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

Bimzelx 320 mg solution for injection in pre-filled pen

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Bimzelx 320 mg solution for injection in pre-filled pen

Each pre-filled pen contains 320 mg of bimekizumab in 2 mL
Bimekizumab is a humanised IgG1monoclonal antibody produced in a genetically engineered Chinese hamster ovary (CHO) cell line 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 to slightly opalescent and, colourless to pale brownish yellow.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Plaque psoriasis
Bimzelx is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

Psoriatic arthritis

Bimzelx, alone or in combination with methotrexate, is indicated for the treatment of active psoriatic arthritis in adults who have had an inadequate response or who have been intolerant to one or more disease-modifying antirheumatic drugs (DMARDs).
Axial spondyloarthritis

Non-radiographic axial spondyloarthritis (nr-axSpA)

Bimzelx is indicated for the treatment of adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) who have responded inadequately or are intolerant to non-steroidal anti-inflammatory drugs (NSAIDs).

Ankylosing spondylitis (AS, radiographic axial spondyloarthritis)

Bimzelx is indicated for the treatment of adults with active ankylosing spondylitis who have responded inadequately or are intolerant to conventional therapy.

Hidradenitis suppurativa (HS)

Bimzelx is indicated for the treatment of active moderate to severe hidradenitis suppurativa (acne inversa) in adults with an inadequate response to conventional systemic HS therapy (see section 5.1).

4.2 Posology and method of administration

Bimzelx is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of conditions for which Bimzelx is indicated.

Posology

Plaque psoriasis
The recommended dose for adult patients with plaque psoriasis is 320 mg (given as 2 subcutaneous injections of 160 mg or 1 subcutaneous injection of 320 mg) at week 0, 4, 8, 12, 16 and every 8 weeks thereafter.

Psoriatic arthritis

The recommended dose for adult patients with active psoriatic arthritis is 160 mg (given as 1 subcutaneous injection of 160 mg) every 4 weeks.

For psoriatic arthritis patients with coexistent moderate to severe plaque psoriasis, the recommended dose is the same as for plaque psoriasis [320 mg (given as 2 subcutaneous injections of 160 mg or 1 subcutaneous injection of 320 mg) at week 0, 4, 8, 12, 16 and every 8 weeks thereafter]. After 16 weeks, regular assessment of efficacy is recommended and if a sufficient clinical response in joints cannot be maintained, a switch to 160 mg every 4 weeks can be considered.

Axial spondyloarthritis (nr-axSpA and AS)
The recommended dose for adult patients with axial spondyloarthritis is 160 mg (given as 1 subcutaneous injection of 160 mg) every 4 weeks.

Hidradenitis suppurativa
The recommended dose for adult patients with hidradenitis suppurativa is 320 mg (given as 2 subcutaneous injections of 160 mg or 1 subcutaneous injection of 320 mg) every 2 weeks up to week 16 and every 4 weeks thereafter.

For above indications, consideration should be given to discontinuing treatment in patients who have shown no improvement by 16 weeks of treatment.

Special populations

Overweight patients with plaque psoriasis

For some patients with plaque psoriasis (including psoriatic arthritis with coexistent moderate to severe psoriasis) and a body weight ≥120 kg who did not achieve complete skin clearance at week 16, 320 mg every 4 weeks after week 16 may further improve treatment response (see section 5.1).

Elderly (≥65 years)

No dose adjustment is required (see section 5.2).

Renal or hepatic impairment

Bimekizumab has not been studied in these patient populations. Dose adjustments are not considered necessary based on pharmacokinetics (see section 5.2).

Paediatric population

The safety and efficacy of bimekizumab in children and adolescents below the age of 18 years have not been established. No data are available.

Method of administration

This medicinal product is administered by subcutaneous injection. A 320 mg dose can be given as 2 subcutaneous injections of 160 mg or 1 subcutaneous injection of 320 mg.

Suitable areas for injection include thigh, abdomen and upper arm. Injection sites should be rotated and injections should not be given into psoriasis plaques or areas where the skin is tender, bruised, erythematous, or indurated. Administration in the upper arm may only be performed by a healthcare professional or caregiver.

The pre-filled syringe or pre-filled pen must not be shaken.

After proper training in subcutaneous injection technique, patients may self-inject Bimzelx with a pre-filled syringe or pre-filled pen if their physician determines that it is appropriate and with medical follow-up as necessary. Patients should be instructed to inject the full amount of Bimzelx according to the instructions for use provided in the package leaflet.

4.3 Contraindications

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

Bimekizumab may increase the risk of infections such as upper respiratory tract infections and oral candidiasis (see section 4.8).

Caution should be exercised when considering the use of bimekizumab in patients with a chronic infection or a history of recurrent infection. Treatment with bimekizumab must not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated (see section 4.3).

Patients treated with bimekizumab should be instructed to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops an infection, the patient should be carefully monitored. If the infection becomes serious or is not responding to standard therapy, treatment should be discontinued until the infection resolves.

Pre-treatment evaluation for tuberculosis (TB)

Prior to initiating treatment with bimekizumab, patients should be evaluated for TB infection. Bimekizumab should not be given in patients with active TB (see section 4.3). Patients receiving bimekizumab should be monitored for signs and symptoms of active TB. Anti-TB therapy should be considered prior to initiating bimekizumab in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed.

Inflammatory bowel disease

Cases of new or exacerbations of inflammatory bowel disease have been reported with bimekizumab (see section 4.8). Bimekizumab is not recommended in patients with inflammatory bowel disease. If a patient develops signs and symptoms of inflammatory bowel disease or experiences an exacerbation of pre-existing inflammatory bowel disease, bimekizumab should be discontinued and appropriate medical management should be initiated.

Hypersensitivity
Serious hypersensitivity reactions including anaphylactic reactions have been observed with IL-17 inhibitors. If a serious hypersensitivity reaction occurs, administration of bimekizumab should be discontinued immediately and appropriate therapy initiated.

Vaccinations

Prior to initiating therapy with bimekizumab, completion of all age appropriate immunisations according to current immunisation guidelines should be considered.

Live vaccines should not be given in patients treated with bimekizumab.

Patients treated with bimekizumab may receive inactivated or non-live vaccinations. Healthy individuals who received a single 320 mg dose of bimekizumab two weeks prior to vaccination with an inactivated seasonal influenza vaccine had similar antibody responses compared to individuals who did not receive bimekizumab prior to vaccination.

Excipients

This medicinal product contains 0.4 mg of polysorbate 80 in each 1 mL solution. Polysorbates may cause allergic reactions.

This medicinal product contains less than 1 mmol (23 mg) sodium per dose, that is to say essentially “sodium free”.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

There is no direct evidence for the role of IL-17A or IL-17F in the expression of CYP450 enzymes. The formation of some CYP450 enzymes is suppressed by increased levels of cytokines during chronic inflammation. Thus, anti-inflammatory treatments, such as with the IL-17A and IL-17F inhibitor bimekizumab, may result in normalisation of CYP450 levels with accompanying lower exposure of CYP450-metabolised medicinal products. Therefore, a clinically relevant effect on CYP450 substrates with a narrow therapeutic index, in which the dose is individually adjusted (e.g. warfarin) cannot be excluded. On initiation of bimekizumab therapy in patients being treated with these types of medicinal products, therapeutic monitoring should be considered.

Population pharmacokinetic (PK) data analyses indicated that concomitant administration of conventional disease modifying antirheumatic drugs (cDMARDs) including methotrexate or prior exposure to biologics have no clinically relevant impact on the clearance of bimekizumab.

Live vaccines should not be given concurrently with bimekizumab (see section 4.4).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential should use an effective method of contraception during treatment and for at least 17 weeks after treatment.

Pregnancy

There is a limited amount of data on the use of bimekizumab 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 Bimzelx during pregnancy.

Breast-feeding

It is unknown whether bimekizumab is excreted in human milk. A risk to the newborn/infant cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Bimzelx therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility

The effect of bimekizumab 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

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

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported adverse reactions were upper respiratory tract infections (14.5%, 14.6%, 16.3%, 8.8% in plaque psoriasis, psoriatic arthritis, axial spondyloarthritis (axSpA) and hidradenitis suppurativa respectively) and oral candidiasis (7.3%, 2.3%, 3.7%, 5.6% in PSO, PsA, axSpA and HS respectively).

Tabulated list of adverse reactions

Adverse reactions from clinical studies and post-marketing reports (Table 1) 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).

A total of 5862 patients have been treated with bimekizumab in blinded and open-label clinical studies in plaque psoriasis (PSO), psoriatic arthritis (PsA), axial spondyloarthritis (nr-axSpA and AS) and hidradenitis suppurativa (HS) representing 11468.6 patient-years of exposure. Of these, over 4660 patients were exposed to bimekizumab for at least one year. Overall, the safety profile of bimekizumab is consistent across all indications.

Table 1: List of adverse reactions

System Organ Class	Frequency	Adverse reaction
Infections and infestations	Very common	Upper respiratory tract infections

	Common	Oral candidiasis, Tinea infections, Ear infections, Herpes simplex infections, Oropharyngeal candidiasis, Gastroenteritis, Folliculitis, Vulvovaginal mycotic infection (including vulvovaginal candidiasis)
	Uncommon	Mucosal and cutaneous candidiasis (including oesophageal candidiasis), Conjunctivitis
Blood and lymphatic system disorders	Uncommon	Neutropenia
Nervous System disorders	Common	Headache
Gastrointestinal disorders	Uncommon	Inflammatory bowel disease
Skin and subcutaneous tissue disorders	Common	Rash, dermatitis and eczema, Acne
General disorders and administration site conditions	Common	Injection site reactions[a], Fatigue
[a)] Includes: injection site erythema, reaction, oedema, pain, swelling, haematoma.		

Description of selected adverse reactions

Infections

In the placebo-controlled period of Phase III clinical studies in plaque psoriasis, infections were reported in 36.0% of patients treated with bimekizumab for up to 16 weeks compared with 22.5% of patients treated with placebo. Serious infections occurred in 0.3% of patients treated with bimekizumab and 0% treated with placebo.

The majority of infections consisted of non-serious mild to moderate upper respiratory tract infections such as nasopharyngitis. There were higher rates of oral and oropharyngeal candidiasis in patients treated with bimekizumab consistent with the mechanism of action (7.3% and 1.2% respectively compared to 0% for placebo-treated patients). More than 98% of cases were non-serious, mild or moderate in severity, and did not require treatment discontinuation. A slightly higher incidence of oral candidiasis was reported in patients <70 kg (8.5% *versus* 7.0% in patients ≥70 kg).

Over the entire treatment period of Phase III studies in plaque psoriasis, infections were reported in 63.2% of patients treated with bimekizumab (120.4 per 100 patient-years). Serious infections were reported in 1.5% of patients treated with bimekizumab (1.6 per 100 patient-years) (see section 4.4).

Infection rates observed in PsA and axSpA (nr-axSpA and AS) Phase III clinical studies were similar to those observed in plaque psoriasis apart from oral and oropharyngeal candidiasis rates in patients treated with bimekizumab, which were

lower at 2.3% and 0% respectively in PsA and 3.7% and 0.3% respectively in axSpA compared to 0% with placebo.

Infection rates observed in HS Phase III clinical studies were similar to those observed in other indications. In the placebo-controlled period, oral and oropharyngeal candidiasis rates in patients treated with bimekizumab were 7.1% and 0% respectively compared to 0% with placebo.

Neutropenia

Neutropenia was observed with bimekizumab in Phase III clinical studies in plaque psoriasis. Over the entire treatment period of Phase III studies, neutropenia grade 3/4 were observed in 1% of patients treated with bimekizumab.

The frequency of neutropenia in PsA, axSpA (nr-axSpA and AS) and HS clinical studies was similar to that observed in plaque psoriasis studies.

Most cases were transient and did not require treatment discontinuation. No serious infections were associated with neutropenia.

Hypersensitivity

Serious hypersensitivity reactions including anaphylactic reactions have been observed with IL-17 inhibitors.

Immunogenicity

Plaque psoriasis

Approximately 45% of plaque psoriasis patients treated with bimekizumab up to 56 weeks at the recommended dosing regimen (320 mg every 4 weeks up to week 16 and 320 mg every 8 weeks thereafter) developed anti-drug antibodies. Of the patients who developed anti-drug antibodies, approximately 34% (16% of all patients treated with bimekizumab) had antibodies that were classified as neutralising.

