ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 02/22/2016

ClinicalTrials.gov ID: NCT01066871

Study Identification

Unique Protocol ID:	EMR700692_003
Brief Title:	Sprifermin (AS902330) in Cartilage Injury Repair (CIR)
Official Title:	A Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group Phase II Trial to Investigate the Efficacy and Safety of Weekly Intra-articular (i.a.) Injections of 10, 30, and 100 µg of AS902330 for Three Consecutive Weeks in Patients With Acute Cartilage Injury of the Knee
Secondary IDs:	

Study Status

Record Verification:	February 2016
Overall Status:	Terminated
Study Start:	March 2010
Primary Completion:	April 2013 [Actual]
Study Completion:	April 2013 [Actual]

Sponsor/Collaborators

Sponsor:	Merck KGaA
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	No

IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: ZS EK 12 563/09 Board Name: Ethikkommission des Landes Berlin, Landesamt für Gesundheit und Soziales Board Affiliation: Institutional Review Board Phone: 49 030-90127640 Email: ethik-kommission@lageso.verwalt-berlin.de
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	Bulgaria: Bulgarian Drug Agency, Ethics Committee for Multicenter Trials Canada: Health Canada, Ethics Review Committee Germany: Bundesinstitut für Arzneimittel und Medizinproducckte (BfArM), Federal Institute for Drugs and Medical Devices, Ethics Commission Poland: Office for Registration of Medicinal Products, Medical Devices and Biocidal Products, Ethics Review Committee Serbia: Agency for Drugs and Medicinal Devices, Ethics Review Committee South Africa: Medicines Control Council, Ethics Committee of the University of the Free State Slovenia: Agency for Medicinal Products - Ministry of Health Hungary: National Institute of Pharmacy

Study Description

Brief Summary:	Several people all over the world suffer from cartilage injuries in the knee. Symptoms include pain, joint swelling, and loss of function. Without repair, cartilage injury may ultimately lead to osteoarthritis (OA). Natural healing is poor, and to date treatment is available only for deep cartilage defects involving also the underlying bone. A promising candidate for drug treatment of cartilage injury is sprifermin (AS902330), a recombinant form of the human fibroblast growth factor (FGF) 18. So far, the drug has been used in subjects with different stages of knee OA in two ongoing studies without emerging safety issues following single and multiple intra-articular injections of ascending doses. However, OA represents late-stage cartilage injury, where repair might be difficult due to diffuse damage, reduced responsiveness of the cartilage, and/or the involvement of other joint structures. This clinical trial is meant to provide the proof of concept and to identify an efficacious dose of sprifermin (AS902330) for the treatment of adult subjects with acute cartilage injuries of the knee. The first subject for this trial was treated on the 19th of April 2010.
Detailed Description:	

Conditions

Conditions:	Isolated Cartilage Injury of the Knee
Keywords:	Knee cartilage injury

fibroblast growth factor 18
FGF18

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Parallel Assignment
Number of Arms:	4
Masking:	Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	74 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Sprifermin (AS902330) 10 mcg	Drug: Sprifermin (AS902330) 10 mcg Sprifermin (AS902330) will be administered at a dose of 10 microgram (mcg) as intra-articular injection once every week for 3 consecutive weeks.
Experimental: Sprifermin (AS902330) 30 mcg	Drug: Sprifermin (AS902330) 30 mcg Sprifermin (AS902330) will be administered at a dose of 30 mcg as intra-articular injection once every week for 3 consecutive weeks.
Experimental: Sprifermin (AS902330) 100 mcg	Drug: Sprifermin (AS902330) 100 mcg Sprifermin (AS902330) will be administered at a dose of 100 mcg as intra-articular injection once every week for 3 consecutive weeks.
Placebo Comparator: Placebo	Placebo Placebo matched to sprifermin (AS902330) will be administered as intra-articular injection once every week for 3 consecutive weeks.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age: 45 Years

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Acute cartilage lesion of ICRS grade 2 to 4 at the femoral condyle of the knee (= target knee)
- Age: 18 to 45 years
- Sex: male or female. Women of childbearing potential (that is, all female subjects after puberty unless they are post-menopausal for at least 2 years or surgically sterile) must have negative serum and urine pregnancy tests at screening and Visit 1, respectively, and must use a highly effective method of contraception.
- History of pain and effusion of the target knee post-injury
- Injury within 4 to 12 weeks prior to 1st treatment with investigational medicinal product (IMP)
- Written informed consent prior to any trial-related activity

Exclusion Criteria:

- Personal medical history of osteoarthritis OA in either knee
- Any previous surgery on the target knee
- History of swelling of the target knee along with pain on weight-bearing, or arthroscopy for diagnostic purposes during the 12 months preceding injury
- Corticosteroid (intra-articular) injection into the target knee during the preceding 12 months
- Any other intra-articular injection into the target knee during the preceding 3 months
- Any concurrent injury (for example, arthrolith, anterior cruciate ligament rupture, meniscus tear) of the target knee requiring surgical intervention
- OA or any pre-existing cartilage damage in the target knee, as revealed by MRI
- Legal incapacity or limited legal capacity
- Subjects who are imprisoned or institutionalized by regulatory or court order
- Pregnancy or lactation
- Participation in another clinical trial within the past 30 days
- Any condition or findings in the medical history or in the pre-trial assessments that in the opinion of the Investigator constitutes a risk or contraindication for participation in the trial or that could interfere with the trial objectives, conduct or evaluation
- Known hypersensitivity to the trial treatment or diluents
- Significant renal or hepatic impairment, as indicated by: Aspartate aminotransferase (AST), alanine aminotransferase (ALT), or alkaline phosphatase (ALP) greater than (>) 3 times the upper limit of normal (ULN); total bilirubin >1.5 times ULN (except in case of Gilbert's syndrome); creatinine >1.5 times ULN; hemoglobin less than (<5.5) millimole per liter (mmol/L), white blood cell count (WBC) <2.5 * 10^9 per liter, or platelets <75 *10^9 per liter)
- Any suspicion of intra-articular infection
- Any known active infections that may compromise the immune system such as human immunodeficiency virus (HIV), Hepatitis B or C infection

- History of sarcoma and/or of other active malignancy within five years, except adequately treated basal cell or squamous cell carcinoma of the skin
- Open growth plate, as revealed by MRI
- Diagnostic arthroscopy after injury and within 4 weeks prior to treatment start

Contacts/Locations

Study Officials: Medical Responsible
Study Director
Merck KGaA, Darmstadt, Germany

Locations: Germany
Please contact the Merck KGaA Communication Center
Darmstadt, Germany

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) was administered at a dose of 10 microgram (mcg) as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) was administered at a dose of 30 mcg as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 100 mcg	Sprifermin (AS902330) was administered at a dose of 100 mcg as intra-articular injection once every week for 3 consecutive weeks.
Placebo	Placebo matched to sprifermin (AS902330) was administered as intra-articular injection once every week for 3 consecutive weeks.

