SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Tremfya 100 mg solution for injection in pre-filled syringe

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pre-filled syringe contains 100 mg of guselkumab in 1 mL solution.

Guselkumab is a fully human immunoglobulin G1 lambda (IgG1λ) monoclonal antibody (mAb) produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection (injection)

The solution is clear and colourless to light yellow, with target pH of 5.8 and approximate osmolarity of 367.5 mOsm/L.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Paediatric plaque psoriasis

Tremfya is indicated for the treatment of moderate to severe plaque psoriasis in children and adolescents from the age of 6 years who are candidates for systemic therapy.

4.2 Posology and method of administration

This medicinal product is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of plaque psoriasis.

Posology

Paediatric plaque psoriasis (6 to 17 years)

Children from the age of 6 years with a body weight of 40 kg or more

The recommended dose is 100 mg by subcutaneous injection at weeks 0 and 4, followed by a maintenance dose every 8 weeks (q8w).

Children from the age of 6 years with a body weight less than 40 kg

For children with a body weight less than 40 kg a 45 mg/0.45 mL pre-filled pen is available. For the posology and method of administration, see section 4.2 of the Tremfya 45 mg/0.45 mL prefilled pen Summary of Product Characteristics.

Consideration should be given to discontinuing treatment in paediatric patients who have shown no response after 24 weeks of treatment.

Missed dose

If a dose is missed, the dose should be administered as soon as possible. Thereafter, dosing should be resumed at the regular scheduled time.

Special populations

Renal or hepatic impairment

Tremfya has not been studied in these patient populations. These conditions are generally not expected to have any significant impact on the pharmacokinetics of monoclonal antibodies, and no dose adjustments are considered necessary. For further information on elimination of guselkumab, see section 5.2.

Paediatric population

The safety and efficacy of Tremfya in patients less than 6 years have not been established. No data are available.

Method of administration

Subcutaneous use. If possible, areas of the skin that show psoriasis should be avoided as injection sites.

Tremfya is not intended for paediatric self-administration. After proper training in subcutaneous injection technique, a caregiver may inject Tremfya if a physician determines that this is appropriate. However, the physician should ensure appropriate medical follow-up of patients. Caregivers should be instructed to inject the full amount of solution according to the 'Instructions for use' provided in the carton.

For instructions on preparation of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Serious hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Clinically important active infections (e.g. active tuberculosis, see section 4.4).

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.

Infections

Guselkumab may increase the risk of infection. Treatment should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated.

Patients treated with guselkumab should be instructed to seek medical advice if signs or symptoms of clinically important chronic or acute infection occur. If a patient develops a clinically important or serious infection or is not responding to standard

therapy, the patient should be monitored closely and treatment should be discontinued until the infection resolves.

Pre-treatment evaluation for tuberculosis

Prior to initiating treatment, patients should be evaluated for tuberculosis (TB) infection. Patients receiving guselkumab should be monitored for signs and symptoms of active TB during and after treatment. Anti-TB therapy should be considered prior to initiating treatment in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed.

Hypersensitivity

Serious hypersensitivity reactions, including anaphylaxis, have been reported in the post-marketing setting (see section 4.8). Some serious hypersensitivity reactions occurred several days after treatment with guselkumab, including cases with urticaria and dyspnoea. If a serious hypersensitivity reaction occurs, administration of guselkumab should be discontinued immediately and appropriate therapy initiated.

Hepatic transaminase elevations

In psoriatic arthritis clinical studies, an increased incidence of liver enzyme elevations was observed in patients treated with guselkumab q4w compared to patients treated with guselkumab q8w or placebo (see section 4.8).

Immunisations

Prior to initiating therapy, completion of all age-appropriate immunisations should be considered according to current immunisation guidelines. Live vaccines should not be used concurrently in patients treated with guselkumab. No data are available on the response to live or inactive vaccines.

Before live viral or live bacterial vaccination, treatment should be withheld for at least 12 weeks after the last dose and can be resumed at least 2 weeks after vaccination. Prescribers should consult the Summary of Product Characteristics of the specific vaccine for additional information and guidance on concomitant use of immunosuppressive agents post-vaccination.

Excipients

Polysorbate 80 content

This medicinal product contains 0.5 mg of polysorbate 80 (E433) in each dosage unit which is equivalent to 0.5 mg/mL. Polysorbates may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

Interactions with CYP450 substrates

In a Phase I study in subjects with moderate to severe plaque psoriasis, changes in systemic exposures (C_{max} and AUC_{inf}) of midazolam, S-warfarin, omeprazole, dextromethorphan, and caffeine after a single dose of guselkumab were not clinically relevant, indicating that interactions between guselkumab and substrates of various CYP enzymes (CYP3A4, CYP2C9, CYP2C19, CYP2D6, and CYP1A2) are unlikely. There is no need for dose adjustment when co-administering guselkumab and CYP450 substrates.

Concomitant immunosuppressive therapy or phototherapy

In psoriasis studies, the safety and efficacy of guselkumab in combination with immunosuppressants, including biologics, or phototherapy have not been evaluated.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential should use effective methods of contraception during treatment and for at least 12 weeks after treatment.

Pregnancy

There are limited data from the use of guselkumab in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonic/foetal development, parturition or postnatal development (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Tremfya during pregnancy.

Breast-feeding

It is unknown whether guselkumab is excreted in human milk. Human IgGs are known to be excreted in breast milk during the first few days after birth, and decrease

to low concentrations soon afterwards; consequently, a risk to the breast-fed infant during this period cannot be excluded. A decision should be made whether to discontinue breast-feeding or to abstain from Tremfya therapy, taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. See section 5.3 for information on the excretion of guselkumab in animal (cynomolgus monkey) milk.

Fertility

The effect of guselkumab on human fertility has not been evaluated. Animal studies do not indicate direct or indirect harmful effects with respect to fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Tremfya 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 was respiratory tract infections in approximately 15% of patients in the psoriasis and psoriatic arthritis clinical studies.

Tabulated list of adverse reactions

Table 1 provides a list of adverse reactions from psoriasis and psoriatic arthritis clinical studies as well as from post-marketing experience. The adverse reactions are classified by MedDRA System Organ Class and frequency, using the following convention: 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), not known (cannot be estimated from the available data).

Table 1: List of adverse reactions

System Organ Class	**Frequency**	**Adverse reactions**
Infections and infestations	Very common	Respiratory tract infections
	Uncommon	Herpes simplex infections

	Uncommon	Tinea infections
	Uncommon	Gastroenteritis
Immune system disorders	Rare	Hypersensitivity
	Rare	Anaphylaxis
Nervous system disorders	Common	Headache
Gastrointestinal disorders	Common	Diarrhoea
Skin and subcutaneous tissue disorders	Uncommon	Urticaria
	Common	Rash
Musculoskeletal and connective tissue disorders	Common	Arthralgia
General disorders and administration site conditions	Common	Injection site reactions
Investigations	Common	Transaminases increased
	Uncommon	Neutrophil count decreased

Description of selected adverse reactions

Transaminases increased

In two Phase III psoriatic arthritis clinical studies, through the placebo-controlled period, adverse events of increased transaminases (includes ALT increased, AST increased, hepatic enzyme increased, transaminases increased, liver function test abnormal, hypertransaminasaemia) were reported more frequently in the guselkumab-treated groups (8.6% in the 100 mg subcutaneous q4w group and 8.3% in the 100 mg subcutaneous q8w group) than in the placebo group (4.6%). Through 1-year, adverse events of increased transaminases (as above) were reported in 12.9% of patients in the q4w group and 11.7% of patients in the q8w group.