Psoriatic arthritis

Approximately 31% of patients with psoriatic arthritis treated with bimekizumab at the recommended dosing regimen (160 mg every 4 weeks) up to 16 weeks had anti-drug antibodies. Of the patients with anti-drug antibodies, about 33% (10% of all patients treated with bimekizumab) had antibodies that were classified as neutralising. By week 52, approximately 47% of biologic disease-modifying anti-rheumatic drug (bDMARD) treatment naïve patients with psoriatic arthritis in the BE OPTIMAL study treated with bimekizumab at the recommended dosing regimen (160 mg every 4 weeks) had anti-drug antibodies. Of the patients with anti-drug antibodies, about 38% (18% of all patients in the BE OPTIMAL study treated with bimekizumab) had antibodies that were classified as neutralising.

Axial spondyloarthritis (nr-axSpA and AS)

Approximately 57% of patients with nr-axSpA treated with bimekizumab up to 52 weeks at the recommended dosing regimen (160 mg every 4 weeks) had anti-drug antibodies. Of the patients with anti-drug antibodies, approximately 44% (25% of all patients treated with bimekizumab) had antibodies that were classified as neutralising.

Approximately 44% of patients with AS treated with bimekizumab up to 52 weeks at the recommended dosing regimen (160 mg every 4 weeks) had anti-drug antibodies. Of the patients with anti-drug antibodies, approximately 44% (20% of all patients treated with bimekizumab) had antibodies that were classified as neutralising.

Hidradenitis suppurativa

Approximately 59% of HS patients treated with bimekizumab up to 48 weeks at the recommended dosing regimen (320 mg every 2 weeks up to week 16 and 320 mg every 4 weeks thereafter) developed anti-drug antibodies. Of the patients who developed anti-drug antibodies, approximately 63% (37% of all patients treated with bimekizumab) had antibodies that were classified as neutralising.

Across indications, no clinically meaningful impact on clinical response was associated with anti-bimekizumab antibodies development and an association between immunogenicity and treatment emergent adverse events has not been clearly established.

Elderly patients (≥65 years)
Exposure is limited in elderly subjects.

Elderly patients may be more likely to experience certain adverse reactions such as oral candidiasis, dermatitis and eczema when using bimekizumab.

In the placebo-controlled period of Phase III clinical studies in plaque psoriasis, oral candidiasis was observed in 18.2% of patients ≥65 years *versus* 6.3% in <65 years, dermatitis and eczema in 7.3% of patients ≥65 years *versus* 2.8% in <65 years.

In the placebo-controlled period of Phase III clinical studies in psoriatic arthritis, oral candidiasis was observed in 7.0% of patients ≥65 years versus 1.6% in <65 years, dermatitis and eczema in 1.2% of patients ≥65 years versus 2.0% in <65 years.

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

4.9 Overdose

Single doses of 640 mg intravenously or 640 mg subcutaneously, followed by 320 mg subcutaneously every two weeks for five doses have been administered in clinical studies without dose-limiting toxicity. In the event of overdose, it is recommended that the patient be monitored for any signs and symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, interleukin inhibitors, ATC code: L04AC21

Mechanism of action

Bimekizumab is a humanised IgG1/κ monoclonal antibody that selectively binds with high affinity to IL-17A, IL-17F and IL-17AF cytokines, blocking their interaction with the IL-17RA/IL-17RC receptor complex. Elevated concentrations of IL-17A and IL-17F have been implicated in the pathogenesis of several immune-mediated inflammatory diseases including plaque psoriasis, psoriatic arthritis, axial spondyloarthritis and hidradenitis suppurativa. IL-17A and IL-17F cooperate and/or synergise with other inflammatory cytokines to induce inflammation. IL17-F is produced in significant amount by innate immune cells. This production can be independent of IL-23. Bimekizumab inhibits the proinflammatory cytokines, resulting in the normalisation of skin inflammation and substantial decrease of local and systemic inflammation, and as a consequence improvement in clinical signs and symptoms associated with psoriasis, psoriatic arthritis, axial spondyloarthritis and hidradenitis suppurativa. From *in vitro* models, bimekizumab was shown to inhibit psoriasis-related gene expression, cytokine production, the migration of inflammatory cells and pathological osteogenesis to a greater extent than inhibition of IL-17A alone.

Clinical efficacy and safety

Plaque psoriasis

The safety and efficacy of bimekizumab was evaluated in 1,480 patients with moderate to severe plaque psoriasis in three Phase 3 multicentre, randomised, placebo and/or active comparator-controlled studies. Patients were at least 18 years of age, had a Psoriasis Area and Severity Index (PASI) score ≥12 and Body Surface Area (BSA) affected by psoriasis (PSO) ≥10%, an Investigators Global Assessment (IGA) score ≥3 on a 5-point scale and were candidates for systemic psoriasis therapy and/or phototherapy. The efficacy and safety of bimekizumab were evaluated *versus* placebo and ustekinumab (BE VIVID – PS0009), *versus* placebo (BE READY – PS0013) and *versus* adalimumab (BE SURE - PS0008).

The BE VIVID study evaluated 567 patients for 52 weeks where patients were randomised to receive either bimekizumab 320 mg every 4 weeks, ustekinumab (45 mg or 90 mg, depending on patient weight, at baseline and week 4 and then every 12 weeks), or placebo for an initial 16 weeks, followed by bimekizumab 320 mg every 4 weeks.

The BE READY study evaluated 435 patients for 56 weeks. Patients were randomised to receive bimekizumab 320 mg every 4 weeks or placebo. At week 16, patients who achieved a PASI 90 response entered the 40-week randomised withdrawal period. Patients initially randomised to bimekizumab 320 mg every 4 weeks were re-randomised to either bimekizumab 320 mg every 4 weeks or bimekizumab 320 mg every 8 weeks or placebo (i.e. withdrawal of bimekizumab). Patients initially randomised to placebo continued to receive placebo provided they were PASI 90 responders. Patients who did not achieve a PASI 90 response at week 16 entered an open-label escape arm and received bimekizumab 320 mg every 4 weeks for 12 weeks. Patients who relapsed (did not achieve PASI 75 response) during the randomised withdrawal period also entered the 12-week escape arm.

The BE SURE study evaluated 478 patients for 56 weeks. Patients were randomised to receive either bimekizumab 320 mg every 4 weeks through week 56, bimekizumab 320 mg every 4 weeks through week 16 followed by bimekizumab 320 mg every 8 weeks through week 56 or adalimumab as per labelling recommendation through week 24 followed by bimekizumab 320 mg every 4 weeks through week 56.

Baseline characteristics were consistent across all 3 studies: patients were predominantly male (70.7%) and white (84.1%), with a mean age of 45.2 years (18 to 83 years), and 8.9% were ≥65 years of age. The median baseline BSA was 20%, the median baseline PASI score was 18 and the baseline IGA score was severe in 33% of patients. The median baseline scores for Patient Symptoms Diary (PSD) pain, itch and scaling items ranged between 6 and 7 on a 0-10 points scale and the median baseline Dermatology Life Quality Index (DLQI) total score was 9.

Across all 3 studies, 38% of patients had received a prior biologic therapy; 23% had received at least one anti-IL17 agent (primary anti-IL17 failures were excluded) and 13% had received at least one TNF-antagonist. Twenty-two percent were naïve to any systemic therapy (including non-biologic and biologic) and 39% of patients had received prior phototherapy or photochemotherapy.

The efficacy of bimekizumab was evaluated with respect to impact on skin disease overall, specific body locations (scalp, nails, palms and soles), patient reported symptoms and impact on quality of life. The two co-primary endpoints in all 3 studies were the proportion of patients who achieved 1) a PASI 90 response and 2) an IGA “clear or almost clear” (IGA 0/1with at least two points improvement from baseline) response at week 16. PASI 100, IGA 0 response at week 16 and PASI
75 response at week 4 were secondary endpoints in all 3 studies.

Skin disease overall

Treatment with bimekizumab resulted in significant improvement across efficacy endpoints compared to placebo, ustekinumab or adalimumab at week 16. The main efficacy results are shown in Table 2.

Table 2: Summary of clinical responses in BE VIVID, BE READY and BE SURE

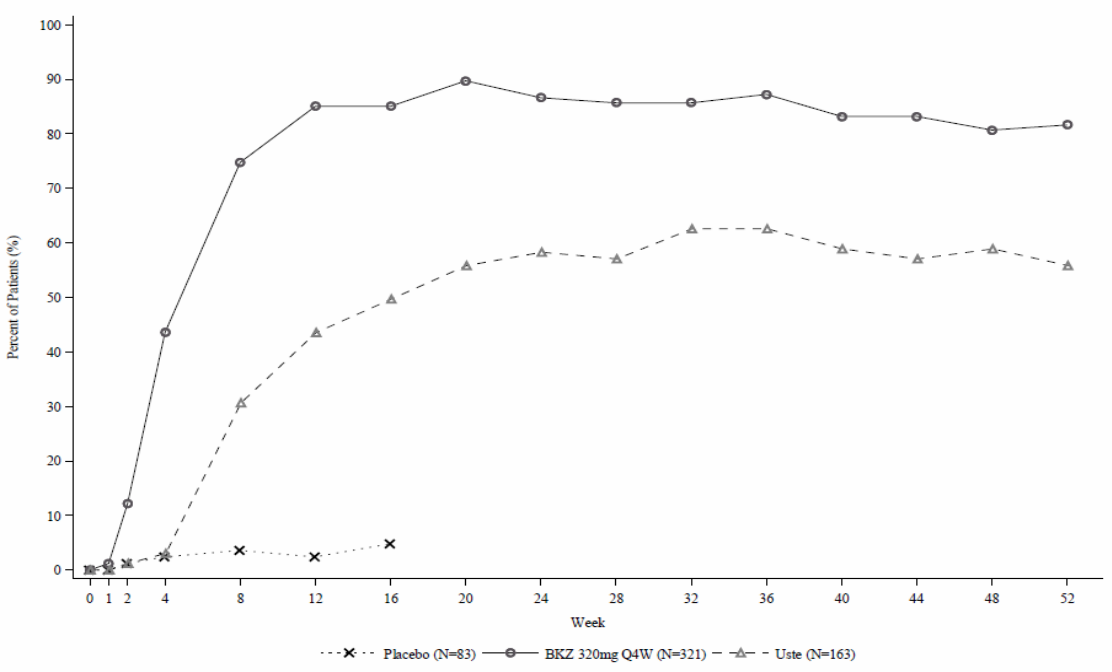
	BE VIVID			BE READY		BE SURE	
	Placebo (N= 83) n (%)	**Bimekizumab 320 mg Q4W (N= 321) n (%)**	**Ustekinumab (N=163) n (%)**	**Placebo (N= 86) n (%)**	**Bimekizumab 320 mg Q4W (N= 349) n (%)**	**Bimekizumab 320 mg Q4W (N= 319) n (%)**	**Adalimumab (N= 159) n (%)**
PASI 100							
Week 16	0 (0.0)	188 (58.6)[a]	34 (20.9)	1 (1.2)	238 (68.2)[a]	194 (60.8)[a]	38 (23.9)
PASI 90							
Week 16	4 (4.8)	273 (85.0)[a, b]	81 (49.7)	1 (1.2)	317 (90.8)[a]	275 (86.2)[a]	75 (47.2)
PASI 75							
Week 4	2 (2.4)	247 (76.9)[a, b]	25 (15.3)	1 (1.2)	265 (75.9)[a]	244 (76.5)[a]	50 (31.4)
Week 16	6 (7.2)	296 (92.2)	119 (73.0)	2 (2.3)	333 (95.4)	295 (92.5)	110 (69.2)
IGA 0							
Week 16	0 (0.0)	188 (58.6)[a]	36 (22.1)	1 (1.2)	243 (69.6)[a]	197 (61.8)	39 (24.5)
IGA 0/1							
Week 16	4 (4.8)	270 (84.1)[a, b]	87 (53.4)	1 (1.2)	323 (92.6)[a]	272 (85.3)[a]	91 (57.2)
Absolute PASI ≤ 2							
Week 16	3 (3.6)	273 (85.0)	84 (51.5)	1 (1.2)	315 (90.3)	280 (87.8)	86 (54.1)
PSD Pain improvement ≥4 (N)	**(N=48)**	**(N=190)**	**(N=90)**	**(N=49)**	**(N=209)**	**(N=222)**	**(N=92)**
Week 16	5 (10.4)	140 (73.7)	54 (60.0)	0 (0.0)	148 (70.8)	143 (64.4)	43 (46.7)
PSD Itch improvement ≥4 (N)	**(N=53)**	**(N=222)**	**(N=104)**	**(N=60)**	**(N=244)**	**(N=248)**	**(N=107)**
Week 16	6 (11.3)	151 (68.0)	57 (54.8)	0 (0.0)	161 (66.0)	153 (61.7)	42 (39.3)
PSD Scaling improvement ≥4 (N)	**(N=56)**	**(N=225)**	**(N=104)**	**(N=65)**	**(N=262)**	**(N=251)**	**(N= 109)**
Week 16	6 (10.7)	171 (76.0)	59 (56.7)	1 (1.5)	198 (75.6)	170 (67.7)	42 (38.5)

Bimekizumab 320 mg Q4W= bimekizumab every 4 weeks. Non-Responder Imputation (NRI) is used.
IGA 0/1 response was defined as Clear (0) or Almost Clear (1) with at least a 2-category improvement from Baseline at week 16. IGA 0 response was defined as Clear (0) with at least a 2-category improvement from Baseline at week 16. PSD is a Patient Symptoms Diary, also referred to as Psoriasis Symptoms and Impacts Measure (P-SIM), measuring psoriasis symptom severity on a scale from 0 (no symptoms) to 10 (very severe symptoms). Response is defined as a decrease ≥4 from baseline to week 16 for pain, itch and scaling on a scale from 0 to 10.
a) p<0.001 *versus* placebo (BE VIVID and BE READY), *versus* adalimumab (BE SURE), adjusted for multiplicity.
b) p<0.001 *versus* ustekinumab (BE VIVID), adjusted for multiplicity.

