Clinical trial results:
A Phase 1/2, randomised, placebo-controlled study of EDP2939 in healthy volunteers and participants with moderate plaque psoriasis.

Summary

EudraCT number	2022-001631-82
Trial protocol	PL BG
Global end of trial date	06 September 2023

Results information

Result version number	v1 (current)
This version publication date	13 December 2023
First version publication date	13 December 2023

Trial information

Trial identification

Sponsor protocol code	EDP2939-101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Evelo Biosciences Ltd
Sponsor organisation address	One Kendall Square, 600/700 Ste7-201, Cambridge, United States, MA 02139
Public contact	Duncan McHale, Evelo Biosciences Ltd, duncan@evelobio.com
Scientific contact	Duncan McHale, Evelo Biosciences Ltd, duncan@evelobio.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 October 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 September 2023
Global end of trial reached?	Yes
Global end of trial date	06 September 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To demonstrate the superiority of EDP2939 compared to placebo on the proportion of participants with moderate plaque psoriasis achieving PASI-50

Protection of trial subjects:

The study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki, ICH GCP, and all applicable country and local regulations. A written informed consent was obtained from each participant before entering the study or performing any non routine procedure. Each prospective participant or his or her legal guardian was given a full explanation of the study, was allowed to read the approved ICF, and had any questions answered. Participants were free to withdraw their consent at any point during the study.

Background therapy:

No background therapy. All prior and concomitant medications were listed.

Evidence for comparator:

This was a placebo-controlled study.

Actual start date of recruitment	12 December 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 66
Country: Number of subjects enrolled	Bulgaria: 22
Country: Number of subjects enrolled	Canada: 28
Country: Number of subjects enrolled	United Kingdom: 35
Worldwide total number of subjects	151
EEA total number of subjects	88

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	138
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects who met all of the inclusion and none of the exclusion criteria were enrolled into the study.
Part A: A total of 35 participants in 3 dose-ascending cohorts (3.9 x10^12, 1.95x10^13, 1.12x10^14 eTPN QD), received EDP2939 or placebo (2:1)
Part B: A total of 116 participants received 3.9 x10^12 EDP2939 or placebo (1:1)

Pre-assignment

Screening details:

Both Parts A and B consisted of a Screening period of 4 weeks.
Part A consisted of healthy volunteers aged 18-65 years. Part B consisted of participants aged 18-75 years with a documented diagnosis of plaque psoriasis, patient-/clinician-reported disease duration>=6 months with PGA=3, BSA5-20% and PASI score of 5-20 at screening and baseline.

Period 1

Period 1 title	Treatment Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Data analyst, Carer, Subject, Assessor

Blinding implementation details:

Part A of the study was participant-blind and investigator-blind, but the treatment allocations were unblinded for the sponsor with the exception of the medical monitor. The random treatment allocation was implemented by the sponsor using a central randomisation schedule.
Part B of the study was participant-blind, investigator-blind and sponsor-blind. The random treatment allocation was implemented using an IRT system.
No unblinding occurred prior to the locking of the clinical databases.

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A Cohort 1 EDP2939 Low Dose

Arm description:

1 capsule of EDP2939 3.9x10^12 eTPN (equivalent total particle number) once daily for 10 days

Arm type	Experimental
Investigational medicinal product name	EDP2939 1 Capsule Low Dose
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One polymer-coated capsule containing 3.9 x 10^12 equivalent total particle number (eTPN) of EDP2939 was self-administered orally once per day for 10 days. Total daily dose was 3.9 x 10^12 eTPN of EDP2939.

Arm title	Part A Cohort 2 EDP2939 Medium Dose

Arm description:

5 Capsules of EDP2939 3.9 x 10^12 eTPN (equivalent total particle number) once daily for 10 days

Arm type	Experimental
Investigational medicinal product name	EDP2939 5 Capsules Low Dose
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Five polymer-coated capsules each containing 3.9 x 10^12 equivalent total particle number (eTPN) of EDP2939 was self-administered orally once per day for 10 days. Total daily dose was 1.95 x 10^13 eTPN of EDP2939.

Arm title	Part A Cohort 3 EDP2939 High Dose

Arm description:

2 capsules of EDP2939 5.6 x 10^13 eTPN (equivalent total particle number), once daily for 10 days

Arm type	Experimental
Investigational medicinal product name	EDP2939 1 Capsule High Dose
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Two polymer-coated capsules each containing 5.6 x 10^13 equivalent total particle number (eTPN) of EDP2939 was self-administered orally once per day for 10 days. Total daily dose was 1.12 x 10^14 eTPN of EDP2939.

