two studies had an IGA score ≥ 3, severe pruritus as defined by a weekly average of the peak pruritus numeric rating scale (PP-NRS) score of ≥7 on a scale of 0 to 10, and greater than or equal to 20 nodular lesions. OLYMPIA 1 and OLYMPIA 2 assessed the effect of Nemluvio monotherapy on the signs and symptoms of prurigo nodularis, targeting improvement in skin lesions and pruritus over 16 weeks. OLYMPIA 1 had a 24-week treatment period and OLYMPIA 2 a 16-week treatment period.

Subjects completing OLYMPIA 1 and OLYMPIA 2 had the opportunity to enrol into the open-label trial (OLYMPIA LTE) and receive treatment with Nemluvio every 4 weeks up to 184 weeks.

Subjects weighing less than 90 kg in the Nemluvio monotherapy group received subcutaneous injections of Nemluvio 60 mg (2 injections of 30 mg) at Week 0, followed by 30 mg injections every 4 weeks. Subjects weighing 90 kg or more in the Nemluvio monotherapy group received subcutaneous injections of Nemluvio 60 mg (2 injections of 30 mg) at Week 0 and every 4 weeks.

Endpoints

Both OLYMPIA 1 and OLYMPIA 2 assessed the same two primary endpoints:

- Proportion of subjects with an improvement of ≥4 from baseline in Peak Pruritus Numeric Rating Scale (PP NRS) at Week 16
- Proportion of subjects with an IGA success (defined as an IGA of 0 [Clear] or 1 [Almost Clear], and a ≥2-point improvement from baseline) at Week 16

Key secondary endpoints included PP NRS improvement ≥4 from baseline at Week 4, PP NRS <2 at Week 4 and Week 16, SD NRS improvement ≥4 from baseline at Week 4 and 16. Other secondary endpoints included the change from baseline to week 16 in PP NRS, SD NRS, PN-associated pain frequency and intensity and the Dermatology Life Quality Index (DLQI).

Baseline characteristics

In these studies, at baseline, 59.6% of subjects were female, 81.4% were white, 25.4% of subjects were older than 65 years of age. The baseline weekly average PP NRS score was a mean (SD) of 8.4 (0.9). Fifty-eight (58) % of subjects had a baseline IGA score of 3 (moderate prurigo nodularis), 42% of subjects had a baseline IGA of 4 (severe prurigo nodularis) and the mean baseline DLQI was 16.9.

Clinical Response

Monotherapy studies (OLYMPIA 1 and OLYMPIA 2) – week 0 to week 16

Results of the pivotal studies evaluating treatment of Nemluvio in OLYMPIA 1 and OLYMPIA 2 are presented in Table 9 and show significant improvement in Nemluvio treated subjects, compared to placebo for both primary endpoints (Figure 4 and Figure 5) and key secondary endpoints (Figure 6).

Table 9 - Efficacy Results for Nemluvio monotherapy (Q4W) in OLYMPIA 1 and OLYMPIA 2

	OLYMPIA 1		**OLYMPIA 2**	
	Nemluvio	**Placebo**	**Nemluvio**	**Placebo**
Number of subjects randomized	190	96	183	91
% of subjects with improvement of PP NRS ≥4 from baseline[a]				
Week 4	41.1	6.3	41.0	7.7
Strata-adjusted proportion difference (95%CI)	31.7* (23.0, 40.4)		33.4* (24.3, 42.4)	
Week 16	58.4	16.7	56.3	20.9
Strata-adjusted proportion difference (95%CI)	40.1* (29.4, 50.8)		37.4* (26.3, 48.5)	