Bimekizumab was associated with a rapid onset of efficacy. In BE VIVID, at week 2 and week 4,
PASI 90 response rates were significantly higher for bimekizumab-treated patients (12.1% and 43.6% respectively) compared to placebo (1.2% and 2.4% respectively) and ustekinumab (1.2% and 3.1% respectively).

In the BE VIVID study, at week 52, bimekizumab-treated patients (every 4 weeks) achieved significantly higher response rates than the ustekinumab-treated patients on the endpoints of PASI 90 (81.9% bimekizumab vs 55.8% ustekinumab, p<0.001), IGA 0/1 (78.2% bimekizumab vs 60.7% ustekinumab, p<0.001) and PASI 100 (64.5% bimekizumab vs 38.0% ustekinumab).

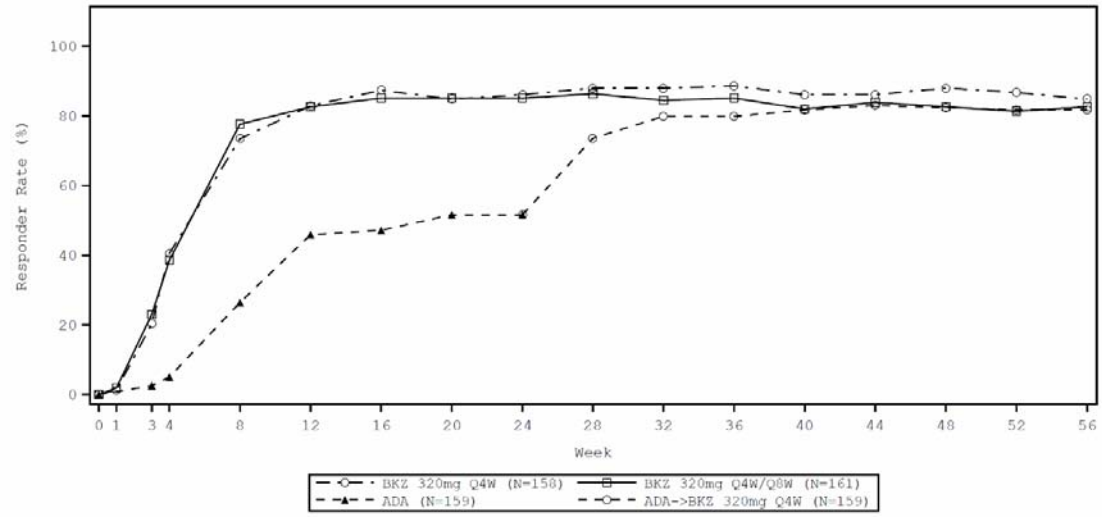
Figure 1: PASI 90 responder rates over time in BE VIVID



BKZ 320 mg Q4W=bimekizumab every 4 weeks; Uste=ustekinumab. NRI is used.

In the BE SURE study at week 24, a significantly higher percentage of patients treated with bimekizumab (Q4W/Q4W and Q4W/Q8W combined dosing arms) achieved PASI 90 and IGA 0/1 responses as compared with adalimumab (85.6% and 86.5% respectively vs 51.6% and 57.9% respectively, p<0.001). At week 56, 70.2% of patients treated with bimekizumab Q8W achieved a PASI 100 response. Among the 65 adalimumab non-responders at week 24 (< PASI 90), 78.5% achieved a PASI 90 response after 16 weeks of treatment with bimekizumab. The safety profile observed in patients who switched from adalimumab to bimekizumab without a wash-out period was similar to patients who initiated bimekizumab after wash-out of prior systemic therapies.

Figure 2: PASI 90 responder rates over time in BE SURE



BKZ 320 mg Q4W = bimekizumab every 4 weeks; BKZ 320 mg Q8W = bimekizumab every 8 weeks; ADA= adalimumab. Patients in the BKZ Q4W/Q8W group switched from Q4W to Q8W dosing at week 16. Patients in the ADA/BKZ 320 mg Q4W group switched from ADA to BKZ Q4W at week 24. NRI is used.

The efficacy of bimekizumab was demonstrated regardless of age, gender, race,

disease duration, body weight, PASI baseline severity and previous treatment with a biologic. Bimekizumab was efficacious in prior biologic exposed patients, including anti-TNF / anti IL-17 and in systemic treatment-naïve patients. Efficacy in patients with primary failure to anti-IL17 has not been investigated.

Based on population PK/ PD analysis and supported by clinical data, patients with higher body weight (≥120 kg) who did not achieve complete skin clearance at week 16 benefited from continued bimekizumab 320 mg every four weeks (Q4W) after the initial 16 weeks of treatment. In the BE SURE study, patients received bimekizumab 320 mg Q4W through week 16, followed by either Q4W or every eight weeks (Q8W) dosing through week 56, regardless of responder status at week 16. Patients in the ≥120 kg group (N=37) on the Q4W maintenance regimen showed greater improvement in PASI100 between week 16 (23.5%) and week 56 (70.6%) compared to those on the Q8W maintenance regimen (week 16: 45.0% vs week 56: 60.0%).

Improvements were observed in psoriasis involving the scalp, nails, palms and soles in patients treated with bimekizumab at week 16 (see Table 3).

Table 3: Scalp, palmoplantar and nail responses in BE VIVID, BE READY and BE SURE at week 16

	BE VIVID			**BE READY**		**BE SURE**	
	Placebo	**Bimekizumab 320 mg Q4W**	**Ustekinumab**	**Placebo**	**Bimekizumab 320 mg Q4W**	**Bimekizumab 320 mg Q4W**	**Adalimumab**
Scalp IGA (N)[a]	(72)	(285)	(146)	(74)	(310)	(296)	(138)
Scalp IGA 0/1, n (%)	11 (15.3)	240 (84.2)[b]	103 (70.5)	5 (6.8)	286 (92.3)[b]	256 (86.5)	93 (67.4)
pp-IGA (N)[a]	(29)	(105)	(47)	(31)	(97)	(90)	(34)
pp-IGA 0/1, n (%)	7 (24.1)	85 (81.0)	39 (83.0)	10 (32.3)	91 (93.8)	75 (83.3)	24 (70.6)
mNAPSI 100 (N)[a]	(51)	(194)	(109)	(50)	(210)	(181)	(95)
mNAPSI 100, n (%)	4 (7.8)	57 (29.4)	15 (13.8)	3 (6.0)	73 (34.8)	54 (29.8)	21 (22.1)

Bimekizumab 320 mg Q4W= bimekizumab every 4 weeks. Non responder imputation (NRI) is used.
Scalp IGA 0/1 and pp-IGA 0/1 responses were defined as Clear (0) or Almost Clear (1) with ≥2 category improvement relative to Baseline.
[a)] Include only patients with a scalp Investigator Global Assessment (IGA) of 2 or greater, a palmoplantar IGA of 2 or greater and a modified Nail Psoriasis and Severity Index (mNAPSI) score > 0 at baseline.
[b)] p<0.001 *versus* placebo, adjusted for multiplicity

Scalp IGA and palmoplantar IGA responses in bimekizumab-treated patients were maintained through week 52 / 56. Nail psoriasis continued to improve beyond week 16. In BE VIVID, at week 52, 60.3% of patients treated with bimekizumab 320 mg every 4 weeks achieved complete nail clearance (mNAPSI 100). In BE READY, at week 56, 67.7% and 69.8% of week 16 PASI 90 responders achieved complete nail clearance with bimekizumab 320 mg every 8 weeks and bimekizumab 320 mg every 4 weeks respectively.

Maintenance of response

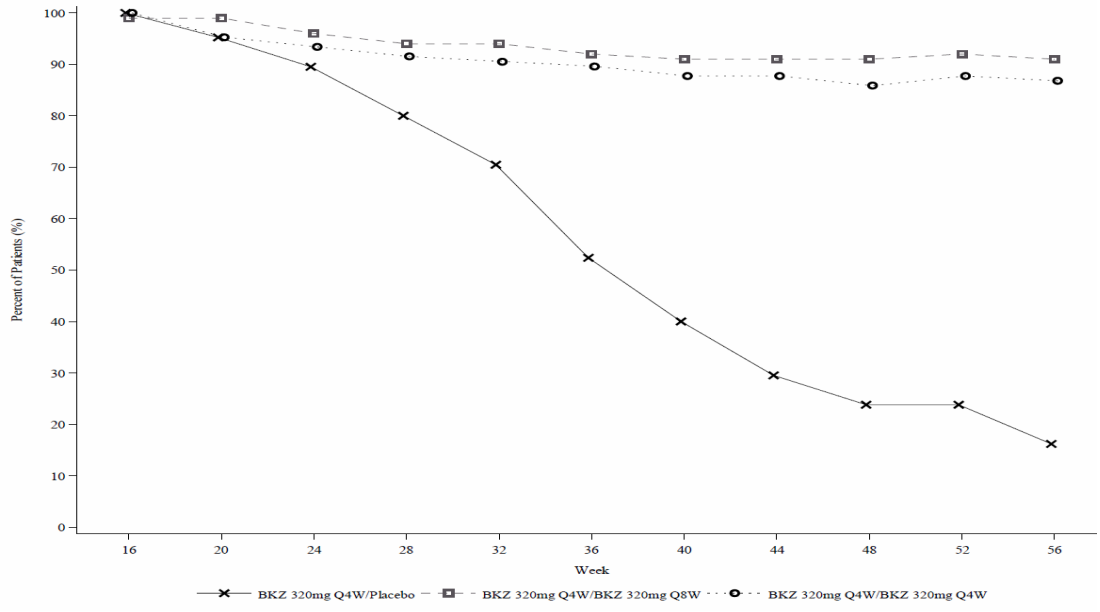
Table 4: Maintenance of responses with bimekizumab at week 52 in PASI100, PASI90, IGA 0/1 and Absolute PASI ≤ 2 responders at week 16*

PASI 100		PASI 90		IGA 0/1		Absolute PASI ≤ 2	
320mg Q4W (N=355) n (%)	320mg Q8W (N=182) n (%)	320mg Q4W (N=516) n (%)	320mg Q8W (N=237) n (%)	320mg Q4W (N=511) n (%)	320mg Q8W (N=234) n (%)	320mg Q4W (N=511) n (%)	320mg Q8W (N= 238) n (%)
295 (83.1)	161 (88.5)	464 (89.9)	214 (90.3)	447 (87.5)	214 (91.5)	460 (90.0)	215 (90.3)

* Integrated analysis of BE VIVID, BE READY and BE SURE. NRI is used.
320 mg Q4W: bimekizumab 320 mg every 4 weeks followed by bimekizumab 320 mg every 4 weeks from week 16.
320 mg Q8W: bimekizumab 320 mg every 4 weeks followed by bimekizumab 320 mg every 8 weeks from week 16.

Durability of response (after bimekizumab discontinuation)

Figure 3: PASI 90 responder rates over time for PASI 90 responders at week 16 – Randomised withdrawal period in BE READY



NRI is used.
At week 16, 105 study participants started the Randomised-Withdrawal Period in the bimekizumab 320 mg Q4W/placebo group, 100 in the bimekizumab 320 mg Q4W/Q8W group, and 106 in the bimekizumab 320 mg Q4W/Q4W group.