Arm title	Part B EDP2939

Arm description:

1 capsule of EDP2939 3.9 x10^12 equivalent total particle equivalent (eTPN), once daily for 16 weeks

Arm type	Experimental
Investigational medicinal product name	EDP2939 1 Capsule
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One polymer-coated capsule containing 3.9 x 10^12 equivalent total particle number (eTPN) of EDP2939 was self-administered orally once per day for16 weeks. Total daily dose was 3.9 x 10^12 eTPN of EDP2939.

Arm title	Part B Placebo

Arm description:

1 capsule of placebo matching Part B EDP2939, once daily for 16 weeks

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One placebo capsule self-administered orally once per day for16 weeks. Placebo was identical to Part B EDP2939 capsules but did not contain active pharmaceutical ingredient.

Arm title	Part A Placebo

Arm description:

1 (Cohort 1), 5 (Cohort 2) or 2 (Cohort 3) capsules of placebo matching relevant Part A EDP2393 administered once daily for 10 days

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Cohort 1: 1 capsule placebo matching EDP2939 low dose; Cohort 2: 5 capsules placebo matching EDP2939 low dose; Cohort 3: 2 capsules placebo matching EDP2939 high dose. Capsules were self-administered orally once per day for 10 days. Placebo was identical to corresponding EDP2939 capsules but did not contain active pharmaceutical ingredient.

Number of subjects in period 1	Part A Cohort 1 EDP2939 Low Dose	Part A Cohort 2 EDP2939 Medium Dose	Part A Cohort 3 EDP2939 High Dose
Started	8	8	7
Completed	8	8	7
Not completed	0	0	0
Consent withdrawn by subject	-	-	-
Unable to attend final dose visit, personal reason	-	-	-
Lost to follow-up	-	-	-
Randomised in error, not treated	-	-	-
Lack of efficacy	-	-	-
Protocol deviation	-	-	-

Number of subjects in period 1	Part B EDP2939	Part B Placebo	Part A Placebo
Started	58	58	12
Completed	47	44	11
Not completed	11	14	1
Consent withdrawn by subject	5	3	-
Unable to attend final dose visit, personal reason	-	-	1
Lost to follow-up	1	-	-
Randomised in error, not treated	-	1	-
Lack of efficacy	4	9	-
Protocol deviation	1	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Part A Cohort 1 EDP2939 Low Dose
Reporting group description:	
1 capsule of EDP2939 3.9x10^12 eTPN (equivalent total particle number) once daily for 10 days	
Reporting group title	Part A Cohort 2 EDP2939 Medium Dose
Reporting group description:	
5 Capsules of EDP2939 3.9 x 10^12 eTPN (equivalent total particle number) once daily for 10 days	
Reporting group title	Part A Cohort 3 EDP2939 High Dose
Reporting group description:	
2 capsules of EDP2939 5.6 x 10^13 eTPN (equivalent total particle number), once daily for 10 days	
Reporting group title	Part B EDP2939
Reporting group description:	
1 capsule of EDP2939 3.9 x10^12 equivalent total particle equivalent (eTPN), once daily for 16 weeks	
Reporting group title	Part B Placebo
Reporting group description:	
1 capsule of placebo matching Part B EDP2939, once daily for 16 weeks	
Reporting group title	Part A Placebo
Reporting group description:	
1 (Cohort 1), 5 (Cohort 2) or 2 (Cohort 3) capsules of placebo matching relevant Part A EDP2393 administered once daily for 10 days	

Reporting group values	Part A Cohort 1 EDP2939 Low Dose	Part A Cohort 2 EDP2939 Medium Dose	Part A Cohort 3 EDP2939 High Dose
Number of subjects	8	8	7
Age categorical Units: Subjects			
Adults (18-64 years)	8	8	7
From 65-84 years	0	0	0
Age continuous Units: years			
arithmetic mean	34.0	31.9	28.0
standard deviation	± 11.71	± 10.34	± 9.81
Gender categorical Units: Subjects			
Female	1	1	3
Male	7	7	4