Overall Study

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
Started	20	18	18	18
Completed	16	13	12	13
Not Completed	4	5	6	5
Lost to Follow-up	0	2	2	0
Protocol Violation	1	0	3	2
Lack of Efficacy	0	0	0	1
Withdrawal by Subject	3	1	0	0
Unspecified	0	2	1	2

Baseline Characteristics

Analysis Population Description

The intention-to-treat (ITT) population included all participants randomized to a trial treatment.

Reporting Groups

	Description
Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) was administered at a dose of 10 microgram (mcg) as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) was administered at a dose of 30 mcg as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 100 mcg	Sprifermin (AS902330) was administered at a dose of 100 mcg as intra-articular injection once every week for 3 consecutive weeks.
Placebo	Placebo matched to sprifermin (AS902330) was administered as intra-articular injection once every week for 3 consecutive weeks.

Baseline Measures

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo	Total
Number of Participants	20	18	18	18	74

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo	Total
Age, Customized [units: participants]					
Less than (<) 40 years	16	15	14	16	61
Greater than or equal to (>=) 40 years	4	3	4	2	13
Gender, Male/Female [units: participants]					
Female	5	5	7	3	20
Male	15	13	11	15	54

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percent Change From Baseline in Cartilage Defect Volume at Month 12
Measure Description	Percent change in cartilage defect volume was calculated based on central magnetic resonance imaging (MRI): (volume at Month 12 minus volume at baseline)*100/volume at baseline.
Time Frame	Baseline, Month 12
Safety Issue?	No

Analysis Population Description

The modified intent-to-treat (mITT) analysis set included all participants from the ITT analysis set who had at least 1 post-treatment magnetic resonance imaging assessment. "N" (number of participants analyzed) signifies the participants who were evaluable for this outcome measure.

Reporting Groups

	Description
Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) was be administered at a dose of 10 microgram (mcg) as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) was administered at a dose of 30 mcg as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 100 mcg	Sprifermin (AS902330) was administered at a dose of 100 mcg as intra-articular injection once every week for 3 consecutive weeks.
Placebo	Placebo matched to sprifermin (AS902330) was administered as intra-articular injection once every week for 3 consecutive weeks.

Measured Values

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
Number of Participants Analyzed	16	14	15	16
Percent Change From Baseline in Cartilage Defect Volume at Month 12 [units: Percent change] Mean (Standard Deviation)	-14.4 (27.17)	-17.8 (29.24)	-12.0 (34.80)	-17.0 (26.65)

2. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline in Cartilage Defect Volume and Cartilage Defect Thickness in the Target Knee at Months 3 and 6
Measure Description	Percent change in cartilage defect volume and cartilage defect thickness at Months 3 and 6 based on central MRI was calculated as: ([volume or thickness at Months 3 and 6 minus volume or thickness at baseline, respectively]*100)/ volume or thickness at baseline.
Time Frame	Baseline, Months 3 and 6
Safety Issue?	No

Analysis Population Description

The mITT analysis set included all participants from the ITT analysis set who had at least 1 post-treatment magnetic resonance imaging assessment. "n" signifies the participants who were evaluable for this outcome measure for each group, respectively.

Reporting Groups

	Description
AS902330 10 mcg	AS902330 was administered at a dose of 10 microgram (mcg) as intra-articular injection once every week for 3 consecutive weeks.
AS902330 30 mcg	AS902330 was administered at a dose of 30 mcg as intra-articular injection once every week for 3 consecutive weeks.
AS902330 100 mcg	AS902330 was administered at a dose of 100 mcg as intra-articular injection once every week for 3 consecutive weeks.
Placebo	Placebo matched to sprifermin AS902330 was administered as intra-articular injection once every week for 3 consecutive weeks.

Measured Values

	AS902330 10 mcg	AS902330 30 mcg	AS902330 100 mcg	Placebo
Number of Participants Analyzed	19	16	17	17
Percent Change From Baseline in Cartilage Defect Volume and Cartilage Defect Thickness in the Target Knee at Months 3 and 6 [units: Percent change] Mean (Standard Deviation)				
Volume: Month 3 (n=18, 16, 17, 17)	3.097 (24.7727)	-1.596 (22.6831)	-2.054 (28.3639)	-3.307 (12.3879)
Volume: Month 6 (n=17, 15, 17, 16)	0.922 (28.8298)	-11.118 (32.3251)	-7.518 (32.6967)	-6.792 (27.8652)
Thickness: Month 3 (n=18, 16, 17, 17)	3.126 (9.7969)	-1.969 (9.2075)	-1.327 (16.4475)	-0.810 (10.9976)
Thickness: Month 6 (n=17, 15, 17, 16)	3.461 (11.7686)	-3.184 (14.1109)	-5.439 (16.1866)	-3.106 (14.1901)

3. Secondary Outcome Measure:

Measure Title	Change From Baseline in Cartilage Defect Volume in the Target Knee at Months 3, 6 and 12
Measure Description	The change in cartilage defect volume at Months 3, 6 and 12 based on central MRI was calculated as volume at Months 3, 6 and 12 minus volume at baseline, respectively.
Time Frame	Baseline, Months 3, 6 and 12
Safety Issue?	No

Analysis Population Description

The mITT analysis set included all participants from the ITT analysis set who had at least 1 post-treatment magnetic resonance imaging assessment. "n" signifies the participants who were evaluable for this outcome measure for each group, respectively.

Reporting Groups

	Description
Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) was administered at a dose of 10 microgram (mcg) as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) was administered at a dose of 30 mcg as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 100 mcg	Sprifermin (AS902330) was administered at a dose of 100 mcg as intra-articular injection once every week for 3 consecutive weeks.

	Description
Placebo	Placebo matched to sprifermin (AS902330) was administered as intra-articular injection once every week for 3 consecutive weeks.

Measured Values

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
Number of Participants Analyzed	19	16	17	17
Change From Baseline in Cartilage Defect Volume in the Target Knee at Months 3, 6 and 12 [units: microliter] Mean (Standard Deviation)				
Baseline (n=19, 16, 17, 17)	130.689 (83.7032)	190.354 (130.5796)	158.125 (131.2277)	128.982 (116.9241)
Change at Month 3 (n=18, 16, 17, 17)	1.682 (30.2235)	-5.588 (21.5146)	-9.630 (40.2382)	-7.439 (13.7056)
Change at Month 6 (n=17, 15, 17, 16)	-0.540 (34.6432)	-29.830 (47.7638)	-23.469 (59.1138)	-14.511 (28.3908)
Change at Month 12 (n=16, 14, 15, 16)	-13.492 (40.8876)	-35.800 (37.0570)	-39.658 (80.5121)	-25.188 (36.1098)

4. Secondary Outcome Measure:

Measure Title	Change From Baseline in Cartilage Defect Thickness in the Target Knee at Months 3, 6 and 12
Measure Description	The change in cartilage defect thickness at Months 3, 6 and 12 based on central MRI was calculated as thickness at Months 3, 6 and 12 minus thickness at baseline, respectively.
Time Frame	Baseline, Months 3, 6 and 12
Safety Issue?	No

Analysis Population Description

The modified intent-to-treat (mITT) analysis set included all participants from the ITT analysis set who had at least 1 post-treatment magnetic resonance imaging assessment. "n" signifies the participants who were evaluable for this outcome measure for each group, respectively.

