

Schedule of Events – Screening Period Through Week 16

	Screening Period	Pre-Randomization Period	Treatment								End of Treatment Period	Treatment Period Early Termination Visit
Study Week				1	2	4	8	12	16			
Study Day (visit window)	up to -37 to -8	-7 (+3) Pre-Rand Visit	1 Baseline	8 (±1)	16 (±3)	29 (±7)	57 (±7)	85 (±7)	113 (±7)			ET
Visit Number	1	2	3	Ph call 1	4	5	6	7	8			ET
Screening/Baseline:												
Informed Consent	X											
Inclusion/Exclusion	X	X	X									
Geriatrics sub-study informed consent ¹	X											
Medical History	X											
Medication History	X											
Demographics	X											
Height	X											
Bilateral radiograph of knees, hips and shoulders ²	X											
Lumbar spine MRI ³	X											
MRI of any knee or hip with baseline K-L ≥3 ²	X								X			X ⁴
NRS/EDiary training ⁵		X										
Assessment of peripheral or central pain	X											
painDETECT Questionnaire	X											
Randomization			X									
Treatment:												
SC Study Drug Injection ⁶			LOADING DOSE			X	X	X				
IV Study Drug Infusion ⁶			X				X					

FIG. 1A

Schedule of Events-Screening Period Through Week 16

11. In the event that a patient must undergo TJR surgery during the study, the patient will complete the early termination visit and the procedures outlined in the schedule of events for TJR follow-up. The early termination visit should be completed before TJR surgery if at all possible. TJR questionnaires are Knee Society Score questionnaire for knee replacements or Harris Hip Score questionnaire for hip replacements.
12. To be performed only if postmenopausal status has to be assessed for female patients ≤ 59 years of age.
13. In the event of a positive urine pregnancy test result, the patient must have a serum pregnancy test with a negative result in order to continue study participation. If the serum pregnancy test is positive, the patient must be withdrawn from study drug and should be asked to return to the clinic for all remaining study visits per the visit schedule.

FIG. 1D

Schedule of Events – Follow-up Period – Week 20 through Week 36

	Follow-up Period					End of Study	Follow-up Period Early Termination
	Week 20	Week 24	Week 28	Week 32	Week 36		
Study Week							
Study Day (visit window)	141(±7)	169(±7)	197(±7)	225(±7)	253(±7)		
Visit Number	9	Ph call 2	Ph call 3	Ph call 4	10		ET
Treatment:							
Concomitant Meds	X	X	X	X	X		X
Efficacy:							
LBPI NRS	X				X		X
Roland Morris Disability Questionnaire	X				X		X
Patient Global Assessment LBP	X				X		X
MOS Sleep Scale Survey	X				X		X
SF-36	X				X		X
EQ-5D-5L	X				X		X
Safety:							
Vital Signs ¹	X				X		X
Physical Examination					X		X
Electrocardiogram					X		X
Joint Pain Questionnaire	X				X		X
Orthostatic blood pressure	X				X		X
Survey of autonomic symptoms	X				X		X
Neurologic examination	BRIEF				FULL		FULL
Adverse Events	X	X	X	X	X		X
MRI of any knee or hip with baseline K-L ≥3 ²					X		X ³
Pre-op questionnaire (TJR) ³							X
Laboratory Testing:							
Hematology					X		X
Blood Chemistry					X		X
Pregnancy test (WOCBP)					SERUM		SERUM
PK/Drug Concentration and ADA Samples:							
PK/Drug conc. sample	X				X		X

FIG. 2A

Schedule of Events – Follow-up Period – Week 20 through Week 36									
ADA sample		X						X	X
Research serum/plasma sample								X	X
<div>1. If the pulse is less than 45 bpm, an ECG with rhythm strip will be obtained and sent to the central reader to confirm the heart rate and rhythm.</div> <div>2. Imaging assessments (X-rays of the knees, hips, and shoulders, and MRI) need to be repeated only if it has been >30 days since the joint was last imaged. If it has been <30 days since imaging assessments were completed, imaging assessments may be completed at the discretion of the investigator.</div> <div>3. In the event that a patient must undergo TJR surgery during the study, the patient will complete the early termination visit and the procedures outlined in the schedule of events for TJR follow-up. The early termination visit should be completed before TJR surgery if at all possible. TJR questionnaires are Knee Society Score questionnaire for knee replacements or Harris Hip Score questionnaire for hip replacements.</div>									

FIG. 2B

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Schedule of Events - Follow-up for Patients Who Undergo Total Joint Replacement Surgery

	Follow-up Period ¹	
	Post-Operative	Long-Term
Follow-up Study Day (Visit Window)	Follow-up Visit 1 4 weeks after the date of the joint replacement surgery	Follow-up Visit 2 20 weeks after the date of the joint replacement surgery
	F/U Day 29 (±7)	F/U Day 140 (±7)
Treatment:		
Concomitant medications	X	X
Safety:		
Vital signs	X	X
Physical examination with joint exam	X ¹	X
Joint pain questionnaire	X	X
Post-operative assessment questionnaire ²	X	X
Event-triggered imaging ³	X	X
MRI of any knee or hip with a baseline K-L ≥3		X

1. Relevant information related to the surgery should be collected, including placement of the prosthesis and healing of the surgical wound.
2. Formal post-operative assessment of joint replacements will be done by completing the Knee Society Score questionnaire for knee replacements or the Harris Hip Score questionnaire for hip replacements. Full details of these assessments are provided in the study reference manual.
3. Imaging may be performed on any joint following a report of clinically significant worsening or exacerbation of pain in that joint. In cases where the contralateral joint had previously been treated with TJR surgery, an MRI is not required.

FIG. 3

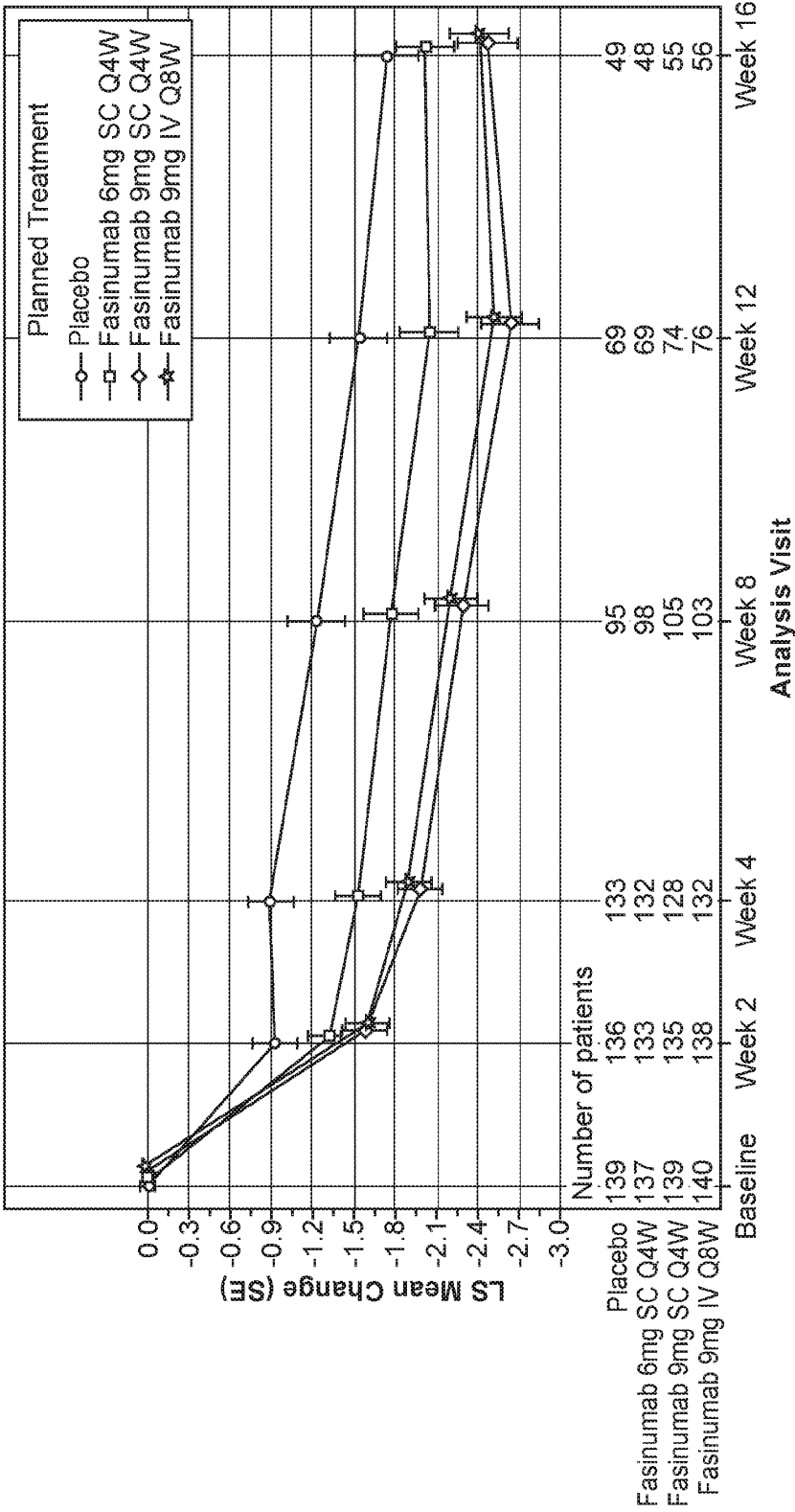


FIG. 4

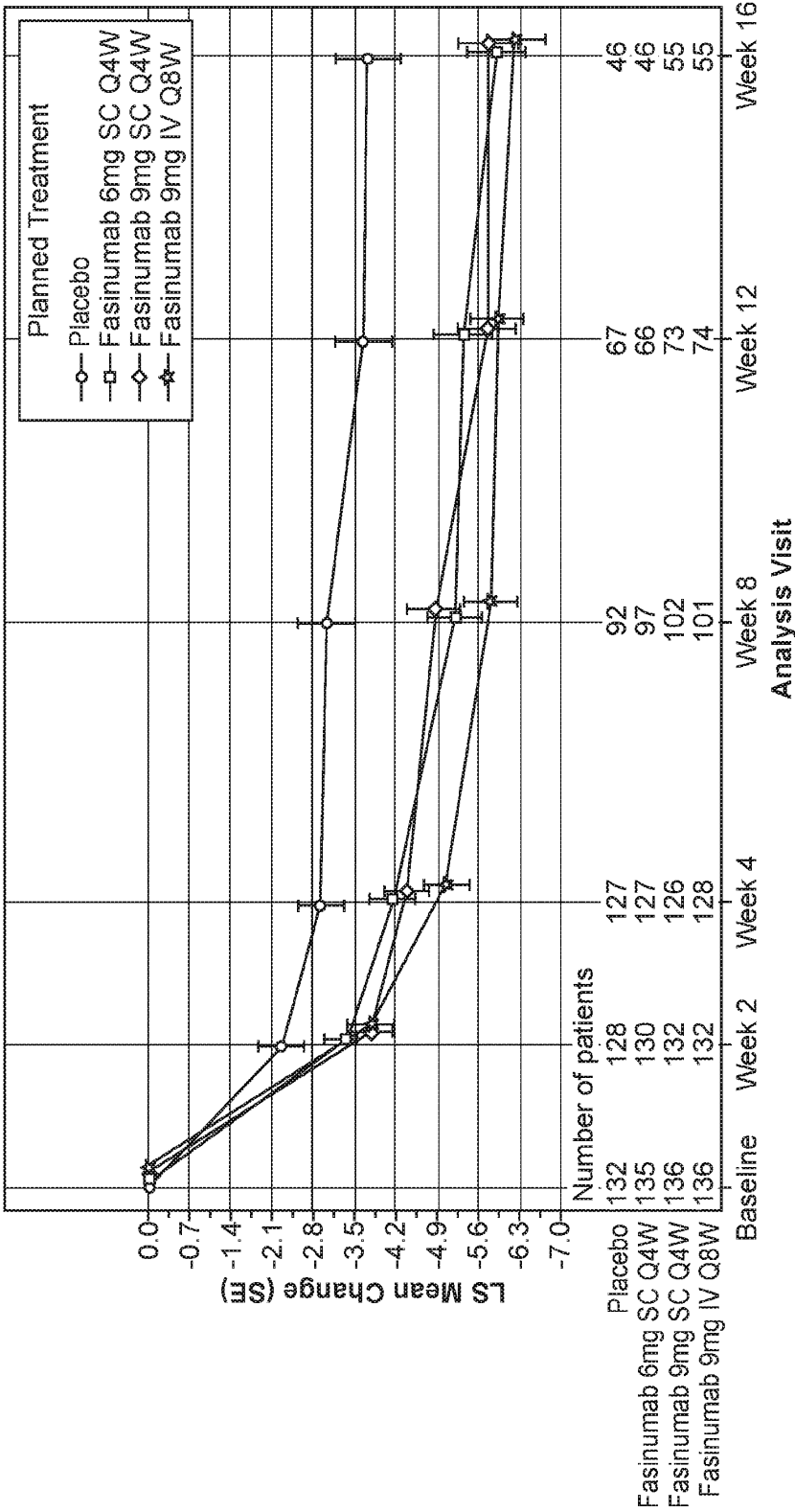


FIG. 5

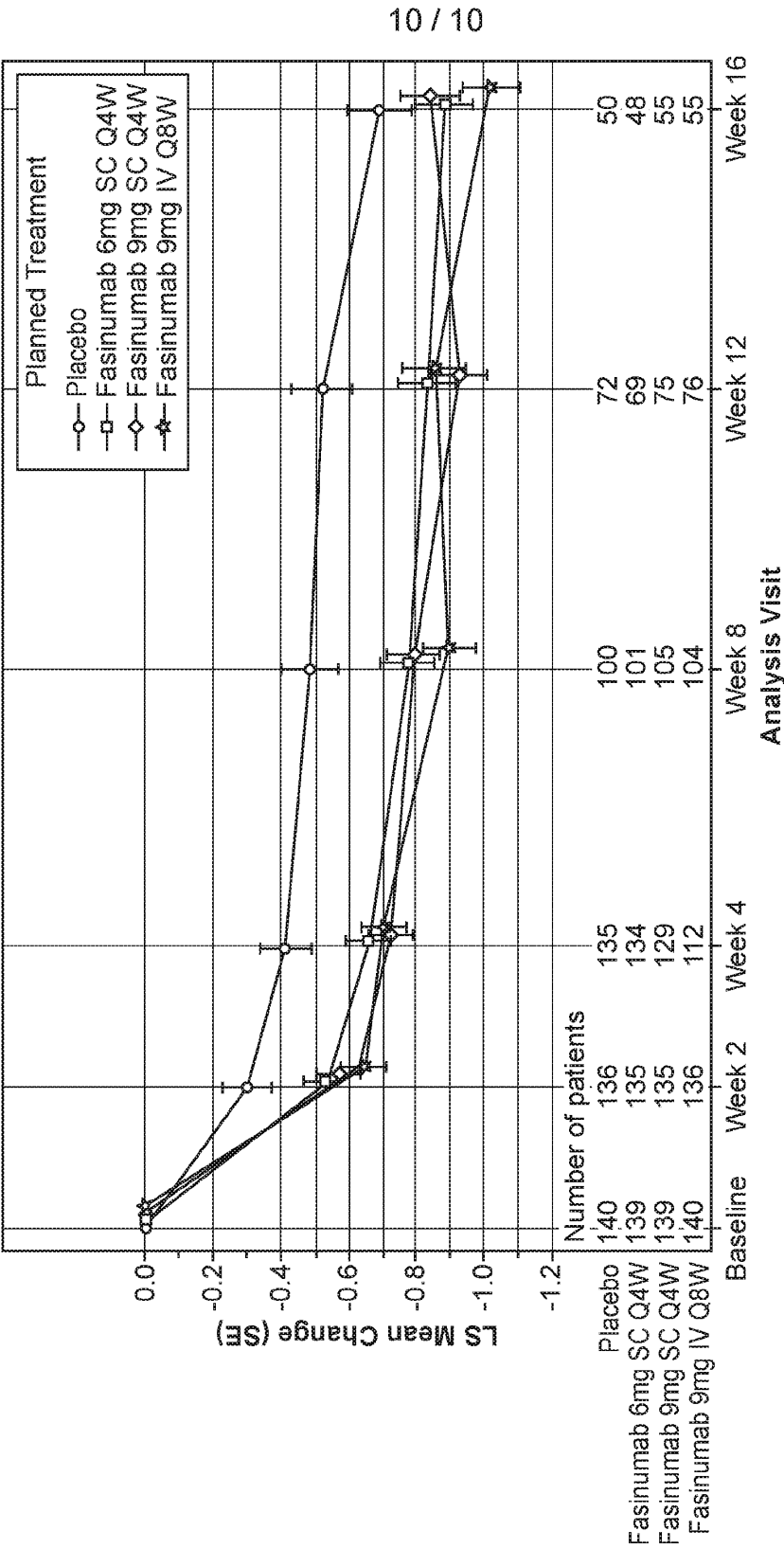


FIG. 6