Reporting group values	Part B EDP2939	Part B Placebo	Part A Placebo
Number of subjects	58	58	12
Age categorical Units: Subjects			
Adults (18-64 years)	51	52	12
From 65-84 years	7	6	0
Age continuous Units: years			
arithmetic mean	45.9	44.1	29.8
standard deviation	± 14.44	± 14.13	± 12.1

Gender categorical Units: Subjects			
Female	22	18	3
Male	36	40	9

Reporting group values	Total		
Number of subjects	151		
Age categorical Units: Subjects			
Adults (18-64 years)	138		
From 65-84 years	13		
Age continuous Units: years arithmetic mean standard deviation	 -		
Gender categorical Units: Subjects			
Female	48		
Male	103		

Subject analysis sets

Subject analysis set title	Part A Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

The Part A Safety Set consists of all participants who received any IMP during Part A of the Study. All analyses using the Safety Set grouped participants according to treatment received.

Subject analysis set title	Part B Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

The Part B Full Analysis Set consists of all participants who were randomised to treatment during Part B of the study. All analyses using the Full Analysis Set grouped participants according to randomised treatment.

Subject analysis set title	Part B Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

The Part B Safety Set consists of all participants who received any IMP during Part B of the Study. All analyses using the Safety Set grouped participants according to treatment received.

Reporting group values	Part A Safety Set	Part B Full Analysis Set	Part B Safety Set
Number of subjects	35	116	115
Age categorical Units: Subjects			
Adults (18-64 years)	35	103	102
From 65-84 years	0	13	13
Age continuous Units: years arithmetic mean standard deviation	 30.8 ± 10.92	 45.0 ± 14.26	 45.2 ± 14.21
Gender categorical Units: Subjects			
Female	8	40	39

Male	27	76	76

End points

End points reporting groups

Reporting group title	Part A Cohort 1 EDP2939 Low Dose
Reporting group description:	
1 capsule of EDP2939 3.9x10^12 eTPN (equivalent total particle number) once daily for 10 days	
Reporting group title	Part A Cohort 2 EDP2939 Medium Dose
Reporting group description:	
5 Capsules of EDP2939 3.9 x 10^12 eTPN (equivalent total particle number) once daily for 10 days	
Reporting group title	Part A Cohort 3 EDP2939 High Dose
Reporting group description:	
2 capsules of EDP2939 5.6 x 10^13 eTPN (equivalent total particle number), once daily for 10 days	
Reporting group title	Part B EDP2939
Reporting group description:	
1 capsule of EDP2939 3.9 x10^12 equivalent total particle equivalent (eTPN), once daily for 16 weeks	
Reporting group title	Part B Placebo
Reporting group description:	
1 capsule of placebo matching Part B EDP2939, once daily for 16 weeks	
Reporting group title	Part A Placebo
Reporting group description:	
1 (Cohort 1), 5 (Cohort 2) or 2 (Cohort 3) capsules of placebo matching relevant Part A EDP2393 administered once daily for 10 days	
Subject analysis set title	Part A Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Part A Safety Set consists of all participants who received any IMP during Part A of the Study. All analyses using the Safety Set grouped participants according to treatment received.	
Subject analysis set title	Part B Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
The Part B Full Analysis Set consists of all participants who were randomised to treatment during Part B of the study. All analyses using the Full Analysis Set grouped participants according to randomised treatment.	
Subject analysis set title	Part B Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Part B Safety Set consists of all participants who received any IMP during Part B of the Study. All analyses using the Safety Set grouped participants according to treatment received.	

Primary: Summary and Analysis of PASI-50 Responders

End point title	Summary and Analysis of PASI-50 Responders[1]
End point description:	
A PASI-50 response is defined as a reduction from baseline of at least 50% in the Psoriasis Area and Severity Index (PASI) Score. The primary estimand used a composite strategy (assumption of non-response) for the use of any prohibited therapy prior to week 16 or where the participant had withdrawn from treatment due to a treatment-failure related reason (related AE, lack of efficacy, requirement for other psoriasis treatment). Withdrawal from treatment for other reasons was considered under a hypothetical strategy with no imputation of missing data after discontinuation of treatment. No other intercurrent events were considered and all other data was analysed as collected.	
End point type	Primary
End point timeframe:	
Week 16	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Part A treatment groups did not form part of the efficacy analysis and were used for safety endpoints only.