% of subjects with PP NRS <2 [a]				
Week 4	21.6	1.0	19.7	2.2
Strata-adjusted proportion difference (95%CI)	18.7* (12.3, 25.0)		18.8* (12.0, 25.7)	
Week 16	34.2	4.2	35.0	7.7
Strata-adjusted proportion difference (95%CI)	30.5* (22.3, 38.7)		30.0* (21.3, 38.6)	
LS Mean change from baseline (%) in PP NRS at Week 16 [b,c]	-54.7	-18.7	-56.2	-18.9
LS mean difference (95%CI)	-36.0[§] (-44.9, -27.1)		-37.4[§] (-46.8, -28.0)	
% of subjects with IGA 0 or 1 at Week 16 [a]	26.3	7.3	37.7	11.0
Strata-adjusted proportion difference (95%CI)	14.6[#] (6.7, 22.6)		28.5* (18.8, 38.2)	
% of subjects with improvement of SD NRS ≥4 from baseline [a]				
Week 4	31.1	5.2	37.2	9.9
Strata-adjusted proportion difference (95%CI)	22.7* (14.7, 30.7)		27.9* (18.4, 37.5)	
Week 16	50.0	11.5	51.9	20.9
Strata-adjusted proportion difference (95%CI)	38.0* (27.8, 48.2)		31.9* (20.7, 43.2)	
LS Mean change from baseline (%) in SD NRS at Week 16 [b,c]	-52.5	-18.8	-53.1	-9.6
LS mean difference (95%CI)	-33.6[§] (-46.1, -21.2)		-43.6[§] (-62.2. -24.9)	

[a] If a subject received any rescue therapy, the underlying data at/after receipt of rescue therapy is set as worst possible value, and the response is derived from underlying data value. Subjects with missing results are considered as non-responders.

[b] Not adjusted for multiplicity

[c] If a subject received any rescue therapy the data at/after receipt of rescue therapy is set as

worst possible value. Missing data is imputed by multiple imputation, assuming missing at random. Least square (LS) means and LS mean differences are strata-adjusted using ANCOVA MI-MAR, based on the randomized stratification variables (analysis center and baseline body weight (<90 kg, ≥90 kg).

*p-value <0.0001, [#]p-value =0.0025 Strata adjusted using the randomized stratification variables (analysis centre and baseline body weight (<90 kg, ≥90 kg)

[§]nominal p-value <0.0001 Strata-adjusted using the randomized stratification variables

Figure 4 – Proportion of Subjects with PP-NRS Improvement ≥4 from baseline to Week 16

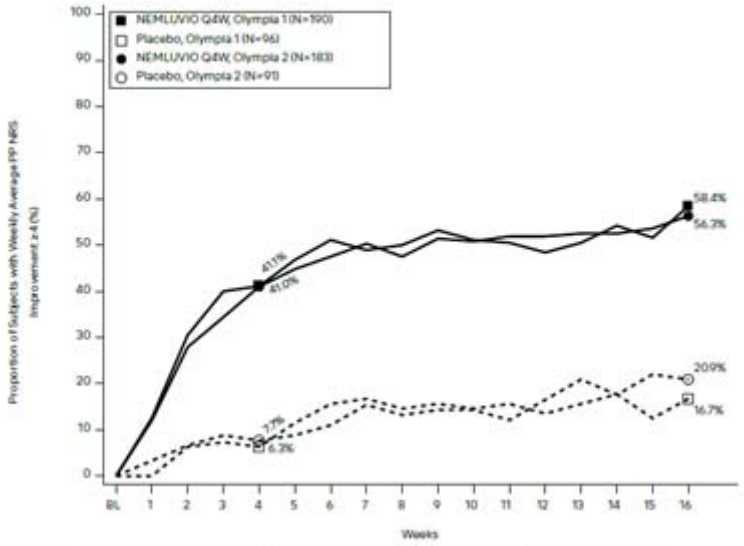


Figure 5 – Proportion of IGA responders from baseline to Week 16

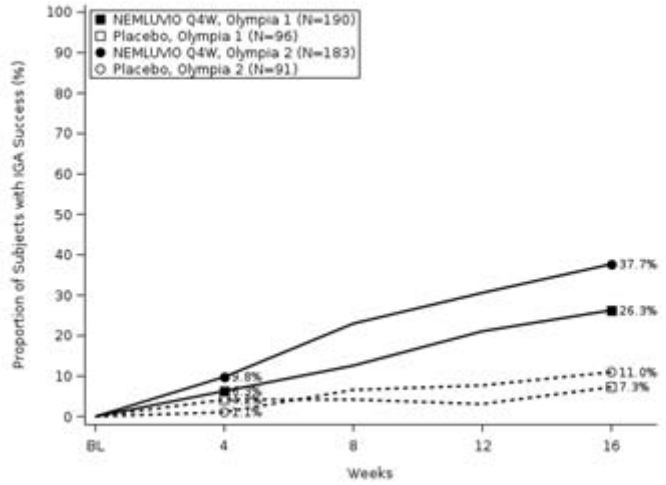
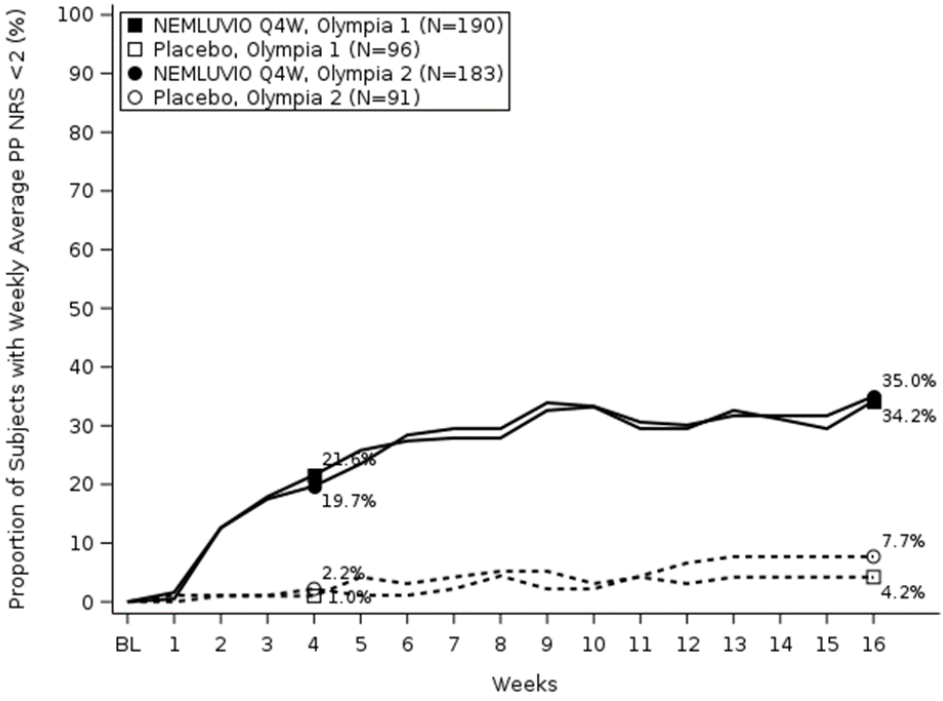


Figure 6 – Proportion of Subjects achieving PP-NRS <2 at Week 4 and Week 16



Treatment effects in subgroups (weight, age, gender, race, history of atopy, and prior treatment, including immunosuppressants) in OLYMPIA 1 and OLYMPIA 2 were generally consistent with the results in the overall study population.

Other Patient-reported outcomes

In both monotherapy studies (OLYMPIA 1 and OLYMPIA 2), Nemluvio significantly improved patient-reported symptoms of PN-associated pain frequency and intensity, and health-related quality of life as measured by DLQI total score (Table 10), at 16 weeks compared to placebo.

Table 10 –Efficacy results on DLQI of Nemluvio Monotherapy (Q4W) in OLYMPIA 1 and OLYMPIA 2 up to week 16

	OLYMPIA 1		**OLYMPIA 2**	
	Nemluvio N=190	**Placebo N=96**	**Nemluvio N=183**	**Placebo N=91**
LS Mean change in DLQI from baseline[a,b]				
At Week 4	-7.8	-3.0	-8.0	-1.9
LS mean difference (95%CI)	-4.8* (-6.3, -3.3)		-6.1* (-7.8, -4.3)	
At Week 16	-8.6	-2.2	-8.9	-0.8
LS mean difference (95%CI)	-6.4* (-8.4, -4.4)		-8.2* (-10.2, -6.1)	
% of subjects with improvement of DLQI ≥4 from baseline[b,c]				
At Week 4	70.0	42.7	68.9	39.6
Strata-adjusted proportion difference (95%CI)	26.5* (14.0, 39.0)		29.9* (17.3, 42.5)	
At Week 16	70.5	42.7	74.9	39.6
Strata-adjusted proportion difference (95%CI)	27.5* (15.8, 39.2)		37.4* (25.7, 49.0)	