Reporting Groups

	Description
Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) was administered at a dose of 10 microgram (mcg) as intra-articular injection once every week for 3 consecutive weeks.

	Description
Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) was administered at a dose of 30 mcg as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 100 mcg	Sprifermin (AS902330) was administered at a dose of 100 mcg as intra-articular injection once every week for 3 consecutive weeks.
Placebo	Placebo matched to sprifermin (AS902330) was administered as intra-articular injection once every week for 3 consecutive weeks.

Measured Values

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
Number of Participants Analyzed	19	16	17	17
Change From Baseline in Cartilage Defect Thickness in the Target Knee at Months 3, 6 and 12 [units: millimeter] Mean (Standard Deviation)				
Baseline (n=19, 16, 17, 17)	1.598 (0.5550)	1.903 (0.5685)	1.758 (0.4901)	1.641 (0.5625)
Change at Month 3 (n=18, 16, 17, 17)	0.028 (0.1441)	-0.029 (0.1847)	-0.046 (0.2544)	-0.005 (0.1633)
Change at Month 6 (n=17, 15, 17, 16)	0.041 (0.1873)	-0.066 (0.2887)	-0.131 (0.2441)	-0.043 (0.2088)
Change at Month 12 (n=16, 14, 15, 16)	-0.058 (0.2648)	-0.101 (0.2318)	-0.176 (0.3274)	-0.179 (0.1661)

5. Secondary Outcome Measure:

Measure Title	Number of Participants With Response to Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) Sub-scales
Measure Description	MOCART scoring system (comprising 9 variables) was used to describe the morphology & signal intensity of the repair tissue following MRI -degree of defect repair [DDR] score 0 (subchondral bone exposed) to 20 (complete repair); integration to the border zone [IBZ] score 0 (> 50% of length of repair tissue) to 15 (complete integration to border zone);surface of repair tissue [SRT] score 0 (>50% surface repair tissue/total degradation) to 10(surface intact);structure of repair tissue [StRT] score 0(inhomogenous/cleft formation) to 5 (homogenous);signal intensity [T2] Mapping Sequence [T2MS] and Hi-Res Sagittal Pharmacodynamic Sequence [Hi-Res SPS] score 0 (marked hyper intense for T2MS and hypo intense for Hi-Res SPS) to 15 (iso intense); subchondral lamina,subchondral bone score 0 (not impact) to 5 (intact);adhesions & effusion score 0 (yes) and 5 (no). Higher values represent more favorable outcome of repair.
Time Frame	Months 3 (M3), 6 (M6) and 12 (M12)

Safety Issue?	No

Analysis Population Description

The mITT analysis set included all participants from the ITT analysis set who had at least 1 post-treatment magnetic resonance imaging assessment. "n" signifies the participants who were evaluable for this outcome measure for each group, respectively.

Reporting Groups

	Description
Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) was administered at a dose of 10 microgram (mcg) as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) was administered at a dose of 30 mcg as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 100 mcg	Sprifermin (AS902330) was administered at a dose of 100 mcg as intra-articular injection once every week for 3 consecutive weeks.
Placebo	Placebo matched to sprifermin (AS902330) was administered as intra-articular injection once every week for 3 consecutive weeks.

Measured Values

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
Number of Participants Analyzed	19	16	17	17
Number of Participants With Response to Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) Sub-scales [units: participants]				
M3, DDR, Complete (n=4, 4, 3, 6)	0	1	0	0
M3, DDR, Hypertrophy (n=4, 4, 3, 6)	0	0	0	0
M3, DDR, incomplete >50% (n=4, 4, 3, 6)	1	1	2	1
M3, DDR, incomplete<50% (n=4, 4, 3, 6)	3	2	1	5
M3, DDR, subchondral bone exposed (n=4, 4, 3, 6)	0	0	0	0
M6, DDR, Complete (n=3, 5, 3, 6)	0	1	0	0
M6, DDR, Hypertrophy (n=3, 5, 3, 6)	0	0	0	0
M6, DDR, incomplete >50% (n=3, 5, 3, 6)	1	1	2	0
M6, DDR, incomplete<50% (n=3, 5, 3, 6)	2	3	1	6

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
M6, DDR, subchondral bone exposed (n=3, 5, 3, 6)	0	0	0	0
M12, DDR, Complete (n=4, 8, 2, 5)	0	1	0	0
M12, DDR, Hypertrophy (n=4, 8, 2, 5)	0	0	0	0
M12, DDR, incomplete >50% (n=4, 8, 2, 5)	3	1	1	0
M12, DDR, incomplete<50% (n=4, 8, 2, 5)	1	6	1	5
M12, DDR, subchondral bone exposed (n=4, 8, 2, 5)	0	0	0	0
M3, IBZ, Complete (n=1, 1, 0, 2)	1	1	0	2
M3, IBZ, Incomplete (split-like) (n=1, 1, 0, 2)	0	0	0	0
M3,IBZ,Defect visible<50% repair tissue(n=1,1,0,2)	0	0	0	0
M3,IBZ,Defect visible>50% repair tissue(n=1,1,0,2)	0	0	0	0
M6, IBZ, Complete (n=1, 2, 0, 2)	1	2	0	2
M6, IBZ, Incomplete (split-like) (n=1, 2, 0, 2)	0	0	0	0
M6,IBZ,Defect visible<50% repair tissue(n=1,2,0,2)	0	0	0	0
M6,IBZ,Defect visible>50% repair tissue(n=1,2,0,2)	0	0	0	0
M12, IBZ, Complete (n=1, 2, 0, 1)	1	2	0	1
M12, IBZ, Incomplete (split-like) (n=1, 2, 0, 1)	0	0	0	0
M12,IBZ,Defect visible<50% repair tissue(n=1,2,0,1	0	0	0	0
M12,IBZ,Defect visible>50% repair tissue(n=1,2,0,1	0	0	0	0
M3, SRT, surface intact (n=1, 1, 0, 2)	1	1	0	2
M3, SRT, surface damaged < 50% (n=1, 1, 0, 2)	0	0	0	0
M3, SRT, surface damaged > 50% (n=1, 1, 0, 2)	0	0	0	0
M6, SRT, surface intact (n=1, 2, 0, 2)	1	2	0	2
M6, SRT, surface damaged <50% (n=1, 2, 0, 2)	0	0	0	0
M6, SRT, surface damaged > 50% (n=1, 2, 0, 2)	0	0	0	0
M12, SRT, surface intact (n=1, 2, 0, 1)	1	2	0	1
M12, SRT, surface damaged <50% (n=1, 2, 0, 1)	0	0	0	0

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
M12, SRT, surface damaged > 50% (n=1, 2, 0, 1)	0	0	0	0
M3, StRT, Homogeneous (n=4, 3, 0, 4)	4	3	0	4
M3, StRT, Inhomogenous (n=4, 3, 0, 4)	0	0	0	0
M6, StRT, Homogeneous (n=3, 4, 0, 3)	3	3	0	3
M6, StRT, Inhomogenous (n=3, 4, 0, 3)	0	1	0	0
M12, StRT, Homogeneous (n=3, 4, 0, 2)	3	3	0	2
M12, StRT, Inhomogenous(n=3, 4, 0, 2)	0	1	0	0
M3, T2MS, Isointense (n=5, 4, 3, 6)	5	4	3	6
M3, T2MS, Moderately hyperintense (n=5, 4, 3, 6)	0	0	0	0
M3, T2MS, Markedly hyperintense (n=5, 4, 3, 6)	0	0	0	0
M6, T2MS, Isointense (n=4, 5, 3, 6)	4	5	3	6
M6, T2MS, Moderately hyperintense (n=4, 5, 3, 6)	0	0	0	0
M6, T2MS, Markedly hyperintense (n=4, 5, 3, 6)	0	0	0	0
M12, T2MS, Isointense (n=4, 8, 2, 5)	4	8	2	5
M12, T2MS, Moderately hyperintense (n=4, 8, 2, 5)	0	0	0	0
M12, T2MS, Markedly hyperintense (n=4, 8, 2, 5)	0	0	0	0
M3, Hi-Res SPS, Isointense (n=5, 4, 3, 6)	5	4	3	6
M3, Hi-Res, Moderately hypointense (n=5, 4, 3, 6)	0	0	0	0
M3, Hi-Res, Markedly hypointense (n=5, 4, 3, 6)	0	0	0	0
M6, Hi-Res SPS, Isointense (n=4, 5, 3, 6)	4	4	3	6
M6, Hi-Res, Moderately hypointense (n=4, 5, 3, 6)	0	1	0	0
M6, Hi-Res, Markedly hypointense (n=4, 5, 3, 6)	0	0	0	0
M12, Hi-Res SPS, Isointense (n=4, 8, 2, 5)	4	6	1	5
M12, Hi-Res, Moderately hypointense (n=4, 8, 2, 5)	0	2	1	0
M12, Hi-Res, Markedly hypointense (n=4, 8, 2, 5)	0	0	0	0
M3, Subchondral Lamina Intact (n=17, 16, 17, 17)	17	16	17	17

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
M3, Subchondral Lamina Not Intact (n=17,16,17,17)	0	0	0	0
M6, Subchondral Lamina Intact (n=16, 15, 17, 16)	16	15	17	16
M6, Subchondral Lamina Not Intact (n=16,15,17,16)	0	0	0	0
M12, Subchondral Lamina Intact (n=15, 14, 15, 16)	15	14	15	16
M12,Subchondral Lamina Not Intact (n=15,14,15,16)	0	0	0	0
M3, Subchondral bone Intact (n=18, 16, 17, 17)	16	16	17	17
M3, Subchondral bone Not Intact (n=18, 16, 17, 17)	2	0	0	0
M6, Subchondral bone Intact (n=17, 15, 17, 16)	14	15	16	15
M6, Subchondral bone Not Intact (n=17, 15, 17, 16)	3	0	1	1
M12, Subchondral bone Intact (n=16, 14, 15, 16)	12	13	14	16
M12, Subchondral bone Not Intact (n=16, 14, 15, 16	4	1	1	0
M3, Adhesions-No (n=2, 3, 1, 2)	2	3	1	2
M3, Adhesions-Yes (n=2, 3, 1, 2)	0	0	0	0
M6, Adhesions-No (n=3, 3, 1, 3)	3	3	1	3
M6, Adhesions-Yes (n=3, 3, 1, 3)	0	0	0	0
M12, Adhesions-No (n=2, 5, 1, 2)	2	5	1	2
M12, Adhesions-Yes (n=2, 5, 1, 2)	0	0	0	0
M3, Effusion-No (n=18, 16, 17, 17)	5	2	1	3
M3, Effusion-Yes (n=18, 16, 17, 17)	13	14	16	14
M6, Effusion-No (n=17, 15, 17, 16)	4	2	3	4
M6, Effusion-Yes (n=17, 15, 17, 16)	13	13	14	12
M12, Effusion-No (n=16, 14, 15, 16)	3	4	1	3
M12, Effusion-Yes (n=16, 14, 15, 16)	13	10	14	13

6. Secondary Outcome Measure:

Measure Title	Change From Baseline in Boston Leeds Osteoarthritis Knee Score (BLOKS) Sub-scale (Bone Marrow Lesion [BML] Size, Osteophyte Size, Meniscal Extrusion Score [MES], and Meniscal Tear Score [MTS]) Scores at Month 12
Measure Description	The BLOKS scoring system assesses intra-articular regions within the knee according to the following features: BML size, cartilage 1, osteophyte size, synovitis, effusion, meniscal extrusion, and meniscal tear. Change from baseline in summary scores for BML size, osteophyte size, MES, and MTS were reported. Summary scores for BML size range from 0 to 27, for osteophyte size range from 0 to 36, for MES range from 0 to 12, and for MTS range from 0 to 32, with lower scores corresponding to favorable outcomes.
Time Frame	Baseline, Month 12
Safety Issue?	No

Analysis Population Description

The mITT analysis set included all participants from the ITT analysis set who had at least 1 post-treatment magnetic resonance imaging assessment. "n" signifies the participants who were evaluable for this outcome measure for each group, respectively.

Reporting Groups

	Description
Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) was administered at a dose of 10 microgram (mcg) as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) was administered at a dose of 30 mcg as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 100 mcg	Sprifermin (AS902330) was administered at a dose of 100 mcg as intra-articular injection once every week for 3 consecutive weeks.
Placebo	Placebo matched to sprifermin (AS902330) was administered as intra-articular injection once every week for 3 consecutive weeks.

Measured Values

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
Number of Participants Analyzed	19	16	17	17
Change From Baseline in Boston Leeds Osteoarthritis Knee Score (BLOKS) Sub-scale (Bone Marrow Lesion [BML] Size, Osteophyte Size, Meniscal Extrusion Score [MES], and Meniscal Tear Score [MTS]) Scores at Month 12 [units: units on a scale]				

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
Mean (Standard Deviation)				
BML: Baseline (n=19, 16, 17, 17)	1.68 (2.262)	1.75 (2.933)	1.24 (1.348)	1.94 (2.512)
BML: Change at Month 12(n=16, 14, 15, 16)	-0.69 (2.089)	-1.07 (3.149)	-0.27 (1.033)	-0.88 (1.455)
Osteophyte: Baseline (n=19, 16, 17, 17)	0.37 (0.831)	0.00 (0.000)	0.88 (1.799)	0.24 (0.664)
Osteophyte: Change at Month12 (n=16, 14, 15, 16)	-0.06 (0.250)	0.07 (0.267)	0.47 (0.990)	0.06 (0.250)
MES: Baseline (n=19, 16, 17, 17)	0.26 (0.452)	0.25 (0.577)	0.47 (0.800)	0.24 (0.562)
MES: Change at Month 12 (n=16, 14, 15, 16)	0.13 (0.342)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)
MTS: Baseline (n=19, 16, 17, 17)	1.05 (1.508)	0.38 (0.719)	0.88 (1.219)	0.53 (0.800)
MTS: Change at Month 12 (n=16, 14, 15, 16)	0.13 (0.500)	0.00 (0.00)	0.00 (0.00)	0.00 (0.365)

7. Secondary Outcome Measure:

Measure Title	Number of Participants With Shift From Baseline in BLOKS Sub-Scales (Cartilage 1, Synovitis, Effusion) Scores at Month 12
Measure Description	The BLOKS scoring system assesses intra-articular regions within the knee according to the following features: BML size, cartilage 1, osteophyte size, synovitis, effusion, meniscal extrusion, and meniscal tear. Total number of participants with shift from baseline in various BLOKS sub-scales (cartilage 1 [patella medial, patella lateral, femur medial trochlea, femur lateral trochlea, medial weight bearing femur, lateral weight bearing femur, tibia medial, tibia lateral], synovitis, and effusion) scores at Month 12 were reported.
Time Frame	Month 12
Safety Issue?	No

Analysis Population Description

The mITT analysis set included all participants from the ITT analysis set who had at least 1 post-treatment magnetic resonance imaging assessment.