In BE READY, for PASI 90 responders at week 16 who were re-randomised to placebo and withdrawn from bimekizumab, the median time to relapse, defined as loss of PASI 75, was approximately 28 weeks (32 weeks after the last bimekizumab dose). Among these patients, 88.1% regained a PASI 90 response within 12 weeks of restarting treatment with bimekizumab 320 mg every 4 weeks.

Health-related Quality of Life / Patient reported outcomes

Across all 3 studies, a greater proportion of patients treated with bimekizumab experienced no impact of psoriasis on their quality of life as measured by the Dermatology Life Quality Index (DLQI) compared to placebo and active comparator-treated patients at week 16 (Table 5).

Table 5: Quality of life in study BE VIVID, BE READY and BE SURE

	BE VIVID			BE READY		BE SURE	
	Placebo (N= 83) n (%)	**Bimekizumab 320 mg Q4W (N= 321) n (%)**	**Ustekinumab (N= 163) n (%)**	**Placebo (N= 86) n (%)**	**Bimekizumab 320 mg Q4W (N= 349) n (%)**	**Bimekizumab 320 mg Q4W (N= 319) n (%)**	**Adalimumab (N= 159) n (%)**
DLQI 0/1[a] Baseline	3 (3.6)	16 (5.0)	5 (3.1)	4 (4.7)	11 (3.2)	10 (3.1)	13 (8.2)
DLQI 0/1[a] Week 16	10 (12.0)	216 (67.3)	69 (42.3)	5 (5.8)	264 (75.6)	201 (63.0)	74 (46.5)

[a)] DLQI absolute score of 0 or 1 indicates no impact of the disease on health-related quality of life. NRI is used.

DLQI 0/1 responses continued to increase beyond week 16 and then were maintained through week 52 / 56. In BE VIVID, DLQI 0/1 response rate at week 52 was 74.8% in patients treated with bimekizumab 320 mg every 4 weeks. In BE SURE at week 56, 78.9% and 74.1% of patients had a DLQI 0/1 with bimekizumab 320 mg every 8 weeks and bimekizumab 320 mg every 4 weeks, respectively.

Phase 3 Open Label Extension study

Patients who completed one of the pivotal phase 3 studies (‘feeder studies’) could enter a 144-week open-label extension study (PS0014) to assess the long-term safety and efficacy of bimekizumab.

344 patients who were treated with bimekizumab 320 mg every 8 weeks (BKZ 320 mg Q8W) or every 4 weeks (BKZ 320 mg Q4W) during the feeder study, and who achieved PASI 90 at the end of the feeder study, received bimekizumab 320 mg Q8W throughout PS0014. Of these, 293 (85.2%) patients completed 144 weeks of treatment with bimekizumab 320 mg Q8W. 48 patients (14.0%) discontinued the study during the treatment period, of which 21 (6.1%) discontinued due to an adverse event and 4 (1.2%) discontinued due to lack of efficacy.

Among the patients remaining in the study, improvements achieved with bimekizumab for the efficacy endpoints PASI 90 and IGA 0/1 in the feeder studies were maintained through an additional 144 weeks of open-label treatment.

Phase 3b direct comparative study versus secukinumab

The efficacy and safety of bimekizumab were also evaluated in a double-blind study compared with secukinumab, an IL-17A inhibitor, (BE RADIANT - PS0015). Patients were randomised to receive bimekizumab (N=373, 320mg at week 0, 4, 8, 12 and 16 (Q4W) followed by 320mg every 4 weeks (Q4W/Q4W) or 320 mg every 8 weeks (Q4W/Q8W)) or secukinumab (N=370, 300 mg at weeks 0,1, 2, 3, 4 followed by 300 mg every 4 weeks). Baseline characteristics were consistent with a population of moderate to severe plaque psoriasis patients with a median BSA of 19% and a median PASI score of 18.

Bimekizumab-treated patients achieved significantly higher response rates compared to secukinumab for the primary endpoint of PASI100 (complete skin clearance) at

week 16. Significantly higher response rates were also achieved with bimekizumab for the secondary endpoint of PASI 100 at week 48 (for both Q4W/Q4W and Q4W/Q8W regimens). Comparative PASI response rates are presented in Table 6. Differences in response rates between bimekizumab and secukinumab-treated patients were noted as early as week 1 for PASI 75 (7.2% and 1.4% respectively) and as early as week 2 for PASI 90 (7.5% and 2.4% respectively).

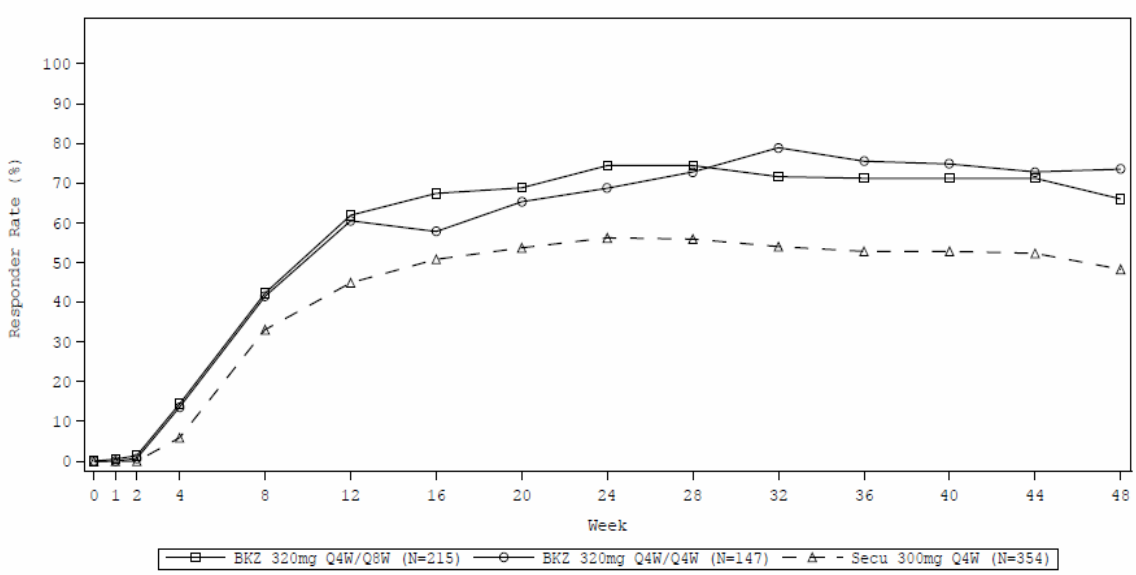
Table 6: PASI response rates from BE RADIANT - bimekizumab versus secukinumab

	Week 4		**Week 16**		**Week 48[a)]**		
	Bimekizumab 320 mg Q4W (N=373) n (%)	**Secukinumab** (N=370) n (%)	**Bimekizumab 320 mg Q4W** (N=373) n (%)	**Secukinumab** (N=370) n (%)	**Bimekizumab 320 mg Q4W/Q4W** (N=147) n (%)	**Bimekizumab 320 mg Q4W/Q8W** (N=215) n (%)	**Secukinumab** (N=354) n (%)
PASI 100	52 (13.9)	23 (6.2)	230 (61.7)*	181 (48.9)	108 (73.5)*	142 (66.0)*	171 (48.3)
PASI 90	134 (35.9)	65 (17.6)	319 (85.5)	275 (74.3)	126 (85.7)	186 (86.5)	261 (73.7)
PASI 75	265 (71.0)*	175 (47.3)	348 (93.3)	337 (91.1)	134 (91.2)	196 (91.2)	301 (85.0)
Absolute PASI<2	151 (40.5)	75 (20.3)	318 (85.3)	283 (76.5)	127 (86.4)	186 (86.5)	269 (76.0)

a) Data are from the Maintenance Set consisting of patients who received at least one dose of study treatment at week 16 or later
*p<0.001 versus secukinumab, adjusted for multiplicity. NRI is used.

Bimekizumab and secukinumab PASI 100 response rates through week 48 are presented in Figure 4.

Figure 4: PASI 100 response rate over time in BE RADIANT



NRI is used. Maintenance Set consisting of patients who received at least one dose of study treatment at week 16 or later

The efficacy of bimekizumab in BE RADIANT was consistent with BE VIVID, BE READY and BE SURE.

Phase 3b Open Label Extension period

At week 48, patients were allowed to enter a 96-week open-label extension period (OLE) and started or continued with bimekizumab 320 mg Q4W or 320 mg Q8W depending on their PASI 90 responder status at week 48. Study participants who initially received bimekizumab 320 mg Q4W during the OLE were switched to bimekizumab 320 mg Q8W at week 72 or later.

231 patients who were treated with bimekizumab 320 mg Q8W or bimekizumab 320 mg Q4W and achieved PASI 90 at week 48 received bimekizumab 320 mg Q8W throughout the OLE. Of these patients, 31 (13.4%) discontinued the study during the OLE, of which 10 (4.3%) discontinued due to an adverse event and 1 (0.4%) discontinued due to lack of efficacy.

116 patients who were treated with secukinumab and achieved PASI 90 at week 48 received bimekizumab 320 mg Q8W throughout the OLE. Of these patients, 16 (13.8%) discontinued the study during the OLE, of which 6 (5.2%) discontinued due to an adverse event and 1 (0.9%) discontinued due to lack of efficacy.

Among the patients remaining in the study, improvements achieved with bimekizumab or secukinumab for the efficacy endpoints PASI 100, PASI 90, PASI 75 and PASI $\leq$2 responder at week 48 were maintained on treatment with bimekizumab 320 mg Q8W through an additional 96 weeks of open-label treatment.

The safety profile of bimekizumab up to week 144 was consistent with the safety profile observed up to 48 weeks.

Psoriatic arthritis (PsA)

The safety and efficacy of bimekizumab were evaluated in 1112 adult patients (at least 18 years of age) with active psoriatic arthritis (PsA) in two multicentre, randomised, double-blind, placebo-controlled studies (PA0010 - BE OPTIMAL and PA0011- BE COMPLETE). The BE OPTIMAL study included an active reference treatment arm (adalimumab) (N=140).

For both studies, patients had a diagnosis of active psoriatic arthritis for at least 6 months based on the Classification Criteria for Psoriatic Arthritis (CASPAR) and had active disease with tender joint count (TJC) $\geq$3 and swollen joint count (SJC) $\geq$3. Patients had a diagnosis of PsA for a median of 3.6 years in BE OPTIMAL and 6.8 years in BE COMPLETE. Patients with each subtype of PsA were enrolled in these studies, including polyarticular symmetric arthritis, oligoarticular asymmetric arthritis, distal interphalangeal joint predominant, spondylitis predominant and arthritis mutilans. At baseline, 55.9% of patients had $\geq$ 3% Body Surface Area (BSA) with active plaque psoriasis. 10.4% of patients had moderate to severe plaque psoriasis and 31.9% and 12.3% had enthesitis and dactylitis at baseline, respectively. The primary efficacy endpoint in both studies was the American College of Rheumatology (ACR) 50 response at week 16.

The BE OPTIMAL study evaluated 852 patients not previously exposed to any biologic disease-modifying anti-rheumatic drug (bDMARD) for the treatment of psoriatic arthritis or psoriasis. Patients were randomized (3:2:1) to receive

bimekizumab 160 mg every 4 weeks through week 52 or placebo up to week 16 followed by bimekizumab 160 mg every 4 weeks through week 52 or an active reference treatment arm (adalimumab 40mg every 2 weeks) up to week 52. In this study, 78.3% of patients had received prior treatment with ≥ 1 cDMARDs and 21.7 % of patients had no prior treatment with cDMARDs. At baseline, 58.2% of patients were receiving concomitant methotrexate (MTX), 11.3% were receiving concomitant cDMARDs other than MTX, and 30.5% were receiving no cDMARDs.

The BE COMPLETE study evaluated 400 patients with an inadequate response (lack of efficacy) or intolerance to treatment with 1 or 2 tumour necrosis factor alpha inhibitors (anti-TNFα – IR) for either psoriatic arthritis or psoriasis. Patients were randomised (2:1) to receive bimekizumab 160 mg every 4 weeks or placebo up to week 16. At baseline, 42.5% of patients were receiving concomitant MTX, 8.0% were receiving concomitant cDMARDs other than MTX, and 49.5% were receiving no cDMARDs. In this study, 76.5% of participants had an inadequate response to 1 TNFα inhibitor, 11.3% had an inadequate response to 2 TNFα inhibitors and 12.3% were intolerant to TNFα inhibitors.