[a] If a subject received any rescue therapy, the data at/after receipt of rescue therapy is set as worst possible value. Missing data is imputed by multiple imputation, assuming missing at random. Least square (LS) means and LS mean differences are strata-adjusted using ANCOVA MI-MAR, based on the randomized stratification variables (analysis center and baseline body weight (<90 kg, ≥90 kg).

[b] Not adjusted for multiplicity

[c] If a subject received any rescue therapy, the underlying data at/after receipt of rescue therapy is set as worst possible value, and the response is derived from underlying data value. Subjects with missing results are considered as non-responders.

*nominal p-value <0.0001 Strata-adjusted using the randomized stratification variables.

5.2 Pharmacokinetic properties

No difference was identified in the nemolizumab PK profiles between subjects with atopic dermatitis and subjects with prurigo nodularis, thus confirming that the disease does not impact the nemolizumab PK profile.

Absorption

Following an initial subcutaneous dose of 60 mg in a phase1 trial (96 subjects per arm), nemolizumab reached peak mean (SD) concentrations (Cmax) of 7.5 (2.31) µg/mL by approximately 6 days post dose.

Following multiple doses of Nemluvio in subjects with atopic dermatitis, the population PK estimated mean (SD) steady-state trough concentrations of nemolizumab were 2.63 (1.27) µg/mL for 30 mg administered Q4W and 0.74 (0.44) µg/mL for 30 mg administered Q8W.

Following multiple doses of Nemluvio in subjects with prurigo nodularis, the population PK estimated mean (SD) steady-state trough concentrations of nemolizumab 3.04 (1.23) µg/mL in patients with body weight <90 kg for 30 mg administered Q4W; and 3.66 (1.63) µg/mL in patients with body weight ≥90 kg for 60 mg administered Q4W.

In both atopic dermatitis and prurigo nodularis population, steady state concentrations of nemolizumab were achieved by week 4 after a 60 mg loading dose and by week 12 without a loading dose.

Distribution

Based on a population PK analysis, the volume of distribution was 7.67 L.

Biotransformation

Specific metabolism studies were not conducted because nemolizumab is a protein. Nemolizumab is expected to be metabolized into small peptides by catabolic pathways.

Elimination

Nemolizumab is expected to be degraded in the same manner as endogenous IgG. In the population PK analysis, the terminal elimination half-life (SD) of nemolizumab estimated to be 18.9 (4.96) days and systemic clearance was estimated to be 0.263 L/day.

Linearity/non-linearity

After a single dose, nemolizumab exhibited linear pharmacokinetics with exposures increasing in dose-proportional manner between 0.03 and 3 mg/kg.

After multiple doses, nemolizumab systemic exposure increased in an approximately dose-proportional manner across the SC dose range up to 30 mg. There was a slight decrease in bioavailability by 9% with the 60 mg SC dose and by 15% with the 90 mg SC dose.

Special populations

Gender, age and race

Gender, age, and race did not have a significant effect on the pharmacokinetics of nemolizumab.

Hepatic impairment

Nemolizumab, as a monoclonal antibody, is not expected to undergo significant hepatic elimination. No clinical studies have been conducted to evaluate the effect of hepatic impairment on the pharmacokinetics of nemolizumab. Mild to moderate hepatic impairment was not found to affect the PK of nemolizumab determined by population PK analysis. No data are available in patients with severe hepatic impairment.

Renal impairment

Nemolizumab, as a monoclonal antibody, is not expected to undergo significant renal elimination. No clinical studies have been conducted to evaluate the effect of renal impairment on the pharmacokinetics of nemolizumab. Population PK analysis did not identify mild or moderate renal impairment as having a clinically meaningful influence on the systemic exposure of nemolizumab. Very limited data are available in patients with severe renal impairment.