Reporting Groups

	Description
Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) was administered at a dose of 10 microgram (mcg) as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) was administered at a dose of 30 mcg as intra-articular injection once every week for 3 consecutive weeks.

	Description
Sprifermin (AS902330) 100 mcg	Sprifermin (AS902330) was administered at a dose of 100 mcg as intra-articular injection once every week for 3 consecutive weeks.
Placebo	Placebo matched to sprifermin (AS902330) was administered as intra-articular injection once every week for 3 consecutive weeks.

Measured Values

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
Number of Participants Analyzed	19	16	17	17
Number of Participants With Shift From Baseline in BLOKS Sub-Scales (Cartilage 1, Synovitis, Effusion) Scores at Month 12 [units: participants]				
Cartilage 1 patella medial	3	1	0	3
Cartilage 1 patella lateral	3	1	3	3
Cartilage 1 femur medial trochlea	2	1	1	1
Cartilage 1 femur lateral trochlea	3	0	1	1
Cartilage 1 medial weight bearing femur	9	4	2	3
Cartilage 1 lateral weight bearing femur	2	3	2	2
Cartilage 1 tibia medial	0	0	1	1
Cartilage 1 tibia lateral	0	2	2	0
Synovitis	0	1	0	0
Effusion	13	11	13	8

8. Secondary Outcome Measure:

Measure Title	Number of Participants With Change From Baseline in International Cartilage Repair Society (ICRS) Grade at Months 6 and 12
Measure Description	The ICRS grading is used to score the amount of cartilage repair and damage. The grades range from 1 to 4 where higher grades indicate more severity of injury. Number of participants with change value of -3, -2, -1, 0, 1, and 2 from baseline in ICRS grade at Months 6 and 12 were reported. Lower change value indicates less severity of injury.

Time Frame	Baseline, Months 6 and 12
Safety Issue?	No

Analysis Population Description

The mITT analysis set included all participants from the ITT analysis set who had at least 1 post-treatment magnetic resonance imaging assessment. "n" signifies the participants who were evaluable for this outcome measure for each group, respectively.

Reporting Groups

	Description
Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) was administered at a dose of 10 microgram (mcg) as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) was administered at a dose of 30 mcg as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 100 mcg	Sprifermin (AS902330) was administered at a dose of 100 mcg as intra-articular injection once every week for 3 consecutive weeks.
Placebo	Placebo matched to sprifermin (AS902330) was administered as intra-articular injection once every week for 3 consecutive weeks.

Measured Values

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
Number of Participants Analyzed	19	16	17	17
Number of Participants With Change From Baseline in International Cartilage Repair Society (ICRS) Grade at Months 6 and 12 [units: participants]				
Month 6: Change value of -3 (n=17, 15, 17, 16)	0	0	0	0
Month 6: Change value of -2 (n=17, 15, 17, 16)	0	3	1	0
Month 6: Change value of -1 (n=17, 15, 17, 16)	1	6	3	5
Month 6: Change value of 0 (n=17, 15, 17, 16)	13	5	11	10
Month 6: Change value of 1 (n=17, 15, 17, 16)	3	0	1	1
Month 6: Change value of 2 (n=17, 15, 17, 16)	0	1	1	0
Month 12: Change value of -3 (n=16, 14, 15, 16)	0	1	0	0
Month 12: Change value of -2 (n=16, 14, 15, 16)	0	1	1	0

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
Month 12: Change value of -1 (n=16, 14, 15, 16)	2	5	3	4
Month 12: Change value of 0 (n=16, 14, 15, 16)	12	6	9	11
Month 12: Change value of 1 (n=16, 14, 15, 16)	2	0	2	1
Month 12: Change value of 2 (n=16, 14, 15, 16)	0	1	0	0

9. Secondary Outcome Measure:

Measure Title	Change From Baseline in Knee Injury and Osteoarthritis Outcome Score (KOOS) Sub-scale Scores and International Knee Documentation Committee (IKDC) Score at Months 3, 6 and 12
Measure Description	The KOOS is a knee-specific self-administered questionnaire that assesses symptoms and problems associated with knee injury and osteoarthritis. It consists of 42 items grouped into 5 sub-scales: symptoms, pain, function in daily living (FDL), function in sports and recreation activities (FSRA), and quality of life (QoL). Sub-scale scores range from 0-100, with 0 representing extreme knee problems and 100 no knee problems. The IKDC consists of 19 items to summarize symptoms such as highest level of activity without significant pain, frequency and severity of pain scales, stiffness and swelling, highest levels of activity without significant swelling or giving way, knee lock or catch, highest level of activity that can be performed on a regular basis, effect of knee on ability to perform set tasks, knee function prior to injury, and current knee function. The IKDC scores range from 0-100 where high score represents high levels of function.
Time Frame	Baseline, Months 3, 6 and 12
Safety Issue?	No

Analysis Population Description

The mITT analysis set included all participants from the ITT analysis set who had at least 1 post-treatment magnetic resonance imaging assessment. "n" signifies the participants who were evaluable for this outcome measure for each group, respectively.

Reporting Groups

	Description
Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) was administered at a dose of 10 microgram (mcg) as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) was administered at a dose of 30 mcg as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 100 mcg	Sprifermin (AS902330) was administered at a dose of 100 mcg as intra-articular injection once every week for 3 consecutive weeks.

	Description
Placebo	Placebo matched to sprifermin (AS902330) was administered as intra-articular injection once every week for 3 consecutive weeks.