End point values	Part B EDP2939	Part B Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	52		
Units: Subjects				
PASI-50 Responder	11	13		

Statistical analyses

Statistical analysis title	PASI-50: EDP2939 vs Placebo

Statistical analysis description:

Estimates come from a generalised linear mixed model (GLMM) with a logit link function, including terms for treatment, visit, baseline PASI score, country, sex and treatment-by-visit interaction.
All visits are included in the model, but only the results for the primary timepoint at Week 16 is shown here.

Comparison groups	Part B EDP2939 v Part B Placebo
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.51
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	1.97

Secondary: Summary and Analysis of PASI-75 Responders

End point title	Summary and Analysis of PASI-75 Responders[2]

End point description:

A PASI-75 response is defined as a reduction from baseline of at least 75% in the Psoriasis Area and Severity Index (PASI) Score.
The primary estimand used a composite strategy (assumption of non-response) for the use of any prohibited therapy prior to week 16 or where the participant had withdrawn from treatment due to a treatment-failure related reason (related AE, lack of efficacy, requirement for other psoriasis treatment). Withdrawal from treatment for other reasons was considered under a hypothetical strategy with no imputation of missing data after discontinuation of treatment. No other intercurrent events were considered and all other data was analysed as collected.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Part A treatment groups did not form part of the efficacy analysis and were used for safety endpoints only.

End point values	Part B EDP2939	Part B Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	52		
Units: Subjects				
PASI-75 Responder	2	4		

Statistical analyses

Statistical analysis title	PASI-75: EDP2939 vs Placebo

Statistical analysis description:

Estimates come from a generalised linear mixed model (GLMM) with a logit link function, including terms for treatment, visit, baseline PASI score, country, sex and treatment-by-visit interaction.
All visits are included in the model, but only the results for the primary timepoint at Week 16 is shown here.

Comparison groups	Part B EDP2939 v Part B Placebo
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.094
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	1.21

Secondary: Summary and Analysis of PGA of 0 or 1 Responders

End point title	Summary and Analysis of PGA of 0 or 1 Responders[3]

End point description:

The estimand used a composite strategy (assumption of non-response) for the use of any prohibited therapy prior to week 16 or where the participant had withdrawn from treatment due to a treatment-failure related reason (related AE, lack of efficacy, requirement for other psoriasis treatment). Withdrawal from treatment for other reasons was considered under a hypothetical strategy with no imputation of missing data after discontinuation of treatment. No other intercurrent events were considered and all other data was analysed as collected.

End point type	Secondary

End point timeframe:

Week 16

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Part A treatment groups did not form part of the efficacy analysis and were used for safety endpoints only.

End point values	Part B EDP2939	Part B Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	52		
Units: Subjects				
PGA 0 or 1 Responders	7	5		

Statistical analyses

Statistical analysis title	PGA 0 or 1: EDP2939 vs Placebo

Statistical analysis description:

Estimates come from a generalised linear mixed model (GLMM) with a logit link function, including terms for treatment, visit, baseline PGA score, country, sex and treatment-by-visit interaction.
All visits are included in the model, but only the results for the primary timepoint at Week 16 is shown here.

Comparison groups	Part B EDP2939 v Part B Placebo
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.649
Method	Mixed models analysis
Parameter estimate	Odds ratio (OR)
Point estimate	1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.35
upper limit	5.29

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Part A: 10 day treatment period + 14 day follow-up period
Part B: 16 week treatment period + 4 week follow-up period

Adverse event reporting additional description:

A treatment-emergent adverse event (TEAE) is defined as an adverse event with onset date and time on or after the date and time of the first dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Part A Cohort 1 EDP2939 Low Dose

Reporting group description:

1 capsule of EDP2939 3.9x10^12 eTPN (equivalent total particle number) once daily for 10 days

Reporting group title	Part A Cohort 2 EDP2939 Medium Dose

Reporting group description:

5 Capsules of EDP2939 3.9 x 10^12 eTPN (equivalent total particle number) once daily for 10 days

Reporting group title	Part A Cohort 3 EDP2939 High Dose

Reporting group description:

2 capsules of EDP2939 5.6 x 10^13 eTPN (equivalent total particle number), once daily for 10 days

Reporting group title	Part A Placebo

Reporting group description:

1 (Cohort 1), 5 (Cohort 2) or 2 (Cohort 3) capsules of placebo matching relevant Part A EDP2393 administered once daily for 10 days

Reporting group title	Part B EDP2939

Reporting group description:

1 capsule of EDP2939 3.9 x10^12 equivalent total particle equivalent (eTPN), once daily for 16 weeks

Reporting group title	Part B Placebo

Reporting group description:

1 capsule of placebo matching Part B EDP2939, once daily for 16 weeks

Serious adverse events	Part A Cohort 1 EDP2939 Low Dose	Part A Cohort 2 EDP2939 Medium Dose	Part A Cohort 3 EDP2939 High Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part A Placebo	Part B EDP2939	Part B Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 58 (0.00%)	1 / 57 (1.75%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 58 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Part A Cohort 1 EDP2939 Low Dose	Part A Cohort 2 EDP2939 Medium Dose	Part A Cohort 3 EDP2939 High Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)	4 / 8 (50.00%)	1 / 7 (14.29%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Headache			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Tension headache			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Gingival swelling			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Abdominal discomfort			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part A Placebo	Part B EDP2939	Part B Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 12 (33.33%)	10 / 58 (17.24%)	5 / 57 (8.77%)

Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 58 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 12 (0.00%)	1 / 58 (1.72%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Tension headache			
subjects affected / exposed	0 / 12 (0.00%)	0 / 58 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Gingival swelling			
subjects affected / exposed	1 / 12 (8.33%)	0 / 58 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Abdominal discomfort			
subjects affected / exposed	1 / 12 (8.33%)	0 / 58 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 58 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 58 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 58 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 12 (8.33%)	0 / 58 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	1 / 12 (8.33%)	0 / 58 (0.00%)	0 / 57 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Gastroenteritis			

subjects affected / exposed	1 / 12 (8.33%)	0 / 58 (0.00%)	1 / 57 (1.75%)
occurrences (all)	1	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	3 / 58 (5.17%)	4 / 57 (7.02%)
occurrences (all)	0	3	4
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	4 / 58 (6.90%)	0 / 57 (0.00%)
occurrences (all)	0	4	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	3 / 58 (5.17%)	1 / 57 (1.75%)
occurrences (all)	0	3	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 May 2022	Change to the reference of enteric-coated capsules to polymer-coated capsules and addition of a footnote to the schedule of activities in Part A to clarify an end of study pregnancy test was to be carried out in all participants. This was not submitted to the competent authorities and ethics committee .
27 June 2022	• Change in study design such that Part B could commence dosing following SRC review of Part A, Cohort 1 (3.9 × 1012 eTPN QD dose level). • Change in Phase 2 (Part B) dose from 7.5 × 1013 to 3.9 × 1012 eTPN QD. • Deletion of reference to Data Monitoring Committee and change in the safety committee from Dose-Level Review Committee to SRC. • Change in minimum number of participants with safety data required for each SRC (changed from 8 to 10 participants). • Update the requirement in Part A for blood samples for biomarkers and systemic levels of EDP2939 to be taken predose on Day 10. • Separate text for Part A and Part B permitted and contraindicated immunizations. • Iteration of specific study halting criteria for Part B. • Specification that SRC review was to be initially performed in a blinded manner. Unblinded review was only to be done if a potential safety signal needed to be confirmed or rejected. This was not submitted to the competent authorities and ethics committee.
23 August 2022	• Change in exclusion criterion number 22 that participants in Part B would be permitted to use unmedicated emollients and moisturizers during the study (but were to be withheld on visit days when skin assessments were made). Other topical treatments were excluded if used within 14 days of randomization. • Change in exclusion criterion number 24 with deletion of "bilirubin >1.5 × upper limit of normal". • Inclusion of monkeypox vaccine in list of live vaccines. • Update of description of the VAS to be rated between 0 (fatigue is no problem) to 100 (fatigue is major problem). • Addition of the Declaration and Signature of the investigator page. This was the first version submitted to regulatory authorities and ethics committees.
14 November 2022	• Change in grading of intensity of AEs for healthy participants in Part A to be mild, moderate, or severe. The CTCAE grading scale was only to be used for participants in Part B. • Deletion of bilateral tubal ligation as a reason to consider a female to be of nonchildbearing potential. • Update in highly effective contraception methods text to change "tubal occlusion" to "tubal occlusion/ligation". • Clarification that Part B investigators would have immediate and unrestricted access within the IRT system to unblind in case of emergency. Additionally, the investigator responsibilities in determining the need for unblinding were clarified and the time frame for sponsor notification were kept the same for Parts A and B.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported