NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

CJM112

Trial Indication(s)

Moderate to severe inflammatory acne

Protocol Number

CCJM112X2203

Protocol Title

A randomized, subject and investigator blinded, placebo-controlled, multi-center study in parallel groups to assess the efficacy and safety of CJM112 in patients with moderate to severe inflammatory acne

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase II

Study Start/End Dates

Study Start Date: December 2016 (Actual)
Primary Completion Date: August 2018 (Actual)
Study Completion Date: August 2018 (Actual)

Reason for Termination (If applicable)

The study was terminated early by the Sponsor, as the results met the pre-planned futility criterion at the pre-planned interim analyses (IA1).

Study Design/Methodology

Randomized, placebo controlled, patient and investigator blinded, multicenter, non-confirmatory, parallel group, proof of concept study in subjects with moderate to severe inflammatory acne

Centers

10 centers in 3 countries: Netherlands(3), Germany(4), United States(3)

Objectives:

Primary:
To assess the efficacy of CJM112 versus placebo on facial inflammatory lesion counts in patients with moderate to severe inflammatory acne
Secondary:
To assess the safety and tolerability of CJM112 in patients with moderate to severe inflammatory acne.
To assess the pharmacokinetics of CJM112 in patients with moderate to severe acne.

Test Product (s), Dose(s), and Mode(s) of Administration

The investigational drug, CJM112 and matching placebo were prepared
and supplied as individual patient packs to be administered via subcutaneous route at the Investigator site.

Subjects were assigned to one of the following 3 treatment arms:

- CJM112 high dose once a month for a total of up to 7 doses
- CJM112 low dose once a month for a total of up to 7 doses
- Placebo once a month for a total of up to 3 doses, followed by re-randomization into either active treatment group for Extension Period 2 for a total of up to 4 active doses

Statistical Methods

The primary variable was the natural log transformed total inflammatory facial lesion counts at week 12. Bayesian model for repeated measurements was used to analyze the log transformed inflammatory facial lesion count.

Efficacy criteria (only for primary endpoint)

- there was at least 90% probability that the treatment effect of CJM112 at Week 12 is better than placebo, AND
- there was at least 50% probability that the treatment effect at Week 12 is at least 30% (hence less than -0.357 on the natural log scale) in favor of CJM112.

The 30% threshold was chosen based on a study showing around 30% difference in inflammatory facial lesion count at Week 12 between a standard care oral antibiotics and placebo.

Futility criterion at IA1:

- there was at least 60% probability that the treatment effect of CJM112 at Week 12 is worse than placebo.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
- Male and female subjects aged 18 to 45 years of age included, and otherwise in good health as determined by medical history, physical examination, vital signs, ECGs and laboratory tests at screening.
- Body weight between 50 and 120 kg, inclusive at screening.

- Patients with papulo-pustular acne vulgaris with between 25 and 100 facial inflammatory lesions (papules, pustules and nodules), and presence of non-inflammatory lesions (open and closed comedones) in the face at screening and baseline, who have failed systemic therapy for inflammatory acne.
- No more than 5 facial inflammatory nodules at screening and baseline.
- Investigator's Global assessment (IGA) score of at least moderate (3) acne severity on the face at screening and baseline.

Exclusion Criteria:
- Appropriate wash out periods are required for investigational drugs, any oral/systemic treatment for acne, systemic or lesional injected (for acne) corticosteroids or systemic immunomodulators, any systemic hormonal treatments, previous treatment with biologics, oral retinoids (in particular isotretinoin) and any topical anti-acne treatment.
- Use of facial medium depth chemical peels (excluding home regimens) within 3 months prior to baseline.
- Any live vaccines (this includes nasal-spray flu vaccine) starting from 6 weeks before baseline.
- Any other forms of acne
- Any severe, progressive or uncontrolled medical or psychiatric condition or other factors at randomization that in the judgment of the investigator prevents the patient from participating in the study.
- History of hypersensitivity or allergy to the investigational compound/compound class being used in this study.
- Active systemic infections (other than common cold) during the 2 weeks prior to baseline.
- History of severe systemic Candida infections or evidence of Candidiasis in the 2 weeks prior to baseline.
- Evidence of active tuberculosis at screening. All patients will be tested for tuberculosis status using a blood test (QuantiFERON®-TB (Tuberculosis) Gold In-Tube). Patients with evidence of tuberculosis may enter the trial afteradequate treatment has been started according to local regulations.
- Patients with known active Crohn's disease
- History of immunodeficiency diseases, including a positive HIV (ELISA and Western blot) test result at screening.
- A positive Hepatitis B surface antigen or Hepatitis C test result at screening
- Pregnant or nursing (lactating) women, where pregnancy is defined

as the state of a female after conception and until the termination of gestation, confirmed by a positive Human chorionic gonadotropin (HCG) laboratory test.
- WOCBP, defined as all women physiologically capable of becoming pregnant, unless they are using highly effective methods of contraception during dosing and for 13 weeks after stopping medication.

Other protocol-defined inclusion/exclusion criteria may apply.

Participant Flow Table

Period 1

	P1: CJM112 high dose / P2: CJM112 high dose	P1: CJM112 low dose / P2: CJM112 low dose	P1: Placebo / P2 CJM112 low dose or high dose	Total
Arm/Group Description	CJM112 high dose in treatment period 1 (Day 1 - 85) ; CJM112 high dose in extension period 2 (Day 86 - 169)	CJM112 low dose in treatment period 1 (Day 1 - 85) ; CJM112 low dose in extension period 2 (Day 86 - 169)	Placebo in treatment period 1 (Day 1 - 85) ; CJM112 low dose or CJM112 high dose in extension period 2 (Day 86 - 169)	
Started	21	13	18	52
Completed	17	10	14	41
Not Completed	4	3	4	11
Study Terminated By Sponsor	2	1	1	4
Withdrawal by Subject	1	2	2	5

Pregnancy	1	0	0	1
Adverse Event	0	0	1	1

Period 2

	P1: CJM112 high dose / P2: CJM112 high dose	P1: CJM112 low dose / P2: CJM112 low dose	P1: Placebo / P2 CJM112 low dose or high dose	Total
Arm/Group Description	CJM112 high dose in treatment period 1 (Day 1 - 85) ; CJM112 high dose in extension period 2 (Day 86 - 169)	CJM112 low dose in treatment period 1 (Day 1 - 85) ; CJM112 low dose in extension period 2 (Day 86 - 169)	Placebo in treatment period 1 (Day 1 - 85) ; CJM112 low dose or CJM112 high dose in extension period 2 (Day 86 - 169)	
Started	17	10	14	41
Completed	14	3	9	26
Not Completed	3	7	5	15
Adverse Event	0	1	0	1
Study Terminated By Sponsor	3	5	4	12
Withdrawal by Subject	0	1	0	1
Lost to Follow-up	0	0	1	1

Baseline Characteristics

	P1: CJM112 high dose / P2: CJM112 high dose	P1: CJM112 low dose / P2: CJM112 low dose	P1: Placebo / P2 CJM112 low dose or high dose	Total
Arm/Group Description	CJM112 high dose in treatment period 1 (Day 1 - 85) ; CJM112 high dose in extension period 2 (Day 86 - 169)	CJM112 low dose in treatment period 1 (Day 1 - 85) ; CJM112 low dose in extension period 2 (Day 86 - 169)	Placebo in treatment period 1 (Day 1 - 85) ; CJM112 low dose or CJM112 high dose in extension period 2 (Day 86 - 169)	
Number of Participants [units: participants]	21	13	18	52
Age Continuous (units: years) Mean ± Standard Deviation				
	23.8±4.19	25.5±5.99	23.9±4.07	24.3±4.62
Sex: Female, Male (units: Participants) Count of Participants (Not Applicable)				
Female	13	8	13	34
Male	8	5	5	18
Race/Ethnicity, Customized (units: Participants) Count of Participants (Not Applicable)				
White	18	10	17	45
Other	3	3	1	7

Summary of Efficacy

Primary Outcome Result(s)

Total inflammatory facial lesion count at day 85

(Time Frame: Day 85)

	P1: CJM112 high dose / P2: CJM112 high dose	P1: CJM112 low dose / P2: CJM112 low dose	P1: Placebo / P2 CJM112 low dose or high dose
Arm/Group Description	CJM112 high dose in treatment period 1 (Day 1 - 85) ; CJM112 high dose in extension period 2 (Day 86 - 169)	CJM112 low dose in treatment period 1 (Day 1 - 85) ; CJM112 low dose in extension period 2 (Day 86 - 169)	Placebo in treatment period 1 (Day 1 - 85) ; CJM112 low dose or CJM112 high dose in extension period 2 (Day 86 - 169)
Number of Participants Analyzed [units: participants]	17	10	15
Total inflammatory facial lesion count at day 85 (units: Lesions) Geometric Mean (90% Confidence Interval)			
	21.9 (16.58 to 29.14)	20.3 (13.76 to 29.66)	18.5 (13.51 to 25.13)

Statistical Analysis

Groups	P1: CJM112 high dose / P2: CJM112 high dose, P1: Placebo / P2 CJM112 low dose or high dose	
Non-Inferiority/Equivalence Test	Superiority	Comparison at end of Period 1 (P1): CJM112 versus Placebo.
Method	Other Bayesian model for repeated measurements	
Other Ratio of geometric means	1.18	Ratio of Geometric Means (CJM112 / Placebo) calculated. A value > 1 indicates a higher number of lesion counts in the CJM112 group. Bayesian analysis. The “credible interval” was calculated and presented under "confidence interval".
90 % Confidence Interval 2-Sided	0.79 to 1.81	

Statistical Analysis

Groups	P1: CJM112 low dose / P2: CJM112 low dose, P1: Placebo / P2 CJM112 low dose or high dose	
Non-Inferiority/Equivalence Test	Superiority	Comparison at end of Period 1 (P1): CJM112 versus Placebo.
Method	Other Bayesian model for repeated measurements	

Other Ratio of geometric means	1.10	Ratio of Geometric Means (CJM112 / Placebo) calculated. A value > 1 indicates a higher number of lesion counts in the CJM112 group. Bayesian analysis. The “credible interval” was calculated and presented under "confidence interval".
90 % Confidence Interval 2-Sided	0.66 to 1.80	

Secondary Outcome Result(s)

Number and severity of adverse events in Period 1

(Time Frame: Day 1 to Day 85)

	P1: CJM112 high dose / P2: CJM112 high dose	P1: CJM112 low dose / P2: CJM112 low dose	P1: Placebo / P2 CJM112 low dose or high dose
Arm/Group Description	CJM112 high dose in treatment period 1 (Day 1 - 85) ; CJM112 high dose in extension period 2 (Day 86 - 169)	CJM112 low dose in treatment period 1 (Day 1 - 85) ; CJM112 low dose in extension period 2 (Day 86 - 169)	Placebo in treatment period 1 (Day 1 - 85) ; CJM112 low dose or CJM112 high dose in extension period 2 (Day 86 - 169)
Number of Participants Analyzed [units: participants]	21	13	18

Number and severity of adverse events in Period 1
(units: Adverse Events)

Number of AEs of mild intensity	27	25	20
Number of AEs of moderate intensity	5	7	9
Number of AEs of severe intensity	0	1	0

Number and severity of adverse events in Period 2

(Time Frame: Day 86 to Day 260)

	P1: CJM112 high dose / P2: CJM112 high dose	P1: CJM112 low dose / P2: CJM112 low dose	P1: Placebo / P2: CJM112 high dose	P1: Placebo / P2: CJM112 low dose
Arm/Group Description	CJM112 high dose in treatment period 1 (Day 1 - 85) ; CJM112 high dose in extension period 2 (Day 86 - 169)	CJM112 low dose in treatment period 1 (Day 1 - 85) ; CJM112 low dose in extension period 2 (Day 86 - 169)	Placebo in treatment period 1; CJM112 high dose in extension period 2	Placebo in treatment period 1; CJM112 low dose in extension period 2
Number of Participants Analyzed [units: participants]	17	10	6	8
Number and severity of adverse events in Period 2 (units: Adverse Events)				
Number of AEs of mild intensity	21	20	6	13

Number of AEs of moderate intensity	6	1	3	1
Number of AEs of severe intensity	1	1	0	0

Pharmacokinetics (PK): Serum trough concentrations of CJM112 in Period 1

(Time Frame: Day 1, Day 29, Day 57 and Day 85)

	P1: CJM112 high dose / P2: CJM112 high dose	P1: CJM112 low dose / P2: CJM112 low dose
Arm/Group Description	CJM112 high dose in treatment period 1 (Day 1 - 85) ; CJM112 high dose in extension period 2 (Day 86 - 169)	CJM112 low dose in treatment period 1 (Day 1 - 85) ; CJM112 low dose in extension period 2 (Day 86 - 169)
Number of Participants Analyzed [units: participants]	21	12
Pharmacokinetics (PK): Serum trough concentrations of CJM112 in Period 1 (units: ng/mL) Mean ± Standard Deviation		
Period 1 Day 1 (Pre Dose)	152 ± 663	0 ± 0
Period 1 Day 29 (Pre Dose)	8670 ± 3370	802 ± 961
Period 1 Day 57 (Pre Dose)	11500 ± 5020	1550 ± 1130
Period 1 Day 85 (Pre Dose)	17000 ± 8080	2040 ± 1570

Pharmacokinetics (PK): Serum trough concentrations of CJM112 in Period 2

(Time Frame: Day 85, Day 113, Day 141 and Day 169)

	P1: CJM112 high dose / P2: CJM112 high dose	P1: CJM112 low dose / P2: CJM112 low dose	P1: Placebo / P2: CJM112 high dose	P1: Placebo / P2: CJM112 low dose
Arm/Group Description	CJM112 high dose in treatment period 1 (Day 1 - 85) ; CJM112 high dose in extension period 2 (Day 86 - 169)	CJM112 low dose in treatment period 1 (Day 1 - 85) ; CJM112 low dose in extension period 2 (Day 86 - 169)	Placebo in treatment period 1; CJM112 high dose in extension period 2	Placebo in treatment period 1; CJM112 low dose in extension period 2
Number of Participants Analyzed [units: participants]	21	12	6	8
Pharmacokinetics (PK): Serum trough concentrations of CJM112 in Period 2 (units: ng/mL) Mean ± Standard Deviation				
Period 2 Day 85 (Pre Dose)	17000 ± 8080	2040 ± 1570	713 ± 1750	0 ± 0
Period 2 Day 113 (Pre Dose)	15900 ± 8140	1890 ± 634	8260 ± 5120	1430 ± 1190
Period 2 Day 141 (Pre Dose)	18700 ± 9450	3140 ± 2180	15700 ± 10700	3700 ± 1250
Period 2 Day 169 (Pre Dose)	19400 ± 9650	3890 ± 1890	16600 ± 6610	2890 ± 672

Number of patients with clinically significant abnormal hematology laboratory parameters

(Time Frame: 38 Weeks)

	P1: CJM112 high dose / P2: CJM112 high dose	P1: CJM112 low dose / P2: CJM112 low dose	P1: Placebo / P2 CJM112 low dose or high dose
Arm/Group Description	CJM112 high dose in treatment period 1 (Day 1 - 85) ; CJM112 high dose in extension period 2 (Day 86 - 169)	CJM112 low dose in treatment period 1 (Day 1 - 85) ; CJM112 low dose in extension period 2 (Day 86 - 169)	Placebo in treatment period 1 (Day 1 - 85) ; CJM112 low dose or CJM112 high dose in extension period 2 (Day 86 - 169)
Number of Participants Analyzed [units: participants]	21	13	18
Number of patients with clinically significant abnormal hematology laboratory parameters (units: Participants) Count of Participants (Not Applicable)			
	0	0	0

Number of patients with clinically significant abnormal clinical chemistry laboratory parameters parameters

(Time Frame: 38 Weeks)

	P1: CJM112 high dose / P2: CJM112 high dose	P1: CJM112 low dose / P2: CJM112 low dose	P1: Placebo / P2 CJM112 low dose or high dose
Arm/Group Description	CJM112 high dose in treatment period 1 (Day	CJM112 low dose in treatment period 1 (Day	Placebo in treatment period 1 (Day 1 - 85) ;

	1 - 85) ; CJM112 high dose in extension period 2 (Day 86 - 169)	1 - 85) ; CJM112 low dose in extension period 2 (Day 86 - 169)	CJM112 low dose or CJM112 high dose in extension period 2 (Day 86 - 169)
Number of Participants Analyzed [units: participants]	21	13	18
Number of patients with clinically significant abnormal clinical chemistry laboratory parameters parameters (units: Participants) Count of Participants (Not Applicable)			
Period 1	3	0	0
Period 2	0	3	2

Number of patients with clinically significant abnormal urinalysis laboratory parameters

(Time Frame: 38 Weeks)

	P1: CJM112 high dose / P2: CJM112 high dose	**P1: CJM112 low dose / P2: CJM112 low dose**	**P1: Placebo / P2 CJM112 low dose or high dose**
Arm/Group Description	CJM112 high dose in treatment period 1 (Day 1 - 85) ; CJM112 high dose in extension period 2 (Day 86 - 169)	CJM112 low dose in treatment period 1 (Day 1 - 85) ; CJM112 low dose in extension period 2 (Day 86 - 169)	Placebo in treatment period 1 (Day 1 - 85) ; CJM112 low dose or CJM112 high dose in extension period 2 (Day 86 - 169)
Number of Participants Analyzed [units: participants]	21	13	18

Number of patients with clinically significant abnormal urinalysis laboratory parameters (units: Participants) Count of Participants (Not Applicable)			
	0	0	0

Summary of Safety

Safety Results

All-Cause Mortality

	Period 1: CJM112 high dose N = 21	Period 1: CJM112 low dose N = 13	Period 1: Placebo N = 18	Period 1: Pooled CJM112 N = 34	Period 2: CJM112 high dose/CJM112 high dose N = 17	Period 2: CJM112 low dose/CJM112 low dose N = 10	Period 2: Placebo/ CJM112 high dose N = 6	Period 2: Placebo/ CJM112 low dose N = 8	Period 2: Pooled CJM112 high dose N = 23	Period 2: Pooled CJM112 low dose N = 18
Arm/Group Description	Period 1: CJM112 high dose	Period 1: CJM112 low dose	Period 1: Placebo	Period 1: Pooled CJM112	CJM112 high dose in treatment period 1; CJM112 high dose in extension period 2	CJM112 low dose in treatment period 1; CJM112 low dose in extension period 2	Placebo in treatment period 1; CJM112 high dose in extension period 2	Placebo in treatment period 1; CJM112 low dose in extension period 2	Period 2: Pooled CJM112 high dose	Period 2: Pooled CJM112 low dose
Total participants affected	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Serious Adverse Events by System Organ Class

Time Frame	38 weeks
Source Vocabulary for Table Default	MedDRA (21.0)
Assessment Type for Table Default	Systematic Assessment

	Period 1: CJM112 high dose N = 21	**Period 1: CJM112 low dose N = 13**	**Period 1: Placebo N = 18**	**Period 1: Pooled CJM112 N = 34**	**Period 2: CJM112 high dose/CJM112 high dose N = 17**	**Period 2: CJM112 low dose/CJM112 low dose N = 10**	**Period 2: Placebo/ CJM112 high dose N = 6**	**Period 2: Placebo/ CJM112 low dose N = 8**	**Period 2: Pooled CJM112 high dose N = 23**	**Period 2: Pooled CJM112 low dose N = 18**
Arm/Group Description	Period 1: CJM112 high dose	Period 1: CJM112 low dose	Period 1: Placebo	Period 1: Pooled CJM112	CJM112 high dose in treatment period 1; CJM112 high dose in extension period 2	CJM112 low dose in treatment period 1; CJM112 low dose in extension period 2	Placebo in treatment period 1; CJM112 high dose in extension period 2	Placebo in treatment period 1; CJM112 low dose in extension period 2	Period 2: Pooled CJM112 high dose	Period 2: Pooled CJM112 low dose
Total participants affected	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)	0 (0.00%)
Hepatobiliary disorders										
Cholelithiasis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)	0 (0.00%)

Other Adverse Events by System Organ Class

Time Frame	38 weeks

Source Vocabulary for Table Default	MedDRA (21.0)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	3%

	Period 1: CJM112 high dose N = 21	**Period 1: CJM112 low dose N = 13**	**Period 1: Placebo N = 18**	**Period 1: Pooled CJM112 N = 34**	**Period 2: CJM112 high dose/CJM112 high dose N = 17**	**Period 2: CJM112 low dose/CJM112 low dose N = 10**	**Period 2: Placebo/ CJM112 high dose N = 6**	**Period 2: Placebo/ CJM112 low dose N = 8**	**Period 2: Pooled CJM112 high dose N = 23**	**Period 2: Pooled CJM112 low dose N = 18**
Arm/Group Description	Period 1: CJM112 high dose	Period 1: CJM112 low dose	Period 1: Placebo	Period 1: Pooled CJM112	CJM112 high dose in treatment period 1; CJM112 high dose in extension period 2	CJM112 low dose in treatment period 1; CJM112 low dose in extension period 2	Placebo in treatment period 1; CJM112 high dose in extension period 2	Placebo in treatment period 1; CJM112 low dose in extension period 2	Period 2: Pooled CJM112 high dose	Period 2: Pooled CJM112 low dose
Total participants affected	16 (76.19 %)	11 (84.62 %)	10 (55.56 %)	27 (79.41 %)	10 (58.82%)	9 (90.00%)	5 (83.33 %)	5 (62.50 %)	15 (65.22 %)	14 (77.78 %)
Blood and lymphatic system disorders										
Increased tendency to bruise	1 (4.76%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiac disorders										
Sinus arrest	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)	0 (0.00%)
Supraventricular extrasystoles	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)	0 (0.00%)

Eye disorders										
Blepharospasm	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	1 (4.35%)	0 (0.00%)
Dry eye	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	1 (5.56%)
Eye irritation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)	0 (0.00%)
Eye pruritus	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	1 (5.56%)
Gastrointestinal disorders										
Diarrhoea	1 (4.76%)	0 (0.00%)	2 (11.11%)	1 (2.94%)	1 (5.88%)	1 (10.00%)	1 (16.67 %)	0 (0.00%)	2 (8.70%)	1 (5.56%)
Flatulence	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Frequent bowel movements	0 (0.00%)	1 (7.69%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Inguinal hernia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)	0 (0.00%)
Lip dry	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)
Nausea	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)	0 (0.00%)
Toothache	1 (4.76%)	1 (7.69%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
General disorders and administration site conditions										
Asthenia	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Fatigue	0 (0.00%)	1 (7.69%)	1 (5.56%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Influenza like illness	1 (4.76%)	0 (0.00%)	1 (5.56%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Injection site bruising	1 (4.76%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Injection site reaction	0 (0.00%)	1 (7.69%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Non-cardiac chest pain	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Sensation of foreign body	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)	0 (0.00%)
Immune system disorders										
Hypersensitivity	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Seasonal allergy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)
Infections and infestations										
Bacterial vaginosis	0 (0.00%)	1 (7.69%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Bronchitis	0 (0.00%)	1 (7.69%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Conjunctivitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	1 (5.56%)
Cystitis	1 (4.76%)	1 (7.69%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Fungal skin infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)	0 (0.00%)
Gastroenteritis	0 (0.00%)	1 (7.69%)	0 (0.00%)	1 (2.94%)	1 (5.88%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	2 (8.70%)	0 (0.00%)
Gastroenteritis viral	0 (0.00%)	1 (7.69%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Helicobacter gastritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)	0 (0.00%)
Laryngitis	1 (4.76%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nasopharyngitis	3 (14.29%)	1 (7.69%)	1 (5.56%)	4 (11.76%)	2 (11.76%)	1 (10.00%)	0 (0.00%)	2 (25.00 %)	2 (8.70%)	3 (16.67%)
Oral herpes	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Pharyngitis	1 (4.76%)	1 (7.69%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Sinusitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	1 (5.56%)
Tonsillitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)	0 (0.00%)
Tooth infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	1 (4.35%)	0 (0.00%)
Upper respiratory tract infection	1 (4.76%)	2 (15.38%)	0 (0.00%)	3 (8.82%)	1 (5.88%)	2 (20.00%)	1 (16.67 %)	0 (0.00%)	2 (8.70%)	2 (11.11%)
Urinary tract infection	1 (4.76%)	1 (7.69%)	1 (5.56%)	2 (5.88%)	2 (11.76%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	2 (8.70%)	1 (5.56%)
Vulvovaginal mycotic infection	1 (4.76%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)
Injury, poisoning and procedural complications										
Concussion	0 (0.00%)	1 (7.69%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Joint dislocation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	1 (4.35%)	0 (0.00%)
Ligament sprain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)	0 (0.00%)
Limb injury	0 (0.00%)	1 (7.69%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Road traffic accident	0 (0.00%)	1 (7.69%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Sports injury	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Wound	1 (4.76%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Investigations										

Alanine aminotransferase increased	1 (4.76%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Aspartate aminotransferase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	1 (5.56%)
Blood creatine phosphokinase increased	1 (4.76%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	2 (20.00%)	1 (16.67 %)	1 (12.50 %)	1 (4.35%)	3 (16.67%)
Blood creatinine increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)
Blood triglycerides increased	1 (4.76%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Glucose urine present	1 (4.76%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Metabolism and nutrition disorders										
Hypoglycaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	1 (4.35%)	0 (0.00%)
Vitamin D deficiency	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)	0 (0.00%)
Musculoskeletal and connective tissue disorders										
Arthritis	0 (0.00%)	1 (7.69%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)
Back pain	0 (0.00%)	1 (7.69%)	1 (5.56%)	1 (2.94%)	1 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)	0 (0.00%)
Joint effusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)
Myalgia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	2 (11.11%)
Neck pain	0 (0.00%)	1 (7.69%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Pain in extremity	1 (4.76%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nervous system disorders										
Headache	1 (4.76%)	3 (23.08%)	1 (5.56%)	4 (11.76%)	1 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)	0 (0.00%)
Psychiatric disorders										
Depression	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal and urinary disorders										
Micturition urgency	1 (4.76%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)
Pollakiuria	1 (4.76%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)
Proteinuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (20.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	3 (16.67%)
Reproductive system and breast disorders										
Dysmenorrhoea	0 (0.00%)	1 (7.69%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders										
Cough	0 (0.00%)	1 (7.69%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dyspnoea	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nasal congestion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)	0 (0.00%)
Oropharyngeal pain	1 (4.76%)	1 (7.69%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	2 (11.11%)
Rhinorrhoea	1 (4.76%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Skin and subcutaneous tissue disorders										
Acne	0 (0.00%)	2 (15.38%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dermal cyst	1 (4.76%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dermatitis	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Diffuse alopecia	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dry skin	2 (9.52%)	0 (0.00%)	2 (11.11%)	2 (5.88%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.56%)
Erythema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)	0 (0.00%)
Papule	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	1 (5.56%)
Pityriasis rosea	0 (0.00%)	1 (7.69%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pruritus	1 (4.76%)	0 (0.00%)	3 (16.67%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	1 (16.67 %)	0 (0.00%)	1 (4.35%)	0 (0.00%)
Psoriasis	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rash maculo-papular	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urticaria	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Other Relevant Findings

NA

Conclusion:

The study was terminated early by the Sponsor, as the results met the pre-planned futility criterion at the pre-planned interim analyses (IA1).

Administration of monthly dose of CJM112 (high and low dose) over 12 weeks in Period 1 followed by Extension Period 2 was safe and well tolerated.

Date of Clinical Trial Report

28-Mar-2019