Body weight

Nemolizumab exposure was lower in subjects with higher body weight.

Table 11 – PK parameters by weight quartile

Body weight (kg)	**1st Quartile [30.8 to 62.0]**	**2nd Quartile [62.0 to 74.0]**	**3rd Quartile [74.0 to 87.1]**	**4th Quartile [87.1 to 181]**
$C_{max,ss}$ (µg/mL)	6.64	5.48	4.86	3.99
$C_{trough,ss}$ (µg/mL)	2.92	2.39	2.18	1.72
$AUC_{□,ss}$ (µg•day/mL)	137	113	101	81.6

$AUC_{t,ss}$ Area under the concentration-time curve during a dosing interval (□ □) at steady state; $C_{max,ss}$ Maximum concentration at steady state; $C_{trough,ss}$ Predose concentration at steady state

PK parameters calculated with population PK model (N=1952)

Atopic Dermatitis

The difference in systemic exposure due to body weight had no clinically meaningful impact on efficacy. Dose adjustment based on body weight is not needed (see section 4.2).

Prurigo Nodularis

The variability in systemic exposure due to body weight had a clinically meaningful impact on skin lesion efficacy as assessed by IGA response but not on pruritus improvement and does require dose adjustment in subjects with prurigo nodularis (see section 4.2).

Paediatric population

Atopic dermatitis

In the population PK analysis, no clinically significant difference in the pharmacokinetics of nemolizumab was estimated in 12-17 years subjects compared to adults. Dose adjustment in this population is not recommended.

5.3 Preclinical safety data

Dedicated animal studies have not been conducted to evaluate the carcinogenic or mutagenic potential of Nemluvio.

Due to its nature and pharmacological properties, direct DNA or other genetic material interaction is not expected for a recombinant humanized monoclonal immunoglobulin such as nemolizumab. Nemluvio and its metabolites (oligo peptides and amino acids) are not deemed to have an intrinsic carcinogenic potential or to be tumor initiators/promotors.

No effects on fertility parameters such as reproductive organs morphology, menstrual cycle length, or sperm/testicular analysis were observed in sexually mature cynomolgus monkey that were chronically administered by the subcutaneous route at doses up to 25 mg/kg/2-week (AUC exposure 43-fold or 34-fold higher than in atopic dermatitis or prurigo nodularis patients respectively, at the 60 mg Maximum Recommended Human Dose.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder for solution for injection:

Sucrose

Trometamol

Trometamol hydrochloride (for pH-adjustment)

L-arginine hydrochloride

Poloxamer 188

Solvent:

Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

36 months

If necessary, the carton containing the pre-filled syringe can be removed from the refrigerator at room temperature (up to 25°C) for a single period up to 90 days. Write the date first removed from the refrigerator in the space provided on the outer carton for the syringe. Do not use Nemluvio beyond the expiration date or 90 days after the date it was first removed from the refrigerator (whichever is earlier).

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C).

Do not freeze.

Store in the original package in order to protect from light.

For storage conditions after reconstitution of the medicinal product, see section 6.6.

6.5 Nature and contents of container

Single-use dual-chamber pre-filled syringe in a borosilicate glass type 1, co-packaged with a 27G needle (stainless steel) with safety shield.

Pack size:

• 1 pre-filled syringe

6.6 Special precautions for disposal

Comprehensive instructions for the administration of Nemluvio in a pre-filled syringe are given at the end of the package leaflet.

Nemluvio must be removed from the refrigerator for 30-45 min before reconstitution. Once reconstitution steps are completed, Nemluvio must be used within 4 hours or discarded.

Inspect Nemluvio visually prior to reconstitution. Nemluvio consists of a white powder and a clear liquid. Do not use if powder is not white, or if liquid is cloudy, or particulate matter is visible. Prior to administration, check that Nemluvio is clear and colourless to slightly yellow and does not contain particles.

The pre-filled syringe should not be exposed to heat or direct sunlight and should not be shaken.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

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NW1 2DX

United Kingdom

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PL 10590/0076

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