Signs and symptoms

In bDMARDs-naïve patients (BE OPTIMAL) and anti-TNFα IR patients (BE COMPLETE) treatment with bimekizumab resulted in significant improvement in signs and symptoms and measures of disease activity compared to placebo at week 16, with similar response rates seen in both patient populations (see Table 7). Clinical responses were sustained up to week 52 in BE OPTIMAL as assessed by ACR 20, ACR 50, ACR 70, MDA, PASI 90, PASI 100 and ACR 50 / PASI 100.

Table 7: Clinical response in study BE OPTIMAL and BE COMPLETE

	BE OPTIMAL (bDMARD-naïve)				**BE COMPLETE (anti TNFα-IR)**		
	Placebo (N=281) n (%)	**BKZ 160mg Q4W (N=431)** n (%)	**Difference from placebo (95% CI)[(d)]**	**Reference Arm[(e)] (Adalimumab) (N=140) n (%)**	**Placebo (N=133)** n (%)	**BKZ 160 mg Q4W (N=267)** n (%)	**Difference from placebo (95% CI)[(d)]**
ACR 20							
Week 16	67 (23.8)	268 (62.2)	38.3 (31.4,	96 (68.6)	21 (15.8)	179 (67.0)	51.2 (42.1,
Week 24	-	282 (65.4)	45.3)	99 (70.7)			60.4)
Week 52		307 (71.2)		102 (72.9)			
ACR 50							
Week 16	28 (10.0)	189 (43.9)*	33.9 (27.4,	64 (45.7)	9 (6.8)	116 (43.4)*	36.7 (27.7,
Week 24	-	196 (45.5)	40.4)	66 (47.1)			45.7)
Week 52		235 (54.5)		70 (50.0)			
ACR 70							
Week16	12 (4.3)	105 (24.4)	20.1 (14.7,	39 (27.9)	1 (0.8)	71 (26.6)	25.8 (18.2,
Week 24	-	126 (29.2)	25.5)	42 (30.0)			33.5)
Week 52		169 (39.2)		53 (37.9)			
MDA[(a)]							
Week 16	37 (13.2)	194 (45.0)*	31.8 (25.2,	63 (45.0)	8 (6.0)	118 (44.2)*	38.2 (29.2,
Week 24	-	209 (48.5)	38.5)	67 (47.9)			47.2)
Week 52		237 (55.0)		74 (52.9)			
Patients with ≥3% BSA	**(N=140)**	**(N=217)**		**(N=68)**	**(N=88)**	**(N=176)**	
PASI 90							
Week 16	4 (2.9)	133 (61.3)*	58.4 (49.9,	28 (41.2)	6 (6.8)	121 (68.8)*	61.9 (51.5,
Week 24	-	158 (72.8)	66.9)	32 (47.1)			72.4)
Week 52		155 (71.4)		41 (60.3)			
PASI 100							
Week 16	3 (2.1)	103 (47.5)	45.3 (36.7,	14 (20.6)	4 (4.5)	103 (58.5)	54.0 (43.1,

Week 24 Week 52	-	122 (56.2) 132 (60.8)	54.0)	26 (38.2) 33 (48.5)			64.8)
ACR50/ PASI 100 Week 16 Week 24 Week 52	0 -	60 (27.6) 68 (31.3) 102 (47.0)	NC (NC, NC)	11 (16.2) 17 (25.0) 24 (35.3)	1 (1.1)	59 (33.5)	32.4 (22.3, 42.5)
Patients with LDI>0 [(b)]	**(N=47)**	**(N=90)**					
Dactylitis free state [(b)] Week 16	24 (51.1)	68 (75.6)***	24.5 (8.4, 40.6)				
Patients with LEI>0 [(c)]	**(N=106)**	**(N=249)**					
Enthesitis free state [(c)] Week 16	37 (34.9)	124 (49.8)**	14.9 (3.7, 26.1)				

ACR50/PASI100= composite ACR50 and PASI100 response. BKZ 160 mg Q4W= bimekizumab 160 mg every 4 weeks. CI= confidence interval. NC=Not calculable

[(a)] A patient was classified as achieving Minimal Disease Activity (MDA) when meeting 5 of the 7 following criteria: tender joint count □1; swollen joint count □1; Psoriasis Activity and Severity Index □1 or body surface area □3; patient pain visual analogue scale (VAS) □15; patient global disease activity VAS □20; Health Assessment Questionnaire Disability Index □0.5; tender entheseal points □1

[(b)] Based on pooled data from BE OPTIMAL and BE COMPLETE studies for patients with baseline Leeds Dactylitis Index (LDI) >0. Dactylitis free state is LDI=0

[(c)] Based on pooled data from BE OPTIMAL and BE COMPLETE studies for patients with baseline Leeds Enthesitis Index (LEI) >0. Enthesitis free state is LEI =0

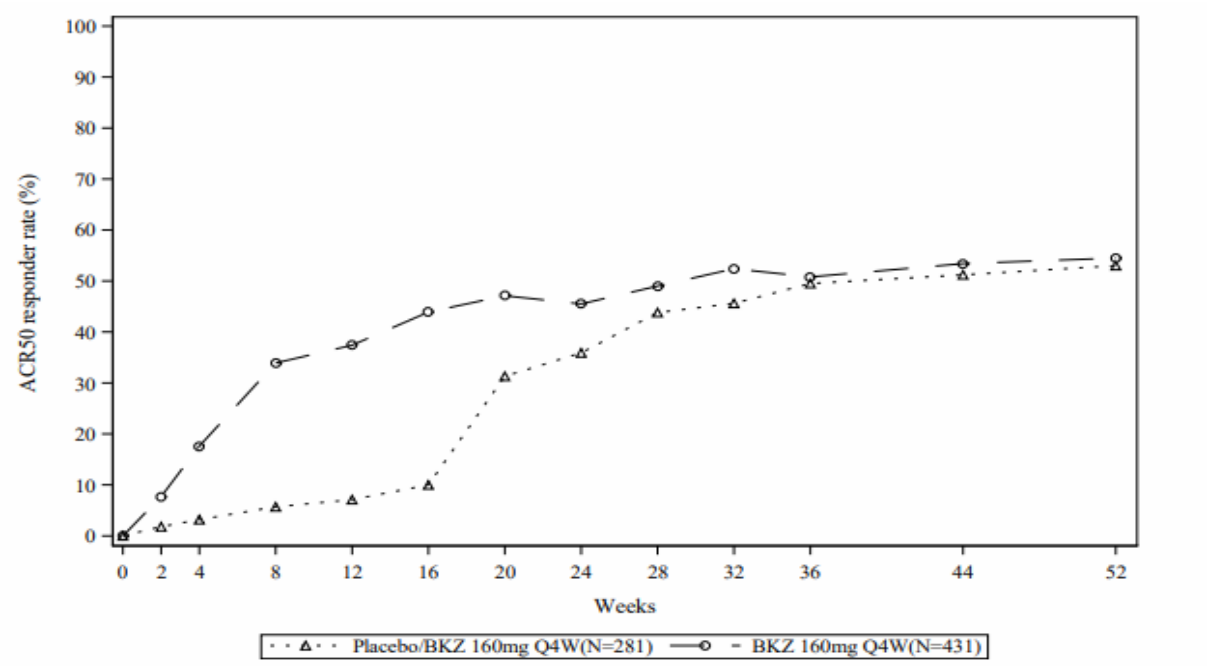
[(d)] Unadjusted differences are shown

[(e)] No statistical comparison to bimekizumab or placebo performed

* p<0.001 versus placebo adjusted for multiplicity. ** p=0.008 versus placebo adjusted for multiplicity. *** p=0.002 versus placebo adjusted for multiplicity. NRI is used. Other endpoints at week 16 and all endpoints at week 24 and week 52 were not part of the sequential testing hierarchy and any comparisons are nominal.

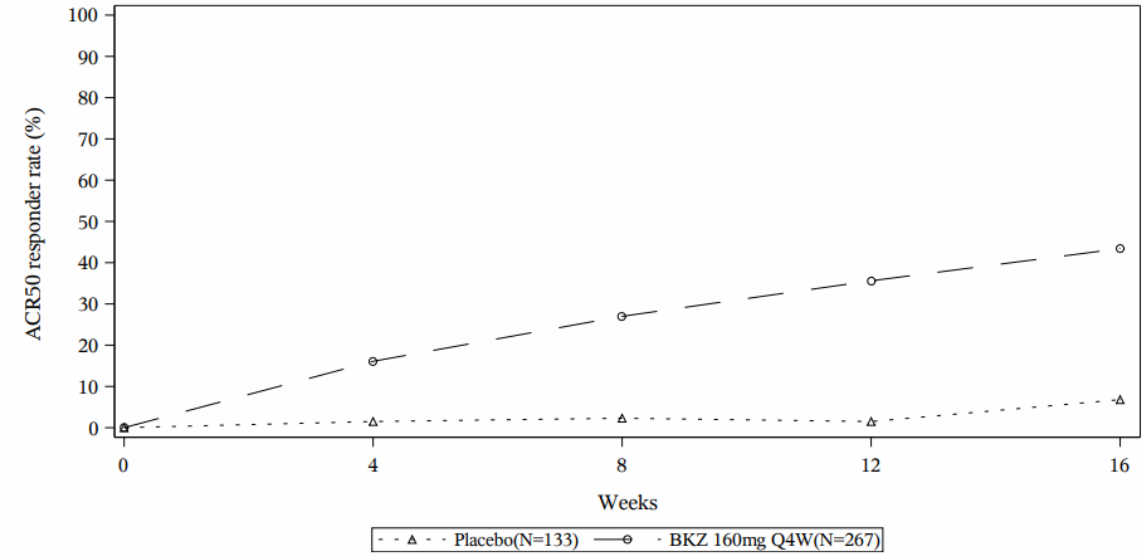
Improvements from baseline were shown in all individual ACR components with bimekizumab at week 16 and were sustained up to week 52 in BE OPTIMAL. Treatment responses on bimekizumab were significantly greater than those on placebo as early as week 2 for ACR 20 (BE OPTIMAL, 27.1% versus 7.8%, nominal p<0.001) and week 4 for ACR 50 (BE OPTIMAL, 17.6% versus 3.2%, nominal p<0.001 and BE COMPLETE, 16.1% versus 1.5%, nominal p<0.001).

Figure 5: ACR 50 response over time up to week 52 in BE OPTIMAL (NRI)



Patients on placebo switched to bimekizumab 160 mg Q4W at week 16.

Figure 6: ACR 50 response over time up to week 16 in BE COMPLETE (NRI)



For the bimekizumab-treated patients who achieved an ACR 50 response at week 16 in BE OPTIMAL, 87.2% maintained this response at week 52.

The efficacy and safety of bimekizumab were demonstrated regardless of age, gender, race, baseline body weight, baseline psoriasis involvement, baseline CRP, disease duration and prior cDMARDs use. In both studies, similar responses were observed with bimekizumab regardless of whether patients were on concomitant cDMARDs, including MTX, or not.

The modified Psoriatic Arthritis Response Criteria (PsARC) is a specific composite responder index comprising of tender joint count, swollen joints count, patient and

physician global assessment. The proportion of patients achieving modified PsARC at week 16 was higher in the bimekizumab-treated patients compared to placebo (80.3% versus 40.2% respectively in BE OPTIMAL and 85.4% versus 30.8% respectively in BE COMPLETE). PsARC response was sustained up to week 52 in BE OPTIMAL.

Radiographic response
In BE OPTIMAL, inhibition of progression of structural damage was assessed radiographically and expressed as the change from baseline in the Van der Heijde modified total Sharp Score (vdHmTSS) and its components, the Erosion Score (ES) and the Joint Space Narrowing score (JSN) at week 16 (see Table 8).