Based on laboratory assessments, most transaminase increases (ALT and AST) were ≤ 3 x upper limit of normal (ULN). Transaminase increases from > 3 to ≤ 5 x ULN and > 5 x ULN were low in frequency, occurring more often in the guselkumab q4w group compared with the guselkumab q8w group (Table 2). A similar pattern of frequency by severity and by treatment group was observed through the end of the 2-year Phase III psoriatic arthritis clinical study.

Table 2: Frequency of patients with transaminase increases post-baseline in two Phase III psoriatic arthritis clinical studies

	Through week 24[a]			**Through 1 year[b]**	
	Placebo N=370[c]	guselkumab 100 mg q8w N=373[c]	guselkumab 100 mg q4w N=371[c]	guselkumab 100 mg q8w N=373[c]	guselkumab 100 mg q4w N=371[c]
ALT					

>1 to ≤3 x ULN	30.0%	28.2%	35.0%	33.5%	41.2%
>3 to ≤ 5 x ULN	1.4%	1.1%	2.7%	1.6%	4.6%
>5 x ULN	0.8%	0.8%	1.1%	1.1%	1.1%
AST					
>1 to ≤3 x ULN	20.0%	18.8%	21.6%	22.8%	27.8%
>3 to ≤ 5 x ULN	0.5%	1.6%	1.6%	2.9%	3.8%
>5 x ULN	1.1%	0.5%	1.6%	0.5%	1.6%

[a] placebo-controlled period

[b] patients randomised to placebo at baseline and crossed over to guselkumab are not included

[c] number of patients with at least one post-baseline assessment for the specific laboratory test within the time period

In the psoriasis clinical studies, through 1 year, the frequency of transaminase increases (ALT and AST) for the guselkumab q8w dose was similar to that observed for the guselkumab q8w dose in the psoriatic arthritis clinical studies. Through 5 years, the incidence of transaminase elevation did not increase by year of guselkumab treatment. Most transaminase increases were ≤ 3 x ULN.

In most cases, the increase in transaminases was transient and did not lead to discontinuation of treatment.

In pooled Phase II and Phase III Crohn's disease clinical studies, through the placebo-controlled period (week 0-12), adverse events of increased transaminases (includes ALT increased, AST increased, hepatic enzyme increased, transaminases increased, and liver function test increased) were reported more frequently in the guselkumab treated groups (1.7% of patients) than in the placebo group (0.6% of patients). In pooled Phase II and Phase III Crohn's disease clinical studies, through the reporting period of approximately one year, adverse events of increased transaminases (includes ALT increased, AST increased, hepatic enzyme increased, transaminases increased, hepatic function abnormal, and liver function test increased) were reported in 3.4% of patients in the guselkumab 200 mg subcutaneous q4w treatment group and 4.1% of patients in the guselkumab 100 mg subcutaneous q8w treatment group compared to 2.4% in the placebo group.

Based on laboratory assessments in pooled Phase II and Phase III Crohn's disease clinical studies, the frequency of ALT or AST elevations were lower than those observed in psoriatic arthritis Phase III clinical studies. In pooled Phase II and Phase III Crohn's disease clinical studies, through the placebo-controlled period (Week 12), ALT (<1% of patients) and AST (<1% of patients) elevations ≥3x ULN were reported in guselkumab treated patients. In pooled Phase II and Phase III Crohn's disease clinical studies, through the reporting period of approximately one year, ALT and/or AST elevations ≥ 3x ULN were reported in 2.7% of patients in the guselkumab 200 mg subcutaneous q4w treatment group and 2.6% of patients in the guselkumab 100 mg subcutaneous q8w treatment group compared to 1.9% in the placebo group. In

most cases, the increase in transaminases was transient and did not lead to discontinuation of treatment.

Neutrophil count decreased

In two Phase III psoriatic arthritis clinical studies, through the placebo-controlled period, the adverse event of decreased neutrophil count was reported more frequently in the guselkumab-treated group (0.9%) than in the placebo group (0%). Through 1 year, the adverse event of decreased neutrophil count was reported in 0.9% of patients treated with guselkumab. In most cases, the decrease in blood neutrophil count was mild, transient, not associated with infection and did not lead to discontinuation of treatment.

Gastroenteritis

In two Phase III psoriasis clinical studies through the placebo-controlled period, gastroenteritis occurred more frequently in the guselkumab-treated group (1.1%) than in the placebo group (0.7%). Through Week 264, 5.8% of all guselkumab-treated patients reported gastroenteritis. Adverse reactions of gastroenteritis were non-serious and did not lead to discontinuation of guselkumab through Week 264. Gastroenteritis rates observed in psoriatic arthritis clinical studies through the placebo-controlled period were similar to those observed in the psoriasis clinical studies.

Injection site reactions

In two Phase III psoriasis clinical studies through Week 48, 0.7% of guselkumab injections and 0.3% of placebo injections were associated with injection site reactions. Through Week 264, 0.4% of guselkumab injections were associated with injection site reactions. Injection site reactions were generally mild to moderate in severity; none were serious, and one led to discontinuation of guselkumab.

In two Phase III psoriatic arthritis clinical studies through Week 24, the number of patients that reported 1 or more injection site reactions was low and slightly higher in the guselkumab groups than in the placebo group; 5 (1.3%) patients in the guselkumab q8w group, 4 (1.1%) patients in the guselkumab q4w group, and 1 (0.3%) patient in the placebo group. One patient discontinued guselkumab due to an injection site reaction during the placebo-controlled period of the psoriatic arthritis clinical studies. Through 1 year, the proportion of patients reporting 1 or more injection site reactions was 1.6% and 2.4% in the guselkumab q8w and q4w groups respectively. Overall, the rate of injections associated with injection site reactions observed in psoriatic arthritis clinical studies through the placebo-controlled period was similar to rates observed in the psoriasis clinical studies.

In Phase II and Phase III Crohn's disease clinical studies through Week 48, the proportion of patients that reported 1 or more injection site reactions to guselkumab was 4.1% (0.8% of injections) in the treatment group which received guselkumab 200 mg intravenous induction followed by 200 mg subcutaneous q4w, and 1.4% (0.6% of injections) of patients in the guselkumab 200 mg intravenous induction followed by 100 mg subcutaneous q8w group. Overall injection site reactions were mild; none were serious.

In a Phase III Crohn's disease clinical study through Week 48, the proportion of patients that reported 1 or more injection site reactions to guselkumab was 7% (1.3% of injections) in the treatment group which received 400 mg subcutaneous induction followed by 200 mg subcutaneous q4w and 4.3% (0.7% of injections) of patients in the 400 mg guselkumab subcutaneous induction followed by 100 mg subcutaneous q8w group. Most injection site reactions were mild; none were serious.

In the Phase III ulcerative colitis maintenance clinical study through Week 44, the proportion of patients that reported 1 or more subcutaneous injection site reactions to guselkumab was 7.9% (2.5% of injections) in the guselkumab 200 mg subcutaneous q4w group and no injections in the guselkumab 100 mg subcutaneous q8w group. Most injection site reactions were mild and none were serious.

Immunogenicity

The immunogenicity of guselkumab was evaluated using a sensitive and drug tolerant immunoassay.

In pooled Phase II and Phase III analyses in patients with psoriasis and psoriatic arthritis, 5% (n=145) of patients treated with guselkumab developed antidrug antibodies in up to 52 weeks of treatment. Of the patients who developed antidrug antibodies, approximately 8% (n=12) had antibodies that were classified as neutralising, which equates to 0.4% of all patients treated with guselkumab. In pooled Phase III analyses in patients with psoriasis, approximately 15% of patients treated with guselkumab developed antidrug antibodies in up to 264 weeks of treatment. Of the patients who developed antidrug antibodies, approximately 5% had antibodies that were classified as neutralising, which equates to 0.76% of all patients treated with guselkumab. Antidrug antibodies were not associated with lower efficacy or development of injection site reactions.

In pooled Phase II and Phase III analyses up to Week 48 in patients with Crohn's disease who were treated with intravenous induction followed by subcutaneous maintenance dose regimen, approximately 5% (n=30) of patients treated with guselkumab developed antidrug antibodies. Of the patients who developed antidrug antibodies, approximately 7% (n=2) had antibodies that were classified as neutralising antibodies, which equates to 0.3% of guselkumab treated patients.

In a Phase III analysis up to Week 48 in patients with Crohn's disease who were treated with subcutaneous induction followed by subcutaneous maintenance dose regimen, approximately 9% (n=24) of patients treated with guselkumab developed antidrug antibodies. Of these patients, 13% (n=3) had antibodies that were classified as neutralising antibodies, which equates to 1% of guselkumab treated patients. Antidrug antibodies were not associated with lower efficacy or development of injection site reactions. In pooled Phase II and Phase III analyses in patients with ulcerative colitis who were treated with intravenous induction followed by subcutaneous maintenance, approximately 12% (n=58) of patients treated with guselkumab for up to 56 weeks developed antidrug antibodies. Of the patients who developed antidrug antibodies, approximately 16% (n=9) had antibodies that were classified as neutralising, which equates to 2% of all patients treated with

guselkumab. In a Phase III analysis up to Week 24 in patients with ulcerative colitis who were treated with subcutaneous induction followed by subcutaneous maintenance, approximately 9% (n=24) of patients treated with guselkumab developed antidrug antibodies. Of the patients who developed antidrug antibodies, 12% (n=3) had antibodies that were classified as neutralising antibodies, which equates to 1% of guselkumab-treated patients. Antidrug antibodies were not associated with lower efficacy or the development of injection-site reactions.

In the Phase III paediatric study, 18% (n=21) of paediatric psoriasis patients treated with guselkumab developed antidrug antibodies in up to week 44. Of the patients who developed antidrug antibodies, none had antibodies that were classified as neutralising. Antibodies to guselkumab were not associated with changes in pharmacokinetics, clinical efficacy or development of injection-site reactions. However, the number of patients who were positive for antibodies to guselkumab is too small for definitive conclusions about the impact on efficacy and safety of guselkumab.

Paediatric population

Plaque psoriasis

The safety of guselkumab was assessed in a Phase III placebo- and active-controlled study in paediatric patients with moderate to severe plaque psoriasis. This clinical study evaluated safety for up to 52 weeks in 120 patients 6 to 17 years of age. The safety profile of guselkumab in this study was consistent with the safety profile reported in the adult plaque psoriasis studies.

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 Website: https://yellowcard.mhra.gov.uk or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Single intravenous doses of guselkumab up to 987 mg (10 mg/kg) have been administered in healthy volunteers and single subcutaneous doses of guselkumab up to 300 mg have been administered in patients with plaque psoriasis in clinical studies without dose-limiting toxicity. In the event of overdose, the patient must be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment must be administered immediately.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, interleukin inhibitors, ATC code: L04AC16.

Mechanism of action

Guselkumab is a human IgG1λ monoclonal antibody (mAb) that binds selectively to the interleukin 23 (IL-23) protein with high specificity and affinity. IL-23 is a cytokine that is involved in inflammatory and immune responses. By blocking IL-23 from binding to its receptor, guselkumab inhibits IL-23-dependent cell signalling and release of proinflammatory cytokines.

Levels of IL-23 are elevated in the skin of patients with plaque psoriasis. In *in vitro* models, guselkumab was shown to inhibit the bioactivity of IL-23 by blocking its interaction with cell surface IL-23 receptor, disrupting IL-23-mediated signaling, activation and cytokine cascades. Guselkumab exerts clinical effects in plaque psoriasis and psoriatic arthritis through blockade of the IL-23 cytokine pathway.

Myeloid cells expressing Fc-gamma receptor 1 (CD64) have been shown to be a predominant source of IL-23 in inflamed tissue in psoriasis. Guselkumab has demonstrated *in vitro* blocking of IL-23 and binding to CD64. These results indicate that guselkumab is able to neutralise IL-23 at the cellular source of inflammation.

Pharmacodynamic effects

In a Phase I study, treatment with guselkumab resulted in reduced expression of IL-23/Th17 pathway genes and psoriasis -associated gene expression profiles, as shown by analyses of mRNA obtained from lesional skin biopsies of patients with plaque psoriasis at Week 12 compared to baseline. In the same Phase I study, treatment with guselkumab resulted in improvement of histological measures of psoriasis at Week 12, including reductions in epidermal thickness and T-cell density. In addition, reduced serum IL-17A, IL-17F and IL-22 levels compared to placebo were observed in guselkumab-treated patients in Phase II and Phase III plaque psoriasis studies. These results are consistent with the clinical benefit observed with guselkumab treatment in plaque psoriasis.

In psoriatic arthritis patients in Phase III studies, serum levels of acute phase proteins C-reactive protein, serum amyloid A, and IL-6, and Th17 effector cytokines IL-17A, IL-17F and IL-22 were elevated at baseline. Guselkumab decreased the levels of

these proteins within 4 weeks of initiation of treatment. Guselkumab further reduced the levels of these proteins by Week 24 compared to baseline and also to placebo.

Clinical efficacy and safety

Adult plaque psoriasis

The efficacy and safety of guselkumab was assessed in three randomised, double-blind, active controlled Phase III studies in adult patients with moderate to severe plaque psoriasis, who were candidates for phototherapy or systemic therapy.

VOYAGE 1 and VOYAGE 2

Two studies (VOYAGE 1 and VOYAGE 2) evaluated the efficacy and safety of guselkumab versus placebo and adalimumab in 1829 adult patients. Patients randomised to guselkumab (N=825) received 100 mg at Weeks 0 and 4, and every 8 weeks (q8w) thereafter through Week 48 (VOYAGE 1) and Week 20 (VOYAGE 2). Patients randomised to adalimumab (N=582) received 80 mg at Week 0 and 40 mg at Week 1, followed by 40 mg every other week (q2w) through Week 48 (VOYAGE 1) and Week 23 (VOYAGE 2). In both studies, patients randomised to placebo (N=422) received guselkumab 100 mg at Weeks 16, 20 and q8w thereafter. In VOYAGE 1, all patients, including those randomised to adalimumab at Week 0, started to receive open-label guselkumab q8w at Week 52. In VOYAGE 2, patients randomised to guselkumab at Week 0 who were Psoriasis Area and Severity Index (PASI) 90 responders at Week 28 were re-randomised to either continue treatment with guselkumab q8w (maintenance treatment) or receive placebo (withdrawal treatment). Withdrawal patients re-initiated guselkumab (dosed at time of retreatment, 4 weeks later and q8w thereafter) when they experienced at least a 50% loss of their Week 28 PASI improvement. Patients randomised to adalimumab at Week 0 who were PASI 90 non-responders received guselkumab at Weeks 28, 32 and q8w thereafter. In VOYAGE 2, all patients started to receive open-label guselkumab q8w at Week 76.

Baseline disease characteristics were consistent for the study populations in VOYAGE 1 and 2 with a median body surface area (BSA) of 22% and 24%, a median baseline PASI score of 19 for both studies, a median baseline dermatology quality of life index (DLQI) score of 14 and 14.5, a baseline investigator global assessment (IGA) score of severe for 25% and 23% of patients, and a history of psoriatic arthritis for 19% and 18% of patients, respectively.

Of all patients included in VOYAGE 1 and 2, 32% and 29% were naïve to both conventional systemic and biologic therapy, 54% and 57% had received prior phototherapy, and 62% and 64% had received prior conventional systemic therapy, respectively. In both studies, 21% had received prior biologic therapy, including 11% who had received at least one anti-tumour necrosis factor alpha (TNFα) agent, and approximately 10% who had received an anti-IL-12/IL-23 agent.

The efficacy of guselkumab was evaluated with respect to overall skin disease, regional disease (scalp, hand and foot and nails) and quality of life and patient reported outcomes. The co-primary endpoints in VOYAGE 1 and 2 were the

proportion of patients who achieved an IGA score of cleared or minimal (IGA 0/1) and a PASI 90 response at Week 16 versus placebo (see Table 3).

Overall skin disease

Treatment with guselkumab resulted in significant improvements in the measures of disease activity compared to placebo and adalimumab at Week 16 and compared to adalimumab at Weeks 24 and 48. The key efficacy results for the primary and major secondary study endpoints are shown in Table 3 below.

Table 3: Summary of clinical responses in VOYAGE 1 and VOYAGE 2

	Number of patients (%)					
	VOYAGE 1			VOYAGE 2		
	Placebo (N=174)	guselkumab (N=329)	adalimumab (N=334)	Placebo (N=248)	guselkumab (N=496)	adalimumab (N=248)
Week 16						
PASI 75	10 (5.7)	300 (91.2)[a]	244 (73.1)[b]	20 (8.1)	428 (86.3)[a]	170 (68.5)[b]
PASI 90	5 (2.9)	241 (73.3)[c]	166 (49.7)[b]	6 (2.4)	347 (70.0)[c]	116 (46.8)[b]
PASI 100	1 (0.6)	123 (37.4)[a]	57 (17.1)[d]	2 (0.8)	169 (34.1)[a]	51 (20.6)[d]
IGA 0/1	12 (6.9)	280 (85.1)[c]	220 (65.9)[b]	21 (8.5)	417 (84.1)[c]	168 (67.7)[b]
IGA 0	2 (1.1)	157 (47.7)[a]	88 (26.3)[d]	2 (0.8)	215 (43.3)[a]	71 (28.6)[d]
Week 24						
PASI 75	-	300 (91.2)	241 (72.2)[e]	-	442 (89.1)	176 (71.0)[e]
PASI 90	-	264 (80.2)	177 (53.0)[b]	-	373 (75.2)	136 (54.8)[b]
PASI 100	-	146 (44.4)	83 (24.9)[e]	-	219 (44.2)	66 (26.6)[e]
IGA 0/1	-	277 (84.2)	206 (61.7)[b]	-	414 (83.5)	161 (64.9)[b]
IGA 0	-	173 (52.6)	98 (29.3)[b]	-	257 (51.8)	78 (31.5)[b]
Week 48						
PASI 75	-	289 (87.8)	209 (62.6)[e]	-	-	-
PASI 90	-	251 (76.3)	160 (47.9)[b]	-	-	-
PASI 100	-	156 (47.4)	78 (23.4)[e]	-	-	-
IGA 0/1	-	265 (80.5)	185 (55.4)[b]	-	-	-
IGA 0	-	166 (50.5)	86 (25.7)[b]	-	-	-

[a] $p < 0.001$ for comparison between guselkumab and placebo.

[b] $p < 0.001$ for comparison between guselkumab and adalimumab for major secondary endpoints.

[c] $p < 0.001$ for the comparisons between guselkumab and placebo for the co-primary endpoints.

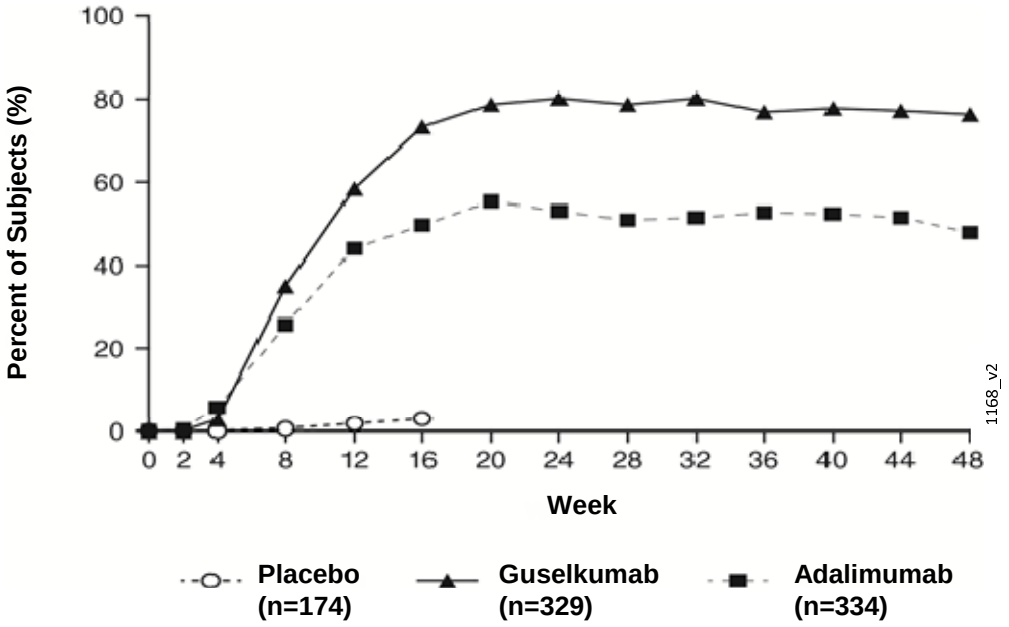
[d] comparisons between guselkumab and adalimumab were not performed.

[e] $p < 0.001$ for comparison between guselkumab and adalimumab.

Response over time

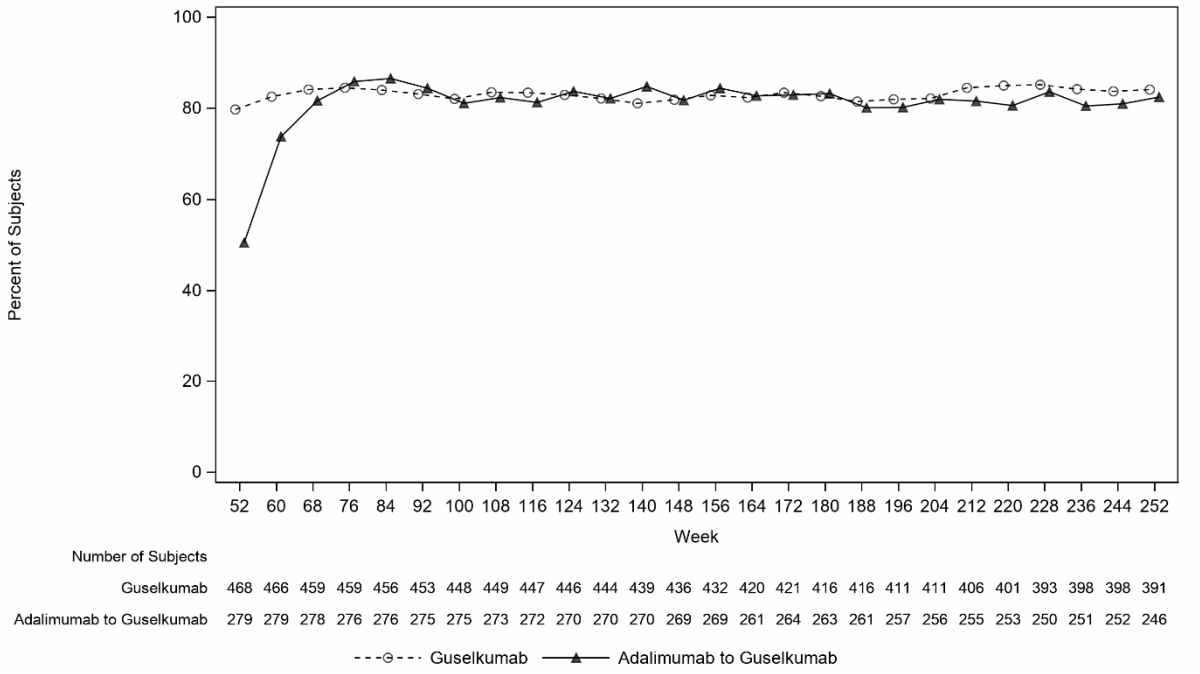
Guselkumab demonstrated rapid onset of efficacy, with a significantly higher percent improvement in PASI as compared with placebo as early as Week 2 ($p < 0.001$). The percentage of patients achieving a PASI 90 response was numerically higher for guselkumab than adalimumab starting at Week 8 with the difference reaching a maximum around Week 20 (VOYAGE 1 and 2) and maintained through Week 48 (VOYAGE 1) (see Figure 1).

Figure 1: Percent of subjects who achieved a PASI 90 response through week 48 by visit (subjects randomised at week 0) in VOYAGE 1



In VOYAGE 1, for patients receiving continuous guselkumab treatment, the PASI 90 response rate was maintained from Week 52 through Week 252. For patients randomised to adalimumab at Week 0 who crossed over to guselkumab at Week 52, the PASI 90 response rate increased from Week 52 through Week 76 and was then maintained through Week 252 (see Figure 2).

Figure 2: Percent of subjects who achieved a PASI 90 response by visit in the open-label phase in VOYAGE 1



The efficacy and safety of guselkumab was demonstrated regardless of age, gender, race, body weight, plaques location, PASI baseline severity, concurrent psoriatic arthritis, and previous treatment with a biologic therapy. Guselkumab was efficacious in conventional systemic-naive, biologic-naive, and biologic-exposed patients.

In VOYAGE 2, 88.6% of patients receiving guselkumab maintenance treatment at Week 48 were PASI 90 responders compared to 36.8% of patients who were withdrawn from treatment at Week 28 ($p < 0.001$). Loss of PASI 90 response was noted as early as 4 weeks after withdrawal of guselkumab treatment with a median time to loss of PASI 90 response of approximately 15 weeks. Among patients who were withdrawn from treatment and subsequently re-initiated guselkumab, 80% regained a PASI 90 response when assessed 20 weeks after initiation of retreatment.

In VOYAGE 2, among 112 patients randomised to adalimumab who failed to achieve a PASI 90 response at Week 28, 66% and 76% achieved a PASI 90 response after 20 and 44 weeks of treatment with guselkumab, respectively. In addition, among 95 patients randomised to guselkumab who failed to achieve a PASI 90 response at Week 28, 36% and 41% achieved a PASI 90 response with an additional 20 and 44 weeks of continued treatment with guselkumab, respectively. No new safety findings were observed in patients who switched from adalimumab to guselkumab.

Regional disease

In VOYAGE 1 and 2, significant improvements were seen in scalp, hand and foot, and nail psoriasis (as measured by the Scalp-specific Investigator Global Assessment [ss-IGA], Physician's Global Assessment of Hands and/or Feet [hf-PGA], Fingernail Physician's Global Assessment [f-PGA] and Nail Psoriasis Severity Index [NAPSI], respectively) in guselkumab-treated patients compared to placebo treated patients at Week 16 ($p < 0.001$, Table 4). Guselkumab demonstrated superiority compared to adalimumab for scalp and hand and foot psoriasis at Week 24 (VOYAGE 1 and 2)

and Week 48 (VOYAGE 1) ($p \leq 0.001$, except for hand and foot psoriasis at Week 24 [VOYAGE 2] and Week 48 [VOYAGE 1], $p < 0.05$).

Table 4: Summary of regional disease responses in VOYAGE 1 and VOYAGE 2

	VOYAGE 1			VOYAGE 2		
	Placebo	guselkumab	adalimumab	Placebo	guselkumab	adalimumab
ss-IGA (N)[a]	145	277	286	202	408	194
ss-IGA 0/1[b], n (%)						
Week 16	21 (14.5)	231 (83.4)[c]	201 (70.3)[d]	22 (10.9)	329 (80.6)[c]	130 (67.0)[d]
hf-PGA (N)[a]	43	90	95	63	114	56
hf-PGA 0/1[b], n (%)						
Week 16	6 (14.0)	66 (73.3)[e]	53 (55.8)[d]	9 (14.3)	88 (77.2)[e]	40 (71.4)[d]
f-PGA (N)[a]	88	174	173	123	246	124
f-PGA 0/1, n (%)						
Week 16	14 (15.9)	68 (39.1)[e]	88 (50.9)[d]	18 (14.6)	128 (52.0)[e]	74 (59.7)[d]
NAPSI (N)[a]	99	194	191	140	280	140
Percent Improvement, mean (SD)						
Week 16	-0.9 (57.9)	34.4 (42.4)[e]	38.0 (53.9)[d]	1.8 (53.8)	39.6 (45.6)[e]	46.9 (48.1)[d]

[a] Includes only subjects with ss-IGA, f-PGA, hf-PGA score ≥ 2 at baseline or baseline NAPSI score > 0.

[b] Includes only subjects achieving ≥ 2-grade improvement from baseline in ss-IGA and/or hf-PGA.

[c] $p < 0.001$ for comparison between guselkumab and placebo for the major secondary endpoint.

[d] comparisons between guselkumab and adalimumab were not performed.

[e] $p < 0.001$ for comparison between guselkumab and placebo.

Health related quality of life / Patient reported outcomes

Across VOYAGE 1 and 2 significantly greater improvements in health related quality of life as measured by Dermatology Life Quality Index (DLQI) and in patient reported psoriasis symptoms (itching, pain, burning, stinging and skin tightness) and signs (skin dryness, cracking, scaling, shedding or flaking, redness and bleeding) as measured by the Psoriasis Symptoms and Signs Diary (PSSD) were observed in guselkumab patients compared to placebo patients at Week 16 (Table 5). Signs of improvement on patient reported outcomes were maintained through Week 24 (VOYAGE 1 and 2) and Week 48 (VOYAGE 1). In VOYAGE 1, for patients receiving continuous guselkumab treatment, these improvements were maintained in the open-label phase through Week 252 (Table 6).

Table 5: Summary of patient reported outcomes at week 16 in VOYAGE 1 and VOYAGE 2

	VOYAGE 1			VOYAGE 2		
	Placebo	guselkumab	adalimumab	Placebo	guselkumab	adalimumab
DLQI, subjects with baseline score	170	322	328	248	495	247
Change from baseline, mean (standard deviation)						
Week 16	-0.6 (6.4)	-11.2 (7.2)[c]	-9.3 (7.8)[b]	-2.6 (6.9)	-11.3 (6.8)[c]	-9.7 (6.8)[b]
PSSD Symptom score, subjects with baseline score > 0	129	248	273	198	410	200
Symptom score = 0, n (%)						
Week 16	1 (0.8)	67 (27.0)[a]	45 (16.5)[b]	0	112 (27.3)[a]	30 (15.0)[b]
PSSD Sign score, subjects with baseline score > 0	129	248	274	198	411	201
Sign score = 0, n (%)						
Week 16	0	50 (20.2)[a]	32 (11.7)[b]	0	86 (20.9)[a]	21 (10.4)[b]

[a] $p < 0.001$ for comparison between guselkumab and placebo.

[b] comparisons between guselkumab and adalimumab were not performed.

[c] $p < 0.001$ for comparison between guselkumab and placebo for major secondary endpoints.

Table 6: Summary of patient reported outcomes in the open-label phase in VOYAGE 1

	guselkumab			adalimumab-guselkumab		
	Week 76	Week 156	Week 252	Week 76	Week 156	Week 252
DLQI score > 1 at baseline, n	445	420	374	264	255	235
Subjects with DLQI 0/1	337 (75.7%)	308 (73.3%)	272 (72.7%)	198 (75.0%)	190 (74.5%)	174 (74.0%)
PSSD Symptom Score, subjects with baseline score > 0	347	327	297	227	218	200
Symptom score = 0, n (%)	136 (39.2%)	130 (39.8%)	126 (42.4%)	99 (43.6%)	96 (44.0%)	96 (48.0%)
PSSD Sign score, subjects with baseline score > 0	347	327	297	228	219	201
Sign score = 0, n (%)	102 (29.4%)	94 (28.7%)	98 (33.0%)	71 (31.1%)	69 (31.5%)	76 (37.8%)

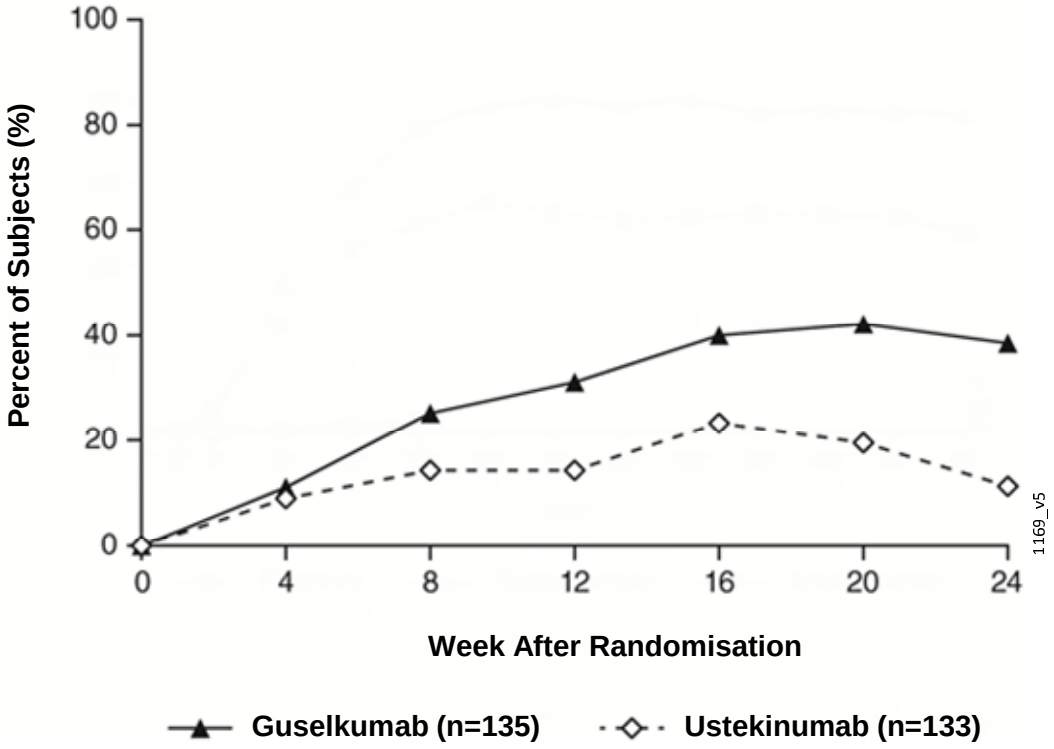
In VOYAGE 2, guselkumab patients had significantly greater improvement from baseline compared to placebo in health-related quality of life, anxiety and depression, and work limitation measures at Week 16, as measured by the 36-item Short Form (SF-36) health survey questionnaire, Hospital Anxiety and Depression Scale (HADS), and Work Limitations Questionnaire (WLQ), respectively. The improvements in SF-36, HADS and WLQ were all maintained through Week 48 and in the open-label phase through Week 252 among patients randomised to maintenance therapy at Week 28.

NAVIGATE

The NAVIGATE study examined the efficacy of guselkumab in patients who had an inadequate response (ie, who had not achieved a 'cleared' or 'minimal' response defined as IGA ≥ 2) to ustekinumab at Week 16. All patients (N=871) received open-label ustekinumab (45 mg ≤100 kg and 90 mg >100 kg) at Weeks 0 and 4. At Week 16, 268 patients with an IGA ≥ 2 score were randomised to either continue ustekinumab treatment (N=133) q12w, or to initiate guselkumab treatment (N=135) at Weeks 16, 20, and q8w thereafter. Baseline characteristics for randomised patients were similar to those observed in VOYAGE 1 and 2.

After randomisation, the primary endpoint was the number of post-randomisation visits between Weeks 12 and 24 at which patients achieved an IGA score 0/1 and had ≥ 2 grade improvement. Patients were examined at four-week intervals for a total of four visits. Among patients who inadequately responded to ustekinumab at the time of randomisation, significantly greater improvement of efficacy was observed in patients who switched to guselkumab treatment compared to patients who continued ustekinumab treatment. Between 12 and 24 weeks after randomisation, guselkumab patients achieved an IGA score 0/1 with ≥ 2 grade improvement twice as often as ustekinumab patients (mean 1.5 vs 0.7 visits, respectively, $p < 0.001$). Additionally, at 12 weeks after randomisation a higher proportion of guselkumab patients compared to ustekinumab patients achieved an IGA score 0/1 and ≥ 2 grade improvement (31.1% vs. 14.3%, respectively; $p = 0.001$) and a PASI 90 response (48% vs 23%, respectively, $p < 0.001$). Differences in response rates between guselkumab and ustekinumab treated patients were noted as early as 4 weeks after randomisation (11.1% and 9.0%, respectively) and reached a maximum 24 weeks after randomisation (see Figure 3). No new safety findings were observed in patients who switched from ustekinumab to guselkumab.

Figure 3: Percent of subjects who achieved an IGA Score of cleared (0) or minimal (1) and at least a 2-grade improvement in IGA from week 0 through week 24 by visit after randomisation in NAVIGATE



ECLIPSE

Efficacy and safety of guselkumab were also investigated in a double-blind study compared to secukinumab. Patients were randomised to receive guselkumab (N=534; 100 mg at Week 0, 4 and q8w thereafter), or secukinumab (N=514; 300 mg at Week 0, 1, 2, 3, 4, and q4w thereafter). The last dose was at week 44 for both treatment groups.

Baseline disease characteristics were consistent with a population of moderate to severe plaque psoriasis with a median BSA of 20%, a median PASI score of 18, and an IGA score of severe for 24% of patients.

Guselkumab was superior to secukinumab as measured by the primary endpoint of PASI 90 response at Week 48 (84.5% versus 70.0%, $p < 0.001$). Comparative PASI response rates are presented in Table 7.

Table 7: PASI response rates in ECLIPSE

	Number of patients (%)	
	guselkumab (N=534)	secukinumab (N=514)
Primary Endpoint		
PASI 90 response at Week 48	451 (84.5%) [a]	360 (70.0%)
Major Secondary Endpoints		
PASI 75 response at both Week 12 and Week 48	452 (84.6%) [b]	412 (80.2%)

PASI 75 response at Week 12	477 (89.3%) [c]	471 (91.6%)
PASI 90 response at Week 12	369 (69.1%) [c]	391 (76.1%)
PASI 100 response at Week 48	311 (58.2%) [c]	249 (48.4%)

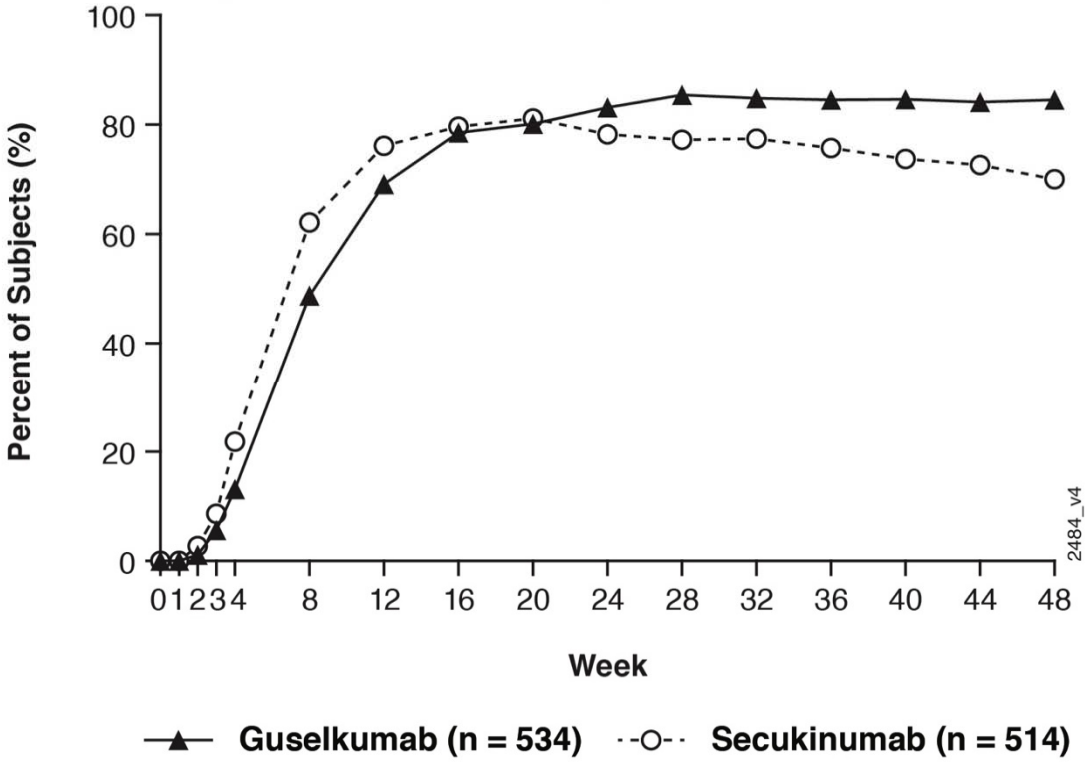
[a] $p < 0.001$ for superiority

[b] $p < 0.001$ for non-inferiority, $p=0.062$ for superiority

[c] formal statistical testing was not performed

Guselkumab and secukinumab PASI 90 response rates through Week 48 are presented in Figure 4.

Figure 4: Percent of subjects who achieved a PASI 90 response through week 48 by visit (Subjects randomised at Week 0) in ECLIPSE



Paediatric population

Paediatric plaque psoriasis

The safety and efficacy of guselkumab were assessed in one multicentre, randomised, placebo- and active biological comparator-controlled study (PROTOSTAR) in 120 paediatric patients 6 to 17 years of age with moderate to severe plaque psoriasis who were candidates for phototherapy or systemic therapy and were inadequately controlled by phototherapy and/or topical therapies. PROTOSTAR was conducted in two parts. Part 1 consisted of a 16-week randomised, placebo and active comparator-controlled period followed by an uncontrolled period of withdrawal and retreatment or initiation of treatment with guselkumab through Week 52. Part 2 consisted of an open-label guselkumab arm through Week 52.

Enrolled patients had an IGA score of ≥3 (“moderate”) on a 5-point scale of overall disease severity, a PASI ≥12, and a minimum affected BSA of ≥10%, and at least one of the following: 1) very thick lesions, 2) clinically relevant facial, genital, or hand/foot involvement, 3) PASI ≥20, 4) BSA >20%, or 5) IGA=4. Subjects with guttate, erythrodermic, or pustular psoriasis were excluded.

In Part 1, 92 patients 6 to 17 years of age were randomised to receive subcutaneous injection of either guselkumab (n=41) or placebo (n=25) at Week 0, 4, and 12, or an active biological comparator (n=26) weekly. In Part 2, 28 additional adolescent patients 12 to 17 years of age were enrolled to receive subcutaneous injection of guselkumab at Week 0, 4, and every 8 weeks thereafter. In the guselkumab group, patients with a body weight less than 70 kg received 1.3 mg/kg administered with the 45 mg/0.45 mL pre-filled pen, and patients with a body weight of 70 kg or more received 100 mg administered with the pre-filled syringe.

The co-primary endpoints were the proportion of patients who achieved a PASI 75 response and the proportion of patients who achieved an IGA score of 0 (“cleared”) or 1 (“minimal”) at Week 16. Secondary endpoints included but were not limited to the proportion of patients who achieved a PASI 90 response, an IGA score of 0 (“cleared”) or a PASI 100 response at Week 16.

Of the 92 patients in the controlled part of the study, baseline demographic characteristics were generally comparable across treatment groups. Overall, over 55% were male, 85% were white, the mean body weight was approximately 57.3 kg, and the mean age was 12.9 years with 33% of the patients less than 12 years.

The baseline disease characteristics were generally comparable across treatment groups with median baseline BSA of 20%, median baseline PASI score of approximately 17, and baseline IGA score of severe for 20% (placebo) and 24% (guselkumab) of patients, and a history of psoriatic arthritis for <5% of patients.

Overall skin disease

Treatment with guselkumab resulted in significant improvements in the outcome measures of disease activity compared to placebo at Week 16. The key efficacy results for the study endpoints are shown in Table 8 below.

Table 8: Summary of endpoints at week 16 in PROTOSTAR

	Placebo (N=25) n (%)	**Guselkumab (N=41) n (%)**	**P-value**
IGA scores of cleared (0) or minimal (1)	4 (16.0%)	27 (65.9%)	<0.001
IGA scores of cleared (0)	1 (4.0%)	16 (39.0%)	0.004

PASI 75 responders	5 (20.0%)	31 (75.6%)	<0.001
PASI 90 responders	4 (16.0%)	23 (56.1%)	0.003
PASI 100 responders	0	14 (34.1%)	0.002

Beyond the 16-week placebo-controlled period in Part 1 of PROTOSTAR, the guselkumab-treated patients who achieved PASI 90 at Week 16 were withdrawn from treatment. Loss of PASI 90 response was noted as early as 12 weeks after withdrawal of guselkumab treatment with a median time to loss of PASI 90 response of approximately 24 weeks. Of the guselkumab-treated patients who failed to achieve a PASI 90 response at Week 16, 72.2% of patients that received an additional 32 weeks of continued guselkumab treatment were PASI 75 responders at Week 52, and 61.1% achieved a PASI 90 response at Week 52.

In patients randomised to placebo at Week 0 who failed to achieve a PASI 90 response at Week 16 and crossed over to receive guselkumab 95.0% and 65.0% achieved PASI 75 and PASI 90 response, respectively, at Week 52.

In the open-label Part 2 of PROTOSTAR, 92.9% and 82.1% of adolescent patients receiving continuous guselkumab treatment achieved PASI 75 and PASI 90 response, respectively, at Week 52.

Health-related quality of life outcomes

Change from baseline in the Children's Dermatology Life Quality Index (CDLQI) score at Week 16 showed a significantly greater improvement in the CDLQI score in the guselkumab group compared with the placebo group.

Changes from baseline in the Family Dermatology Life Quality Index (FDLQI) score at Week 16 also showed a numerically greater improvement in the FDLQI score in the guselkumab group compared with the placebo group (see Table 9).

Table 9: Summary of health-related quality of life outcomes at week 16 in PROTOSTAR

	Placebo (N=25)	**Guselkumab (N=41)**	**P-value**
Change from baseline in CDLQI			
LSMean (95% CI)[a]	-1.88 (-3.81, 0.05)	-7.28 (-8.87, -5.68)	<0.001
Change from baseline in FDLQI			
LSMean (95% CI)[a]	-0.60 (-2.75, 1.55)	-6.04 (-7.83, -4.25)	<0.001[b]

[a] LSMean = least squares mean

[b] p-value for FDLQI is nominal

5.2 Pharmacokinetic properties

Paediatric Patients

Steady-state serum trough concentrations of guselkumab were achieved by Week 20 in paediatric patients 6 to 17 years of age with moderate to severe plaque psoriasis, and were within the range of those observed in adults.

The recommended dosing regimen results in similar predicted serum guselkumab exposure in paediatric patients with plaque psoriasis as compared to adults across the body weight range.

Absorption

Following a single 100 mg subcutaneous injection in healthy subjects, guselkumab reached a mean (± SD) maximum serum concentration (C_{max}) of 8.09 ± 3.68 mcg/mL by approximately 5.5 days post dose.

Steady-state serum guselkumab concentrations were achieved by Week 20 following subcutaneous administrations of 100 mg guselkumab at Weeks 0 and 4, and every 8 weeks thereafter. The mean (± SD) steady-state trough serum guselkumab concentrations in two Phase III studies in patients with plaque psoriasis were 1.15 ± 0.73 mcg/mL and 1.23 ± 0.84 mcg/mL.

The absolute bioavailability of guselkumab following a single 100 mg subcutaneous injection was estimated to be approximately 49% in healthy subjects.

Distribution

Mean volume of distribution during the terminal phase (V_z) following a single intravenous administration to healthy subjects ranged from approximately 7 to 10 L across studies.

Biotransformation

The exact pathway through which guselkumab is metabolised has not been characterised. As a human IgG mAb, guselkumab is expected to be degraded into

small peptides and amino acids via catabolic pathways in the same manner as endogenous IgG.

Elimination

Mean systemic clearance (CL) following a single intravenous administration to healthy subjects ranged from 0.288 to 0.479 L/day across studies. Mean half-life ($T_{1/2}$) of guselkumab was approximately 17 days in healthy subjects and approximately 15 to 18 days in patients with plaque psoriasis across studies.

Population pharmacokinetic analyses indicated that concomitant use of NSAIDs, oral corticosteroids and csDMARDs such as methotrexate, did not affect the clearance of guselkumab.

Linearity/non-linearity

The systemic exposure of guselkumab (C_{max} and AUC) increased in an approximately dose-proportional manner following a single subcutaneous injection at doses ranging from 10 mg to 300 mg in healthy subjects or patients with plaque psoriasis.

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Patients with renal or hepatic impairment

No specific study has been conducted to determine the effect of renal or hepatic impairment on the pharmacokinetics of guselkumab. Renal elimination of intact guselkumab, an IgG mAb, is expected to be low and of minor importance; similarly, hepatic impairment is not expected to influence clearance of guselkumab as IgG mAbs are mainly eliminated via intracellular catabolism.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeat-dose toxicity, toxicity to reproduction and pre- and post-natal development.

In repeat-dose toxicity studies in cynomolgus monkeys, guselkumab was well tolerated via intravenous and subcutaneous routes of administration. A weekly subcutaneous guselkumab dose of 50 mg/kg administered to monkeys resulted in exposure (AUC) values that were at least 23 times the maximum clinical exposures following a guselkumab dose of 200 mg given intravenously. Additionally, there

were no adverse immunotoxicity or cardiovascular safety pharmacology effects noted during the conduct of the repeat-dose toxicity studies or in a targeted cardiovascular safety pharmacology study in cynomolgus monkeys.

There were no preneoplastic changes observed in histopathology evaluations of animals treated up to 24-weeks, or following the 12-week recovery period during which active substance was detectable in the serum.

No mutagenicity or carcinogenicity studies were conducted with guselkumab.

Guselkumab could not be detected in breast milk from cynomolgus monkeys as measured at post-natal day 28.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Histidine

Histidine monohydrochloride monohydrate

Polysorbate 80 (E433)

Sucrose

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

2 years.

6.4 Special precautions for storage

Store in a refrigerator (2°C–8°C). Do not freeze.

Keep the pre-filled syringe in the outer carton in order to protect from light.

6.5 Nature and contents of container

1 mL solution in a pre-filled glass syringe with a fixed needle and a needle shield, assembled in an automatic needle guard. Tremfya is available in a pack containing one pre-filled syringe and in a multipack contain 2 (2 packs of 1) pre-filled syringes.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

After removing the pre-filled syringe from the refrigerator, keep the pre-filled syringe inside the carton and allow to reach room temperature by waiting for 30 minutes before injecting Tremfya. The pre-filled syringe should not be shaken.

Prior to use, a visual inspection of the pre-filled syringe is recommended. The solution should be clear, colourless to light yellow, and may contain a few small white or clear particles. Tremfya should not be used if the solution is cloudy or discoloured, or contains large particles.

Each pack is provided with an ‘Instructions for use’ leaflet that fully describes the preparation and administration of the pre-filled syringe.

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

7 MARKETING AUTHORISATION HOLDER

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