Measured Values

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
Number of Participants Analyzed	19	16	17	17
Change From Baseline in Knee Injury and Osteoarthritis Outcome Score (KOOS) Sub-scale Scores and International Knee Documentation Committee (IKDC) Score at Months 3, 6 and 12 [units: units on a scale] Mean (Standard Deviation)				
KOOS Symptoms: Baseline (n=19, 16, 17, 17)	68.80 (16.955)	67.63 (20.432)	59.66 (17.024)	67.65 (21.297)
KOOS Symptoms:Change at Month 3(n=19, 16, 17, 17)	14.10 (16.940)	12.95 (20.982)	21.01 (13.236)	17.02 (23.095)
KOOS Symptoms: Change at Month 6(n=18, 16, 17, 17)	17.26 (18.385)	17.19 (16.864)	26.47 (11.012)	22.27 (23.975)
KOOS Symptoms: Change at Month 12(n=17, 14, 16,16)	12.61 (20.208)	17.86 (17.994)	29.91 (14.219)	26.12 (23.464)
KOOS Pain: Baseline (n=19, 16, 17, 17)	65.20 (19.074)	67.01 (23.282)	56.70 (20.672)	65.20 (22.569)
KOOS Pain: Change at Month 3 (n=19, 16, 17, 17)	16.23 (19.162)	18.75 (18.799)	24.02 (20.197)	24.02 (25.852)
KOOS Pain: Change at Month 6 (n=18,16,17,17)	19.44 (21.810)	22.40 (19.496)	26.63 (16.169)	27.29 (25.839)
KOOS Pain: Change at Month 12 (n=17, 14, 16, 16)	16.99 (21.603)	18.06 (19.543)	31.60 (14.868)	28.47 (24.163)
KOOS FDL: Baseline (n=19, 16, 17, 17)	69.89 (18.053)	74.17 (19.969)	64.01 (20.694)	73.83 (24.326)
KOOS FDL: Change at Month 3 (n=19, 16, 17, 17)	16.95 (18.630)	14.25 (15.809)	21.80 (19.302)	20.80 (25.123)
KOOS FDL: Change at Month 6 (n=18, 16, 17, 17)	18.14 (18.690)	17.56 (16.883)	25.09 (15.637)	23.05 (25.792)
KOOS FDL: Change at Month 12 (n=17, 14, 16, 16)	16.70 (20.370)	14.92 (19.199)	28.22 (16.183)	24.75 (25.689)
KOOS FSRA: Baseline (n=18, 16, 17, 16)	38.06 (24.920)	46.25 (23.488)	38.82 (18.416)	39.38 (25.747)
KOOS FSRA: Change at Month 3 (n=18, 16, 17, 16)	22.78 (27.074)	25.94 (22.746)	27.06 (25.924)	38.44 (28.619)
KOOS FSRA: Change at Month 6 (n=17, 16, 17, 16)	27.94 (26.224)	32.19 (23.307)	31.47 (23.767)	42.81 (29.550)

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
KOOS FSRA: Change at Month 12 (n=16, 14, 16, 15)	24.38 (28.336)	32.05 (30.070)	40.94 (21.926)	50.33 (29.669)
KOOS QoL: Baseline (n=19, 16, 17, 17)	41.45 (25.277)	41.41 (14.591)	34.19 (15.643)	40.07 (19.398)
KOOS QoL: Change at Month 3 (n=19, 16, 17, 17)	9.54 (24.149)	17.19 (18.042)	16.54 (23.064)	23.16 (25.842)
KOOS QoL: Change at Month 6 (n=18, 16, 17, 17)	13.89 (26.129)	23.44 (20.091)	23.53 (17.888)	27.94 (28.821)
KOOS QoL: Change at Month 12 (n=17, 14, 16, 16)	12.13 (27.729)	16.52 (23.206)	29.69 (17.002)	41.41 (28.401)
IKDC Score: Baseline (n=19, 16, 17, 17)	52.753 (18.8009)	50.431 (12.1996)	46.045 (15.2838)	55.646 (19.0396)
IKDC Score: Change at Month 3 (n=19, 16, 16, 17)	16.999 (16.6813)	23.563 (13.5872)	25.790 (19.6412)	25.152 (20.1268)
IKDC Score: Change at Month 6 (n=18, 16, 17, 16)	21.711 (19.4701)	28.664 (15.2400)	30.494 (18.9965)	27.658 (22.8095)
IKDC Score: Change at Month 12 (n=17, 14, 16, 16)	20.284 (21.2408)	25.944 (17.6274)	31.787 (19.1616)	32.184 (23.3421)

10. Secondary Outcome Measure:

Measure Title	Number of Participants With Global Evaluation of Treatment Benefit
Measure Description	Participants were asked to evaluate and rate the treatment benefit as poor, fair, good, very good or excellent.
Time Frame	Months 3, 6 and 12
Safety Issue?	No

Analysis Population Description

The mITT analysis set included all participants from the ITT analysis set who had at least 1 post-treatment magnetic resonance imaging assessment. "n" signifies the participants who were evaluable for this outcome measure for each group, respectively.

Reporting Groups

	Description
Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) was administered at a dose of 10 microgram (mcg) as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) was administered at a dose of 30 mcg as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 100 mcg	Sprifermin (AS902330) was administered at a dose of 100 mcg as intra-articular injection once every week for 3 consecutive weeks.

	Description
Placebo	Placebo matched to sprifermin (AS902330) was administered as intra-articular injection once every week for 3 consecutive weeks.

Measured Values

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
Number of Participants Analyzed	19	16	17	17
Number of Participants With Global Evaluation of Treatment Benefit [units: participants]				
Poor: Month 3 (n= 19, 16, 17, 17)	1	1	0	1
Fair: Month 3 (n= 19, 16, 17, 17)	3	1	0	3
Good: Month 3 (n= 19, 16, 17, 17)	9	6	3	4
Very Good: Month 3 (n= 19, 16, 17, 17)	4	5	10	2
Excellent: Month 3 (n= 19, 16, 17, 17)	2	3	4	7
Poor: Month 6 (n= 18, 16, 17, 17)	0	0	0	1
Fair: Month 6 (n= 18, 16, 17, 17)	3	0	0	2
Good: Month 6 (n= 18, 16, 17, 17)	7	9	5	6
Very Good: Month 6 (n= 18, 16, 17, 17)	5	4	9	2
Excellent: Month 6 (n= 18, 16, 17, 17)	3	3	3	6
Poor: Month 12 (n= 17, 14, 16, 16)	0	0	0	0
Fair: Month 12 (n= 17, 14, 16, 16)	2	0	0	0
Good: Month 12 (n= 17, 14, 16, 16)	6	3	3	6
Very Good: Month 12 (n= 17, 14, 16, 16)	7	5	7	6
Excellent: Month 12 (n= 17, 14, 16, 16)	2	6	6	4

11. Secondary Outcome Measure:

Measure Title	Number of Participants With Treatment Emergent Adverse Events (TEAEs), Local TEAEs, Systemic TEAEs, TEAEs Leading to Discontinuation and Serious Adverse Events (SAEs)

Measure Description	An adverse event (AE) is defined as any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product, which does not necessarily have a causal relationship with this treatment. An SAE is an AE that resulted in any of the following outcomes: death; life threatening; persistent/significant disability/ incapacity; initial or prolonged inpatient hospitalization; congenital anomaly/birth defect. TEAEs are those AEs that either started or worsened in severity on or after the date of first dose of study drug and on or before Month 12. Local TEAEs are those only related to the target knee. Systemic TEAEs are those that are related to other parts of the body.
Time Frame	Baseline up to Month 12
Safety Issue?	Yes

Analysis Population Description

Safety analysis set included all participants who received at least 1 dose of trial treatment and who had at least 1 post injection safety assessment.