Table 8: Change in vdHmTSS in BE OPTIMAL at Week 16

	Placebo	**BKZ 160mg Q4W**	**Difference from placebo (95% CI)[a)]**
Population with elevated hs-CRP and/or at least 1 bone erosion at baseline	**(N=227)**	**(N=361)**	
Mean change from baseline (SE)	0.36 (0.10)	0.04 (0.05)*	-0.32 (-0.35, -0.30)
Overall population	**(N=269)**	**(N=420)**	
Mean change from baseline (SE)	0.32 (0.09)	0.04 (0.04)*	-0.26 (-0.29, -0.23)

*p =0.001 versus placebo. p-values are based on reference-based imputation using difference in LS Mean using an ANCOVA model with treatment, bone erosion at Baseline and region as fixed effects and Baseline score as a covariate.
Week 16 summary data is based on the first set of reads for the primary analysis.
[a)]Unadjusted differences are shown

Bimekizumab significantly inhibited the progression of joint damage at week 16 in both the population with elevated hs-CRP and/or at least 1 bone erosion at baseline and the overall population compared to placebo. While reference-based imputation was specified as the missing data handling method in the statistical testing procedure comparing bimekizumab versus placebo, changes from baseline were also calculated using standard multiple imputation in both the population with elevated hs-CRP and/or at least 1 bone erosion at baseline and the overall population at week 16 in the bimekizumab arm (mean change from baseline 0.01 and 0.01 respectively) and the adalimumab arm (mean change from baseline -0.05 and -0.03 respectively). Inhibition of the progression of joint damage was sustained in both the population with elevated hs-CRP and/or at least 1 bone erosion at baseline and the overall population to week 52 in both the bimekizumab arm (mean change from baseline 0.10 and 0.10 respectively) and the adalimumab arm (mean change from baseline -0.17 and -0.12 respectively).
The observed percentage of patients with no radiographic joint damage progression (defined as a change from baseline in mTSS of ≤0.5) from randomization to week 52 was 87.9% (N=276/314) for bimekizumab and 84.8% (N=168/198) for placebo study participants switching to bimekizumab and 94.1% (N=96/102) for adalimumab in the population with elevated hs-CRP and/or at least 1 bone erosion. Similar rates were observed in the overall population (89.3% (N=326/365) for bimekizumab and 87.3% (N=207/237) for placebo study participants switching to bimekizumab and 94.1% (N=111/118) for adalimumab).

Physical function and other health-related outcomes

Both bDMARD-naïve (BE OPTIMAL) and anti-TNFα-IR (BE COMPLETE) patients receiving bimekizumab showed significant improvement from baseline in physical function compared to placebo patients at week 16 ($p<0.001$) as assessed by the HAQ-

DI (LS Mean change from baseline: - 0.3 versus - 0.1 in BE OPTIMAL and - 0.3 versus 0 in BE COMPLETE, respectively). In both studies, a greater proportion of patients achieved a clinically meaningful reduction of at least 0.35 in HAQ-DI score from baseline in the bimekizumab group compared with placebo at week 16.

Bimekizumab-treated patients reported significant improvement from baseline in the Short Form-36 item Health Survey Physical Component Summary (SF-36 PCS) score at Week 16 compared to placebo (LS Mean change from baseline: 6.3 versus 1.9, $p<0.001$ in BE OPTIMAL and 6.2 versus 0.1, $p<0.001$ in BE COMPLETE).

In both studies, bimekizumab-treated patients reported meaningful reduction from baseline in fatigue as measured by the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score at week 16 compared to placebo. Meaningful improvement from baseline was also observed in the Psoriatic Arthritis Impact of Disease-12 (PsAID-12) score in the bimekizumab-treated group compared to the placebo group at week 16.
Patients with axial involvement at baseline, approximately 74% of patients, (defined as a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score ≥4) showed greater improvement from baseline in BASDAI compared with placebo at week 16

Improvements achieved at Week 16 in all measures of physical function and other health-related outcomes mentioned above (HAQ-DI, SF-36 PCS, FACIT-Fatigue, PsAID-12 scores and BASDAI) were sustained up to week 52 in BE OPTIMAL.

In BE OPTIMAL, at week 52, 65.5% of patients treated with bimekizumab achieved complete nail clearance (mNAPSI resolution in patients with mNAPSI higher than 0 at Baseline).

Axial spondyloarthritis (nr-axSpA and AS)

The efficacy and safety of bimekizumab was evaluated in 586 adult patients (at least 18 years of age) with active axial spondyloarthritis (axSpA) in two multicentre, randomised, double-blind, placebo-controlled studies, one in non-radiographic axial spondyloarthritis (nr-axSpA) and one in ankylosing spondylitis (AS), also known as radiographic axSpA. The primary endpoint in both studies was the percentage of patients achieving an Assessment of SpondyloArthritis International Society (ASAS) 40 response at week 16. Consistent results were seen across both patient populations.

The BE MOBILE 1 study (AS0010) evaluated 254 patients with active nr-axSpA. Patients had axSpA (age of symptoms onset < 45 years) meeting the ASAS classification criteria and had active disease as defined by a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4 and spinal pain ≥4 on a 0 to 10 numeric rating scale (NRS) (from BASDAI Item 2) and no evidence of radiographic changes in the sacroiliac joints that would meet the modified New York criteria for AS. Patients also had objective signs of inflammation as indicated by elevated C-reactive protein (CRP) level and/or evidence of sacroiliitis on Magnetic Resonance Imaging (MRI) as well as a history of inadequate response to 2 different non-steroidal anti-inflammatory drugs (NSAIDs) or intolerance or contraindication to NSAIDs. Patients were randomized (1:1) to receive bimekizumab 160 mg every 4 weeks up to week 52 or placebo up to week 16 followed by bimekizumab 160 mg every 4 weeks up to week 52. At baseline, patients had symptoms of nr-axSpA for a mean of 9 years (median of 5.5 years). 10.6% of patients were previously treated with an anti-TNFα agent.

The BE MOBILE 2 study (AS0011) evaluated 332 patients with active AS determined by documented radiologic evidence (x-ray) fulfilling the Modified New York criteria for AS. Patients had active disease as defined by a BASDAI ≥4 and spinal pain ≥4 on a 0 to 10 numeric rating scale (NRS) (from BASDAI Item 2). Patients had to have a history of inadequate response to 2 different NSAIDs or intolerance or contraindication to NSAIDs. Patients were randomized (2:1) to receive bimekizumab 160 mg every 4 weeks up to week 52 or placebo up to week 16 followed by bimekizumab 160 mg every 4 weeks up to week 52. At baseline, patients had symptoms of AS for a mean of 13.5 years (median of 11 years). 16.3% of patients were previously treated with an anti-TNFα agent.

Clinical response

Treatment with bimekizumab resulted in significant improvement in signs and symptoms and measures of disease activity compared to placebo at week 16 in both nr-axSpA and AS patient populations (see Table 9). Clinical responses were sustained up to week 52 in both patient populations as assessed by all the endpoints presented in Table 9.

Table 9: Clinical responses in BE MOBILE 1 and BE MOBILE 2

	BE MOBILE 1 (nr-axSpA)			**BE MOBILE 2 (AS)**		
	Placebo (N=126) n (%)	**BKZ 160 mg Q4W (N=128) n (%)**	**Difference from placebo (95% CI)[a)]**	**Placebo (N=111) n (%)**	**BKZ 160 mg Q4W (N=221) n (%)**	**Difference from placebo (95% CI**
ASAS 40 Week 16 Week 52	27 (21.4)	61 (47.7)* 78 (60.9)	26.2 (14.9, 37.5)	25 (22.5)	99 (44.8)* 129 (58.4)	22.3 (11.5, 33.0)
ASAS 40 in anti-TNFα naives Week 16 Week 52	(N=109) 25 (22.9)	(N= 118) 55 (46.6) 73 (61.9)	24.8 (12.4, 37.1)	(N=94) 22 (23.4)	(N=184) 84 (45.7)* 108 (58.7)	22.3 (10.5, 34.0)
ASAS 20 Week 16 Week 52	48 (38.1)	88 (68.8)* 94 (73.4)	30.7 (19.0, 42.3)	48 (43.2)	146 (66.1)* 158 (71.5)	22.8 (11.8, 33.8)
ASAS-partial remission Week 16 Week 52	9 (7.1)	33 (25.8)* 38 (29.7)	18.6 (9.7, 27.6)	8 (7.2)	53 (24.0)* 66 (29.9)	16.8 (8.1, 25.5)
ASDAS-major improvement Week 16 Week 52	9 (7.1)	35 (27.3)* 47 (36.7)	20.2 (11.2, 29.3)	6 (5.4)	57 (25.8)* 71 (32.1)	20.4 (11.7, 29.1)
BASDAI-50 Week 16 Week 52	27 (21.4)	60 (46.9) 69 (53.9)	25.3 (14.0, 36.6)	29 (26.1)	103 (46.6) 119 (53.8)	20.5 (9.6, 31.4)

BKZ 160 mg Q4W = bimekizumab 160 mg every 4 weeks. ASDAS = Ankylosing Spondylitis Disease Activity Score.
NRI is used.
[a)] Unadjusted differences are shown.
*p<0.001 versus placebo, adjusted for multiplicity.

The proportion of patients in BE MOBILE 1 reaching ASDAS <2.1 (combining ASDAS-inactive disease (ID) and ASDAS-low disease (LD)) at week 16 was 46.1% in the bimekizumab group versus 21.1% in the placebo group (multiple imputation). At week 52, 61.6% of patients in the bimekizumab group achieved an ASDAS <2.1, including 25.2% in inactive disease state (ASDAS <1.3).

The proportion of patients in BE MOBILE 2 reaching ASDAS <2.1 (combining ASDAS-ID and ASDAS-LD) at week 16 was 44.8% in the bimekizumab group versus 17.4% in placebo group (multiple imputation). At week 52, 57.1% of patients in the bimekizumab group achieved an ASDAS <2.1, including 23.4 % in inactive disease state (ASDAS <1.3).

All four ASAS 40 components (total spinal pain, morning stiffness, Bath Ankylosing Spondylitis Functional Index [BASFI] and Patient's Global Assessment of Disease Activity [PGADA]) were improved with bimekizumab treatment and contributed to the overall ASAS 40 response at week 16, and these improvements were sustained up to Week 52 in both patient populations.

Improvements in other measures of efficacy are shown in Table 10.

Table 10: Other measures of efficacy in BE MOBILE 1 and BE MOBILE 2

	BE MOBILE 1 (nr-axSpA)		**BE MOBILE 2 (AS)**	
	Placebo (N= 126)	**BKZ 160 mg Q4W (N= 128)**	**Placebo (N= 111)**	**BKZ 160 mg Q4W (N=221)**
Nocturnal spinal pain				
Baseline	6.7	6.9	6.8	6.6
Mean change from baseline at Week 16	-1.7	-3.6*	-1.9	-3.3*
Mean change from baseline at Week 52		-4.3		-4.1
BASDAI				
Baseline	6.7	6.9	6.5	6.5
Mean change from baseline at Week 16	-1.5	-3.1*	-1.9	-2.9*
Mean change from baseline at Week 52		-3.9		-3.6
BASMI				
Baseline	3.0	2.9	3.8	3.9
Mean change from baseline at Week 16	-0.1	-0.4	-0.2	-0.5**
Mean change from baseline at Week 52		-0.6		-0.7
hs-CRP (mg/L)				
Baseline (Geometric Mean)	5.0	4.6	6.7	6.5
Ratio to baseline at Week 16	0.8	0.4	0.9	0.4
Ratio to baseline at Week 52		0.4		0.3

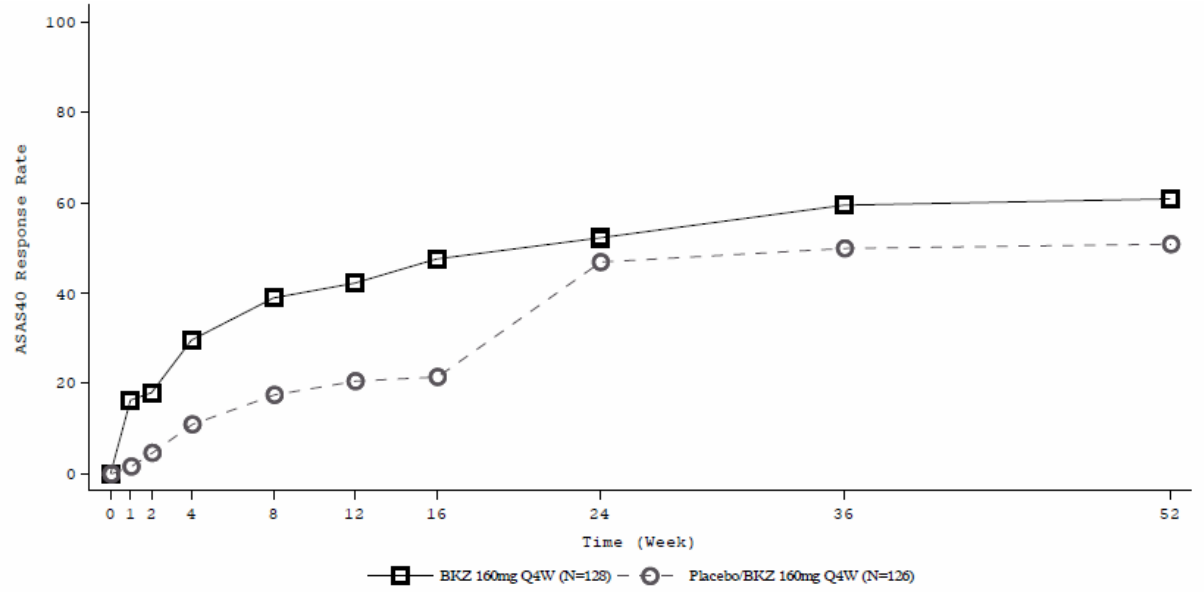
BASMI = Bath Ankylosing Spondylitis Metrology Index. Hs-CRP = high sensitivity C-reactive protein
MI is used.
*p<0.001 reference-based imputation, versus placebo, adjusted for multiplicity. **p<0.01 reference-based imputation, versus placebo, adjusted for multiplicity.

Bimekizumab was associated with a rapid onset of efficacy in both nr-axSpA and AS patient population.

Treatment responses on bimekizumab-treated patients for ASAS 40 were greater than those on placebo as early as week 1 in BE MOBILE 1 (16.4% vs. 1.6%, nominal p<0.001) and Week 2 in BE MOBILE 2 (16.7% vs. 7.2%, nominal p=0.019).

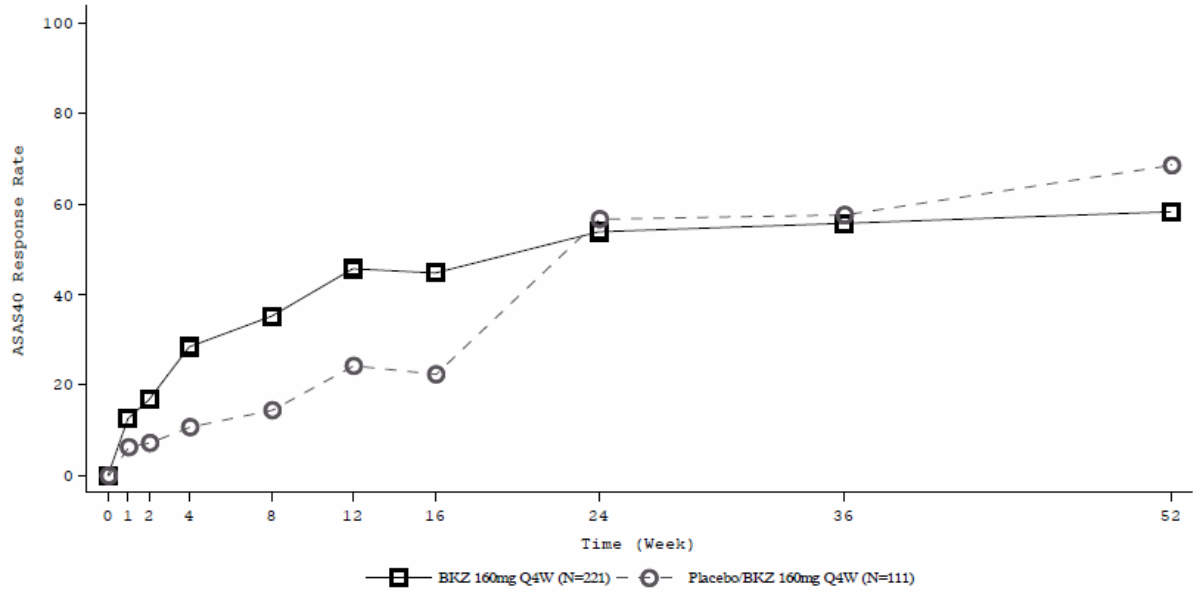
Bimekizumab was also associated with a rapid decrease in systemic inflammation as measured by hs-CRP levels as early as week 2 in both nr-axSpA and AS patient populations, with nominal p-values <0.001 in both studies.

Figure 7: ASAS 40 response over time up to week 52 in BE MOBILE 1 (NRI)



Patients on placebo switched to bimekizumab 160 mg Q4W at week 16

Figure 8: ASAS 40 response over time up to week 52 in BE MOBILE 2 (NRI)



Patients on placebo switched to Bimekizumab 160 mg Q4W at week 16

In an integrated analysis of BE MOBILE 1 and BE MOBILE 2, of bimekizumab-treated patients who achieved an ASAS 40 response at eek 16, 82.1% maintained this response at week 52.

The efficacy of bimekizumab was demonstrated regardless of age, gender, race, disease duration, baseline inflammation status, baseline ASDAS and concomitant cDMARDs.

Similar response in ASAS 40 was seen in patients regardless of prior anti-TNFα exposure.

At week 16, among patients with enthesitis at baseline, the proportion of patients (NRI) with enthesitis resolution as assessed by the Maastricht Ankylosing Spondylitis Enthesitis (MASES) index was greater with bimekizumab compared to placebo (BE MOBILE 1: 51.1% versus 23.9% and BE MOBILE 2: 51.5% versus 32.8%). The resolution of enthesitis with bimekizumab was sustained up to week 52 in both studies (BE MOBILE 1: 54.3% and BE MOBILE 2: 50.8%).

Reduction of inflammation

Bimekizumab reduced inflammation as measured by hs-CRP (see Table 10) and as assessed by MRI in an imaging sub-study. Signs of inflammation were assessed by MRI at baseline and week 16 and expressed as change from baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) score for sacroiliac joints and Ankylosing Spondylitis spine Magnetic Resonance Imagine-activity (ASspiMRI-a score in the Berlin modification) for the spine. Reduction of inflammatory signs in both sacroiliac joints and the spine was observed in patients treated with bimekizumab as compared with placebo (see Table 11). Reduction of inflammation as measured by hs-CRP and as assessed by MRI was sustained to week 52.

Table 11: Reduction of inflammation as assessed by MRI in BE MOBILE 1 and BE MOBILE 2

	BE MOBILE 1 (nr-axSpA)		**BE MOBILE 2 (AS)**	
	Placebo	**BKZ 160 mg Q4W**	**Placebo**	**BKZ 160 mg Q4W**
SPARCC score				
Mean change from baseline [a)] at week 16	-1.56 (N=62)	-6.15 (N=78)	0.59 (N=46)	-4.51 (N=81)
Mean change from baseline [a)] at week 52		-7.57 (N=67)		-4.67 (N=78)
ASspiMRI-a (Berlin modifications) score				
Mean change from baseline [a)] at week 16	0.03 (N=60)	-0.36 (N=74)	-0.34 (N=46)	-2.23 (N=81)
Mean change from baseline [a)] at week 52		-0.70 (N=65)		-2.38 (N=77)

[a)] Change from baseline values are based on observed cases as assessed by central read of week 52 dataset.

Physical function and other health-related outcomes

Patients treated with bimekizumab showed significant improvement from baseline in physical function as assessed by the BASFI compared to placebo (LS Mean change from baseline at Week 16 in BE MOBILE 1: -2.4 versus -0.9, $p<0.001$ and in BE MOBILE 2: -2.0 versus -1.0, $p<0.001$). Patients treated with bimekizumab reported significant improvement from baseline compared to placebo-treated patients in SF-36 PCS score (LS Mean change from baseline at week 16 in BE MOBILE 1: 9.3 versus 5.4, $p<0.001$ and in BE MOBILE 2: 8.5 versus 5.2, $p<0.001$).

Patients treated with bimekizumab reported significant improvement from baseline in health-related quality of life as measured by the AS Quality of Life Questionnaire (ASQoL) compared to placebo (LS Mean change from baseline at week 16 in BE MOBILE 1: -4.9 versus -2.3, $p<0.001$ and in BE MOBILE 2: -4.6 versus -3.0, $p<0.001$) as well as meaningful reduction in fatigue as assessed by the FACIT-Fatigue score (Mean change from baseline at week 16 in BE MOBILE 1: 8.5 for bimekizumab versus 3.9 for placebo and in BE MOBILE 2: 8.4 for bimekizumab versus 5.0 for placebo).

Improvements achieved at week 16 in all measures of physical function and other health-related outcomes mentioned above (BASFI, SF-36 PCS, ASQoL and FACIT-Fatigue scores) were sustained up to week 52 in both studies.

Extra-articular manifestation

In pooled data from BE MOBILE 1 (nr-axSpA) and BE MOBILE 2 (AS), at week 16, the proportion of patients developing a uveitis event was lower with bimekizumab (0.6%) compared to placebo (4.6%). The incidence of uveitis remained low with long-term treatment with bimekizumab (1.2/100 patient-years in the pooled phase 2/3 studies).

Hidradenitis suppurativa

The safety and efficacy of bimekizumab was evaluated in 1014 adult patients (at least 18 years of age) with moderate to severe Hidradenitis Suppurativa (HS) in two Phase 3 multicentre, randomised, double-blind, placebo-controlled studies (HS0003 – BE HEARD I and HS0004 – BE HEARD II). Patients had a diagnosis of HS for at least 6 months with Hurley Stage II or Hurley Stage III disease, and with ≥5 inflammatory lesions (i.e. number of abscesses plus number of inflammatory nodules) and had a history of inadequate response to a course of systemic antibiotics for the treatment of HS.

In both studies patients were randomised (2:2:2:1) to receive bimekizumab 320 mg every 2 weeks for 48 weeks (320 mg Q2W/Q2W) or bimekizumab 320 mg every 4 weeks for 48 weeks (320 mg Q4W/Q4W) or bimekizumab 320 mg every 2 weeks to week 16 followed by 320 mg every 4 weeks up to week 48 (320 mg Q2W/Q4W) or placebo to week 16 followed by bimekizumab 320 mg every 2 weeks up to week 48. Concomitant oral antibiotic use was allowed if the patient was on a stable dose regimen of doxycycline, minocycline, or an equivalent systemic tetracycline for 28 days prior to baseline.

The primary efficacy endpoint in both studies was the Hidradenitis Suppurativa Clinical Response 50 ($HiSCR_{50}$) at week 16, i.e. at least a 50% reduction in the total abscess and inflammatory nodule count with no increase in abscess or draining tunnel count relative to baseline.

Baseline characteristics were consistent across both studies and reflective of a population with moderate to severe HS. Patients had a median disease duration of 5.3 years (mean 8.0 years). The proportions of Hurley Stage II and Stage III patients were 55.7% (50.3% in HS0003 and 61.1% in HS0004) and 44.3% (49.7% in HS0003 and 38.9% in HS0004) respectively, and 8.5% were receiving concomitant antibiotic therapy for HS. The mean baseline Dermatology Life Quality Index (DLQI) total score was 11.4. 56.8% of patients were female and the mean age of all patients was 36.6 years. 79.7% of patients were White, and 10.8% were Black or African American. 45.6% of patients were current smokers.

Clinical response

Treatment with bimekizumab resulted in clinically relevant improvement in disease activity compared to placebo at week 16. Key efficacy results are shown in Table 12 and 13. The results in Table 12 reflect the predefined primary analysis in which any systemic antibiotic use prior to week 16 resulted in imputation of nonresponse. In Table 13, only systemic antibiotic use considered by the Investigator to be rescue treatment for HS resulted in imputation of nonresponse.

Table 12: Response in BE HEARD I and BE HEARD II at week 16 - primary analysis[a]

	BE HEARD I			BE HEARD II		
	Placebo (N=72)	**BKZ 320 mg Q4W (N=144)**	**BKZ 320 mg Q2W (N=289)**	**Placebo (N=74)**	**BKZ 320 mg Q4W (N=144)**	**BKZ 320 mg Q2W (N=291)**
$HiSCR_{50}$, % (95% CI)	28.7 (18.1, 39.3)	45.3 (36.8, 53.8)	47.8* (41.8, 53.7)	32.2 (21.4, 42.9)	53.8* (45.4, 62.1)	52.0* (46.1, 57.8)
$HiSCR_{75}$, % (95% CI)	18.4 (9.3, 27.5)	24.7 (17.3, 32.1)	33.4* (27.8, 39.1)	15.6 (7.2, 24.0)	33.7* (25.7, 41.7)	35.7* (30.1, 41.3)
HSSDD worst skin pain response[b] % (95% CI)	15.0 (3.6, 26.5)	22.1 (12.7, 31.4)	32.3 (25.1, 39.5)	10.9 (1.7, 20.1)	28.6 (19.5, 37.8)	31.8 (25.1, 38.4)

a) Patients who take systemic antibiotics for any reason or who discontinue due to adverse event or lack of efficacy are treated as non-responders at all subsequent visits for responder variables (or are subject to multiple imputation for continuous variables). Other missing data were imputed via multiple imputation.
b) Skin pain response, based on the threshold for within-patient clinically meaningful change (defined as at least a 3-point decrease from Baseline in Hidradenitis Suppurativa Symptom Daily Diary (HSSDD) weekly worst skin pain score) at week 16 among study participants with a score of ≥3 at Baseline. For BE HEARD I: N=46 for placebo, N=103 for BKZ Q4W and N=190 for BKZ Q2W; BE HEARD II: N=49 for placebo, N=108 for BKZ Q4W and N=209 for BKZ Q2W.
*p<0.025 versus placebo, adjusted for multiplicity.

Table 13: Response in BE HEARD I and BE HEARD II at week 16 - supportive analysis[a]

	BE HEARD I			BE HEARD II		
	Placebo (N=72)	**BKZ 320 mg Q4W (N=144)**	**BKZ 320 mg Q2W (N=289)**	**Placebo (N=74)**	**BKZ 320 mg Q4W (N=144)**	**BKZ 320 mg Q2W (N=291)**
$HiSCR_{50}$, % (95% CI)	34.0 (23.0, 45.1)	53.5 (45.0, 62.0)	55.2 (49.2, 61.1)	32.3 (21.5, 43.1)	58.5 (50.2, 66.8)	58.7 (53.0, 64.5)
$HiSCR_{75}$, % (95% CI)	18.3 (9.3, 27.3)	31.4 (23.5, 39.4)	38.7 (32.9, 44.5)	15.7 (7.2, 24.1)	36.4 (28.3, 44.5)	39.7 (34.0, 45.5)
HSSDD worst skin pain response[b] % (95% CI)	16.1 (4.5, 27.8)	25.3 (16.0, 34.7)	36.7 (29.4, 44.1)	11.1 (1.8, 20.4)	32.9 (23.5, 42.4)	36.7 (29.8, 43.6)

a) Post-hoc analysis (modified nonresponder imputation [mNRI]): Patients who take systemic antibiotics as rescue medication for HS as defined by the Investigator or who discontinue due to adverse event or lack of efficacy are treated as non-responders at all subsequent visits for responder variables (or are subject to multiple imputation for continuous variables). Other missing data were imputed via multiple imputation.
b) Skin pain response, based on the threshold for within-patient clinically meaningful change (defined as at least a 3-point decrease from Baseline in Hidradenitis Suppurativa Symptom Daily Diary (HSSDD) weekly worst skin pain score) at week 16 among study participants with a score of ≥3 at Baseline. For BE HEARD I: N=46 for placebo, N=103 for BKZ Q4W and N=190 for BKZ Q2W; BE HEARD II: N=49 for placebo, N=108 for BKZ Q4W and N=209 for BKZ Q2W.

In both studies, the onset of action of bimekizumab occurred as early as week 2.

The efficacy of bimekizumab was demonstrated regardless of prior biologics therapy and systemic antibiotic use at baseline.

Clinical responses were sustained through week 48 in both studies (see Table 14).

Table 14: Response in BE HEARD I and BE HEARD II at week 48 (mNRI*)

	BE HEARD I			BE HEARD II		
	BKZ 320mg Q4W/Q4W (N=144)	**BKZ 320 mg Q2W/Q4W (N=146)**	**BKZ 320 mg Q2W/Q2W (N=143)**	**BKZ 320mg Q4W/Q4W (N=144)**	**BKZ 320 mg Q2W/Q4W (N=146)**	**BKZ 320 mg Q2W/Q2W (N=145)**
$HiSCR_{50}$, %	52.7	61.4	60.6	63.2	63.8	60.6
$HiSCR_{75}$, %	40.5	44.7	47.6	53.9	48.8	47.3

* mNRI (modified non-responder imputation): Patients who take systemic antibiotics as rescue medication for HS as defined by the Investigator or who discontinue due to adverse event or lack of efficacy are treated as non-responders at all subsequent visits for responder variables (or are subject to multiple imputation for continuous variables). Other missing data were imputed via multiple imputation. This exploratory approach to handling missing data was performed post-hoc.

Health-related quality of life

Across both studies, patients treated with bimekizumab experienced greater meaningful improvement compared to placebo in their health-related quality of life as measured by the standard skin-specific DLQI (Table 15).

Table 15: Health-related quality of life in BE HEARD I and BE HEARD II at week 16

	BE HEARD I			BE HEARD II		
	Placebo (N=72)	**BKZ 320 mg Q4W (N=144)**	**BKZ 320 mg Q2W (N=289)**	**Placebo (N=74)**	**BKZ 320 mg Q4W (N=144)**	**BKZ 320 mg Q2W (N=291)**
DLQI total score Mean cfb[a] (SE)	-2.9 (0.8)	-5.4 (0.6)	-5.0 (0.4)	-3.2 (0.6)	-4.5 (0.5)	-4.6 (0.3)

DLQI total score ranges from 0 to 30 with higher scores indicating lower HRQoL.
Patients who take systemic antibiotics as rescue medication for HS as defined by the Investigator or who discontinue due to adverse event or lack of efficacy are subject to multiple imputation. Other missing data were imputed via multiple imputation.
a) cfb: change from baseline

Improvement achieved at week 16 in health-related quality of life measurements with bimekizumab were sustained through week 48.

Paediatric population

The licensing authority has deferred the obligation to submit the results of studies with Bimzelx in one or more subsets of the paediatric population in psoriasis and chronic idiopathic arthritis (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

The pharmacokinetic (PK) properties of bimekizumab were similar in patients with plaque psoriasis, psoriatic arthritis and axial spondyloarthritis (nr-axSpA and AS).

Based on population PK analyses and using a reference bodyweight of 90 kg, the bimekizumab apparent clearance and volume of distribution, respectively, in patients with hidradenitis suppurativa were estimated to be approximately 31 and 18 % higher than for the aforementioned indications, with an estimated half-life in HS of 20 days. Consequently, the median steady state trough concentration at a dose of 320 mg every 4 weeks was approximately 40 % lower in HS compared to other indications.

Absorption

Based on population pharmacokinetic analysis, following a single subcutaneous dose of 320 mg in plaque psoriasis patients, bimekizumab reached a median (2.5th and 97.5th percentile) peak plasma concentration of 25 (12 -50) μg/mL, between 3 and 4 days post dose.

Population pharmacokinetic analysis showed that bimekizumab was absorbed with an average absolute bioavailability of 70.1% in healthy volunteers.

Based on simulated data, the median (2.5th and 97.5th percentile) peak and trough concentration at steady-state following subcutaneous administration of 320 mg every 4 weeks are 43 (20-91) μg/mL and 20 (7-50) μg/mL respectively and steady-state is reached after approximately 16 weeks with every 4 weeks dosing regimen. Compared with exposure after a single dose, the population pharmacokinetic analysis showed that patients exhibited a 1.74-fold increase in peak plasma concentrations and area under the curve (AUC) following repeated four weekly dosing.

After switching from the 320 mg every 4 weeks dosing regimen to 320 mg every 8 weeks dosing regimen at week 16, steady-state is achieved approximately 16 weeks after the switch. Median (2.5th and 97.5th percentile) peak and trough plasma concentrations are 30 (14 -60) μg/mL and 5 (1-16) μg/mL respectively.

Distribution

Based on population pharmacokinetic analyses, the median (coefficient of variation %) volume of distribution (V/F) at steady state was 11.2 (30.5%) L in plaque psoriasis patients.

Biotransformation

Bimekizumab is a monoclonal antibody and is expected to be degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous immunoglobulins.

Elimination

Based on population pharmacokinetic analyses, the median (coefficient of variation %) apparent clearance (CL/F) of bimekizumab was 0.337 L/day (32.7%) and the mean terminal elimination half-life of bimekizumab was 23 days in clinical studies in patients with plaque psoriasis.

Linearity/non-linearity

Bimekizumab exhibited dose-proportional pharmacokinetics in patients with plaque psoriasis over a dose range from 64 mg to 480 mg following multiple subcutaneous administrations, with apparent clearance (CL/F) being independent of dose.

Pharmacokinetic/Pharmacodynamic relationship

A population pharmacokinetic/pharmacodynamic model was developed using all available data in moderate to severe plaque psoriasis patients. The analysis showed that higher bimekizumab concentrations are related to better Psoriasis Area and Severity Index (PASI) and Investigators Global Assessment (IGA) response. A dose of 320 mg every 4 weeks was shown to be an appropriate dose for the initial treatment

period and 320 mg every 8 weeks thereafter is appropriate for the maintenance period for the majority of moderate to severe plaque psoriasis patients (see Special Populations, Body weight).

Special populations

Body weight
Population pharmacokinetic modelling indicated that exposure decreased as body weight increased. The average plasma concentration in adult patients weighing ≥120 kg following a 320 mg subcutaneous injection was predicted to be at least 30% lower than in adult patients weighing 90 kg. Dose adjustment may be appropriate in some patients (see section 4.2).

Elderly
Based on population pharmacokinetic analysis with a limited number of elderly patients (n=355 for age ≥ 65 years and n= 47 for age ≥ 75 years), apparent clearance (CL/F) in elderly patients and patients less than 65 years of age was similar. No dose adjustment is required (see section 4.2).

Renal impairment or hepatic impairment
No specific studies have been conducted to determine the effect of renal or hepatic impairment on the pharmacokinetics of bimekizumab. The renal elimination of intact bimekizumab, an IgG monoclonal antibody, is expected to be low and of minor importance. Similarly, IgGs are mainly eliminated via intracellular catabolism and hepatic impairment is not expected to influence clearance of bimekizumab. Based on population pharmacokinetic analyses, hepatic function markers (ALT/bilirubin) did not have any impact on bimekizumab clearance in patients with plaque psoriasis.

Race
No clinically meaningful differences in bimekizumab exposure were observed in Japanese or Chinese subjects compared to Caucasian subjects in a clinical pharmacokinetic study. No dose adjustment is required.

Gender
Population pharmacokinetic modelling indicated females may have 10% faster apparent clearance (CL/F) compared to males and it is not clinically meaningful. No dose adjustment is required.

5.3 Preclinical safety data

Non-clinical data revealed no special hazard for humans based on tissue cross-reactivity testing, repeat-dose toxicity studies (including safety pharmacology endpoints and assessment of fertility-related endpoints) and evaluation of pre- and postnatal development in the cynomolgus monkey.

In cynomolgus monkeys, bimekizumab-related effects were limited to mucocutaneous changes consistent with pharmacologic modulation of commensal microflora.

No mutagenicity or carcinogenicity studies were conducted with bimekizumab. However monoclonal antibodies are not expected to damage DNA or chromosomes. In a 26-week chronic toxicology study in cynomolgus monkeys there were no pre-neoplastic or neoplastic lesions observed at a dose resulting in 109 times the human

exposure at 320 mg every 4 weeks.

In a peri- and postnatal development study in the cynomolgus monkey, bimekizumab showed no effects on gestation, parturition, infant survival, foetal and postnatal development when administered throughout organogenesis until parturition at a dose resulting in 27 times the human exposure at 320 mg every 4 weeks based on AUC. At birth, serum bimekizumab concentrations in infant monkeys were comparable to those of mothers.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycine
Sodium acetate trihydrate
Glacial acetic acid
Polysorbate 80
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

3 years

6.4 Special precautions for storage

Bimzelx 320 mg solution for injection in pre-filled pen

Store in a refrigerator (2 °C – 8 °C).

Do not freeze.

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

The pre-filled pen may be stored at room temperature (up to 25 °C) for a single period of maximum 25 days with protection from light. Once removed from the refrigerator and stored under these conditions, discard after 25 days or by the expiry date printed

on the container, whichever occurs first. A field for the date is provided on the carton to record the date removed from the refrigerator.

6.5 Nature and contents of container

Bimzelx 320 mg solution for injection in pre-filled pen

Two mL pre-filled pen containing a pre-filled syringe (Type I glass) with a fluoropolymer-laminated bromobutyl rubber stopper, staked 27G, ½" thin wall needle, and a rigid needle shield consisting of a thermoplastic elastomer needle cover and a polypropylene rigid shield.

Pack size of 1 pre-filled pen.
Multipack containing 3 (3 packs of 1) pre-filled pens.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

UCB Pharma Limited
208 Bath Road
Slough
Berkshire
SL1 3WE
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PLGB 00039/0811

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

18/11/2024

10 DATE OF REVISION OF THE TEXT

12/05/2025