Supplementary Table 1. Demographics and baseline characteristics

	Placebo N=8	ACE-536 Treatment (mg/kg)				Overall N=32
		0.0625 N=6	0.125 x 1 N=6	0.125 x 2 N=6	0.25 N=6	
Age (yr), mean (SD), range	58.6 (4.7) 55-69	59.3 (7.5) 49-69	57.7 (5.8) 52-68	60.5 (2.6) 56-64	61.0 (8.7) 50-71	59.4 (5.8) 49-71
Weight (kg), mean (SD)	65.3 (7.5)	71.3 (3.4)	70.5 (7.8)	68.8 (10.6)	69.2 (9.6)	68.8 (7.9)
Height (cm), mean (SD)	163.5 (5.5)	162.0 (6.1)	161.7 (7.6)	166.2 (5.3)	159.2 (6.8)	162.6 (6.2)
BMI (kg/m^2), mean (SD)	24.4 (2.3)	27.3 (3.3)	26.9 (2.2)	24.9 (3.0)	27.2 (2.9)	26.1 (3.0)
Hemoglobin, Screening, (g/dL), mean (SD)	13.1 (0.6)	13.3 (0.5)	13.3 (0.6)	13.1 (1.0)	13.6 (0.5)	13.3 (0.6)
Hemoglobin, Day -1, (g/dL), mean (SD)	13.1 (0.6)	13.2 (0.6)	13.3 (0.3)	13.1 (0.9)	13.2 (0.7)	13.2 (0.6)
Race, n (%)						
American Indian/Alaska Native	1 (13%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	2 (6%)
Black or African American	1 (13%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	2 (6%)
White	6 (75%)	4 (67%)	6 (100%)	6 (100%)	6 (100%)	28 (88%)
Ethnicity n (%)						
Hispanic or Latino	2 (25%)	0 (0%)	3 (50%)	0 (0%)	2 (33%)	7 (22%)
Non-Hispanic or Latino	6 (75%)	6 (100%)	3 (50%)	6 (100%)	4 (67%)	25 (78%)

Supplementary Table 2. Treatment-related adverse events by treatment group, n (%) of subjects

System Organ Class Preferred Term	ACE-536 (mg/kg)				Placebo N=8
	0.0625 N=6	0.125 x 1 N=6	0.125 x 2 N=6	0.25 N=6	
Musculoskeletal and Connective Tissue Disorders					
Myalgia	1 (17%)	-	-	-	-
Muscle spasms	-	-	1 (17%)	-	-
Skin and Subcutaneous Tissue Disorders					
Pruritus generalized	-	-	-	1 (17%)	-
Rash papular	-	-	-	1 (17%)	-
Dry skin	-	-	-	1 (17%)	-
Macule	-	-	1 (17%)	-	-
Nervous System Disorders					
Hyperesthesia		-	-	1(17%)	-
General Disorders and Administrative Site Conditions					
Injection site hemorrhage	1 (17%)	1 (17%)	-	1 (17%)	-
Injection site macule	-	-	1 (17%)	1 (17%)	-
Injection site pain	-	-	-	-	1 (13%)

Supplementary Table 3. Pharmacokinetic parameters for ACE-536 after administration of first SC dose by treatment group, mean (SD).

Parameter	ACE-536 (mg/kg)		
	0.0625 (N=6)	**0.125 (N=12)**	**0.25 (N=6)**
AUC_{0-14}, day*μg/mL	4.7 (1.1)	6.5 (3.2)	19.6 (4.3)
C_{max}, μg/mL[a]	0.4 (0.1)	0.6 (0.2)	1.9 (0.4)
T_{max}, days[a]	7.0 (2.9)	9.8 (2.6)	8.0 (3.2)
$t_{1/2}$, days	NC	16.2 (2.2) N=7	14.9 (1.6) N=5
Cl/F, mL/day/kg	NA	6.4 (3.4) N=7	4.6 (0.5) N=5
V_z/F, mL/kg	NA	142.5 (61.1) N=7	98.9 (17.2) N=5

NC = Not computable; NA = Not applicable

[a] compartmental analysis (otherwise, non-compartmental analysis)