Reporting Groups

	Description
Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) was administered at a dose of 10 microgram (mcg) as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) was administered at a dose of 30 mcg as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 100 mcg	Sprifermin (AS902330) was administered at a dose of 100 mcg as intra-articular injection once every week for 3 consecutive weeks.
Placebo	Placebo matched to sprifermin (AS902330) was administered as intra-articular injection once every week for 3 consecutive weeks.

Measured Values

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
Number of Participants Analyzed	19	18	18	19
Number of Participants With Treatment Emergent Adverse Events (TEAEs), Local TEAEs, Systemic TEAEs, TEAEs Leading to Discontinuation and Serious Adverse Events (SAEs) [units: participants]				
TEAEs	10	11	12	14
Local TEAEs	9	8	11	11
Systemic TEAEs	6	7	5	7
TEAEs Leading to Discontinuation	0	0	0	1

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
SAEs	1	0	2	0

12. Secondary Outcome Measure:

Measure Title	Number of Participants With Acute Inflammatory Reactions
Measure Description	Acute inflammatory reaction (AIR) is defined as an increase of pain by 30 millimeter (mm) on a 100 mm visual analog scale (VAS) associated with a subject-reported synovial fluid effusion within 3 days following intra-articular injection.
Time Frame	Baseline up to Month 12
Safety Issue?	Yes

Analysis Population Description

Safety analysis set included all participants who received at least 1 dose of trial treatment and who had at least 1 post injection safety assessment.
"N" (number of participants analyzed) signifies the participants who were evaluable for this outcome measure.

Reporting Groups

	Description
Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) was administered at a dose of 10 microgram (mcg) as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) was administered at a dose of 30 mcg as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 100 mcg	Sprifermin (AS902330) was administered at a dose of 100 mcg as intra-articular injection once every week for 3 consecutive weeks.
Placebo	Placebo matched to sprifermin (AS902330) was administered as intra-articular injection once every week for 3 consecutive weeks.

Measured Values

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
Number of Participants Analyzed	14	14	15	12
Number of Participants With Acute Inflammatory Reactions [units: participants]	4	0	7	2

13. Secondary Outcome Measure:

Measure Title	Number of Participants With Binding Antibodies (BAbs) and Neutralizing Antibodies (NAbs) to Fibroblast Growth Factor 18 (FGF18)
Measure Description	Number of participants with BAbs and NAbs to FGF18 at Week 1 (pre-dose), Week 2 (pre-dose), Week 4, Months 3 and 12 were reported.
Time Frame	Week 1 (pre-dose), Week 2 (pre-dose), Week 4, Months 3 and 12
Safety Issue?	No

Analysis Population Description

Safety analysis set included all participants who received at least 1 dose of trial treatment and who had at least 1 post injection safety assessment.

Reporting Groups

	Description
Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) was administered at a dose of 10 microgram (mcg) as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) was administered at a dose of 30 mcg as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 100 mcg	Sprifermin (AS902330) was administered at a dose of 100 mcg as intra-articular injection once every week for 3 consecutive weeks.
Placebo	Placebo matched to sprifermin (AS902330) was administered as intra-articular injection once every week for 3 consecutive weeks.

Measured Values

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
Number of Participants Analyzed	19	18	18	19
Number of Participants With Binding Antibodies (BAbs) and Neutralizing Antibodies (NAbs) to Fibroblast Growth Factor 18 (FGF18) [units: participants]				
BAbs: Pre-dose Week 1	1	2	1	1
BAbs: Pre-dose Week 2	1	3	1	1
BAbs: Week 4	1	3	1	1

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
BAbs: Month 3	1	3	0	1
BAbs: Month 12	1	1	0	1
NAbs: Pre-dose Week 1	1	1	1	1
NAbs: Pre-dose Week 2	1	2	1	1
NAbs: Week 4	1	2	1	1
NAbs: Month 3	1	2	0	1
NAbs: Month 12	1	0	0	1

Reported Adverse Events

Time Frame	Baseline Up to Month 12
Additional Description	Safety analysis set included all participants who received at least 1 dose of trial treatment and who had at least 1 post injection safety assessment. One participant randomized to sprifermin (AS902330) 10 mcg group actually received placebo treatment, and therefore was included in placebo group for safety analysis.

Reporting Groups

	Description
Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) was administered at a dose of 10 microgram (mcg) as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) was administered at a dose of 30 mcg as intra-articular injection once every week for 3 consecutive weeks.
Sprifermin (AS902330) 100 mcg	Sprifermin (AS902330) was administered at a dose of 100 mcg as intra-articular injection once every week for 3 consecutive weeks.
Placebo	Placebo matched to sprifermin (AS902330) was administered as intra-articular injection once every week for 3 consecutive weeks.

Serious Adverse Events

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	1/19 (5.26%)	0/18 (0%)	2/18 (11.11%)	0/19 (0%)
Injury, poisoning and procedural complications				
Joint injury [A] *	0/19 (0%)	0/18 (0%)	1/18 (5.56%)	0/19 (0%)
Reproductive system and breast disorders				
Menorrhagia [A] *	1/19 (5.26%)	0/18 (0%)	0/18 (0%)	0/19 (0%)
Vascular disorders				
Hypertension [A] *	0/19 (0%)	0/18 (0%)	1/18 (5.56%)	0/19 (0%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA Version 15.1

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	10/19 (52.63%)	11/18 (61.11%)	13/18 (72.22%)	15/19 (78.95%)
Blood and lymphatic system disorders				
Lymphadenopathy [A] *	1/19 (5.26%)	0/18 (0%)	0/18 (0%)	0/19 (0%)
Cardiac disorders				
Tachycardia paroxysmal [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	0/19 (0%)
Ear and labyrinth disorders				
Ear pain [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	0/19 (0%)
Endocrine disorders				
Hypothyroidism [A] *	1/19 (5.26%)	0/18 (0%)	0/18 (0%)	0/19 (0%)
Eye disorders				

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Eye inflammation [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	0/19 (0%)
Gastrointestinal disorders				
Abdominal pain upper [A] *	1/19 (5.26%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)
Diarrhoea [A] *	1/19 (5.26%)	0/18 (0%)	1/18 (5.56%)	2/19 (10.53%)
Enteritis [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	0/19 (0%)
Gingival inflammation [A] *	1/19 (5.26%)	0/18 (0%)	0/18 (0%)	0/19 (0%)
Toothache [A] *	0/19 (0%)	1/18 (5.56%)	1/18 (5.56%)	0/19 (0%)
Vomiting [A] *	0/19 (0%)	0/18 (0%)	1/18 (5.56%)	0/19 (0%)
General disorders				
Fatigue [A] *	1/19 (5.26%)	0/18 (0%)	0/18 (0%)	0/19 (0%)
Inflammation [A] *	0/19 (0%)	0/18 (0%)	3/18 (16.67%)	0/19 (0%)
Injection site joint pain [A] *	0/19 (0%)	0/18 (0%)	1/18 (5.56%)	0/19 (0%)
Malaise [A] *	0/19 (0%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)
Mucosal inflammation [A] *	0/19 (0%)	0/18 (0%)	1/18 (5.56%)	0/19 (0%)
Pain [A] *	0/19 (0%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)
Hepatobiliary disorders				
Hepatic failure [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	0/19 (0%)
Hepatic steatosis [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	0/19 (0%)
Immune system disorders				
Seasonal allergy [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	0/19 (0%)
Infections and infestations				
Acute sinusitis [A] *	0/19 (0%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Bronchitis [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	0/19 (0%)
Cystitis [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	0/19 (0%)
Influenza [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	2/19 (10.53%)
Nasopharyngitis [A] *	3/19 (15.79%)	6/18 (33.33%)	4/18 (22.22%)	3/19 (15.79%)
Otitis externa [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	0/19 (0%)
Otitis media [A] *	0/19 (0%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)
Pharyngitis [A] *	0/19 (0%)	2/18 (11.11%)	0/18 (0%)	2/19 (10.53%)
Sinusitis [A] *	1/19 (5.26%)	0/18 (0%)	0/18 (0%)	0/19 (0%)
Tonsillitis [A] *	0/19 (0%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)
Tooth abscess [A] *	1/19 (5.26%)	0/18 (0%)	0/18 (0%)	0/19 (0%)
Tooth infection [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	0/19 (0%)
Upper respiratory tract infection [A] *	1/19 (5.26%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)
Injury, poisoning and procedural complications				
Arthropod sting [A] *	0/19 (0%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)
Excoriation [A] *	0/19 (0%)	0/18 (0%)	1/18 (5.56%)	0/19 (0%)
Femur fracture [A] *	1/19 (5.26%)	0/18 (0%)	0/18 (0%)	0/19 (0%)
Joint dislocation [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	0/19 (0%)
Joint injury [A] *	1/19 (5.26%)	1/18 (5.56%)	0/18 (0%)	1/19 (5.26%)
Ligament sprain [A] *	1/19 (5.26%)	0/18 (0%)	0/18 (0%)	0/19 (0%)
Limb injury [A] *	1/19 (5.26%)	0/18 (0%)	0/18 (0%)	0/19 (0%)
Meniscus injury [A] *	1/19 (5.26%)	0/18 (0%)	0/18 (0%)	0/19 (0%)

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Muscle injury [A] *	0/19 (0%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)
Muscle strain [A] *	1/19 (5.26%)	0/18 (0%)	0/18 (0%)	0/19 (0%)
Overdose [A] *	0/19 (0%)	0/18 (0%)	1/18 (5.56%)	0/19 (0%)
Procedural pain [A] *	0/19 (0%)	0/18 (0%)	1/18 (5.56%)	0/19 (0%)
Soft tissue injury [A] *	0/19 (0%)	1/18 (5.56%)	1/18 (5.56%)	0/19 (0%)
Traumatic haematoma [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	0/19 (0%)
Investigations				
Blood creatine increased [A] *	1/19 (5.26%)	0/18 (0%)	0/18 (0%)	0/19 (0%)
Blood creatine phosphokinase increased [A] *	2/19 (10.53%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)
Hepatic enzyme increased [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	0/19 (0%)
Lipase increased [A] *	0/19 (0%)	0/18 (0%)	1/18 (5.56%)	0/19 (0%)
Metabolism and nutrition disorders				
Gout [A] *	0/19 (0%)	0/18 (0%)	1/18 (5.56%)	0/19 (0%)
Hypercholesterolaemia [A] *	0/19 (0%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)
Hypertriglyceridaemia [A] *	0/19 (0%)	0/18 (0%)	1/18 (5.56%)	0/19 (0%)
Hypocalcaemia [A] *	0/19 (0%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)
Musculoskeletal and connective tissue disorders				
Arthralgia [A] *	3/19 (15.79%)	4/18 (22.22%)	5/18 (27.78%)	3/19 (15.79%)
Arthritis [A] *	0/19 (0%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)
Axillary mass [A] *	0/19 (0%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)
Back pain [A] *	1/19 (5.26%)	0/18 (0%)	1/18 (5.56%)	0/19 (0%)
Bursitis [A] *	0/19 (0%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Groin pain [A] *	1/19 (5.26%)	0/18 (0%)	0/18 (0%)	0/19 (0%)
Joint crepitation [A] *	2/19 (10.53%)	0/18 (0%)	0/18 (0%)	0/19 (0%)
Joint effusion [A] *	1/19 (5.26%)	0/18 (0%)	1/18 (5.56%)	0/19 (0%)
Joint swelling [A] *	0/19 (0%)	0/18 (0%)	2/18 (11.11%)	0/19 (0%)
Musculoskeletal chest pain [A] *	1/19 (5.26%)	0/18 (0%)	0/18 (0%)	0/19 (0%)
Musculoskeletal discomfort [A] *	0/19 (0%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)
Musculoskeletal pain [A] *	0/19 (0%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)
Myalgia [A] *	0/19 (0%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)
Neck pain [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	1/19 (5.26%)
Pain in extremity [A] *	0/19 (0%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)
Pain in jaw [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	0/19 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Neoplasm skin [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	0/19 (0%)
Nervous system disorders				
Carpal tunnel syndrome [A] *	0/19 (0%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)
Dizziness [A] *	1/19 (5.26%)	1/18 (5.56%)	0/18 (0%)	0/19 (0%)
Headache [A] *	3/19 (15.79%)	3/18 (16.67%)	0/18 (0%)	1/19 (5.26%)
Migraine [A] *	0/19 (0%)	0/18 (0%)	2/18 (11.11%)	0/19 (0%)
Psychiatric disorders				
Depression [A] *	1/19 (5.26%)	0/18 (0%)	0/18 (0%)	0/19 (0%)
Sleep disorder [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	0/19 (0%)
Renal and urinary disorders				

	Sprifermin (AS902330) 10 mcg	Sprifermin (AS902330) 30 mcg	Sprifermin (AS902330) 100 mcg	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Haematuria [A] *	1/19 (5.26%)	0/18 (0%)	1/18 (5.56%)	0/19 (0%)
Nephrolithiasis [A] *	0/19 (0%)	0/18 (0%)	0/18 (0%)	1/19 (5.26%)
Reproductive system and breast disorders				
Menorrhagia [A] *	0/19 (0%)	0/18 (0%)	0/18 (0%)	0/19 (0%)
Vaginal inflammation [A] *	0/19 (0%)	0/18 (0%)	1/18 (5.56%)	0/19 (0%)
Respiratory, thoracic and mediastinal disorders				
Oropharyngeal pain [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	0/19 (0%)
Rhinitis allergic [A] *	0/19 (0%)	0/18 (0%)	1/18 (5.56%)	0/19 (0%)
Skin and subcutaneous tissue disorders				
Pruritus [A] *	1/19 (5.26%)	0/18 (0%)	0/18 (0%)	0/19 (0%)
Pruritus generalised [A] *	1/19 (5.26%)	0/18 (0%)	0/18 (0%)	0/19 (0%)
Vascular disorders				
Hypertension [A] *	0/19 (0%)	1/18 (5.56%)	0/18 (0%)	0/19 (0%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA Version 15.1

Limitations and Caveats

The study was discontinued due to low recruitment.

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is less than or equal to 60 days from the time submitted to the sponsor for review. The sponsor can with reasonable grounds require changes to the communication which do not change the scientific statement or neutrality of the communication.

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