Table S1. Baseline demographic characteristics and dialysis treatment history in REN-001 and REN-002

	REN-001				
		Sotatercept Dose (Subcutaneous)			
	Placebo n=11	0.3 mg/kg n=9	0.5 mg/kg n=8	0.7 mg/kg n=9	0.7/0.4 mg/kg n=6
Age, mean (SD), years	55.2 (12.57)	59.9 (12.86)	56.9 (12.76)	61.7 (13.44)	55.0 (15.86)
Sex, n (%)					
Male	7 (63.6)	3 (33.3)	7 (87.5)	2 (22.2)	5 (83.3)
Female	4 (36.4)	6 (66.7)	1 (12.5)	7 (77.8)	1 (16.7)
Dialysis					
Pre-dialysis weight, mean (SD), kg	83.6 (24.7)	81.3 (18.9)	82.2 (9.5)	82.8 (19.8)	84.1 (13.3)
Post-dialysis weight, mean (SD), kg	80.9 (23.9)	78.6 (18.4)	79.1 (8.5)	80.8 (19.3)	81.0 (13.4)

	REN-002					
	Sotatercept Administration Route and Dose					
	IV 0.1 mg/kg n=7	IV 0.2 mg/kg n=9	IV 0.1–0.4 mg/kg n=12	SC 0.13 mg/kg n=7	SC 0.26 mg/kg n=9	SC 0.4–0.5 mg/kg n=6
Age, years (SD)	59.1 (15.43)	59.4 (15.80)	61.4 (15.68)	62.3 (13.03)	61.9 (15.43)	53.7 (15.93)
Sex, n (%)						
Male	3 (42.9)	5 (55.6)	7 (58.3)	4 (57.1)	6 (66.7)	3 (50.0)
Female	4 (57.1)	4 (44.4)	5 (41.7)	3 (42.9)	3 (33.3)	3 (50.0)
Dialysis						
Pre-dialysis weight, mean (SD), kg	81.20 (21.53)	75.71 (14.75)	78.33 (15.22)	82.37 (17.33)	82.32 (21.41)	71.43 (15.71)
Post-dialysis weight, mean (SD), kg	78.73 (20.97)	73.84 (14.86)	76.21 (14.79)	79.93 (16.86)	80.42 (21.32)	69.15 (14.74)

Table S2. Concomitant phosphate binding use at baseline

Patients, n (%)	REN-001					
		Sotatercept Dose (Subcutaneous)				All Sotatercept N=32
	Placebo n=11	0.3 mg/kg n=9	0.5 mg/kg n=8	0.7 mg/kg n=9	0.7/0.4 mg/kg n=6	
Calcium-based phosphorus binders						
Calcium acetate	1 (9.1)	3 (33.3)	5 (62.5)	4 (44.4)	1 (16.7)	13 (40.6)
Calcium carbonate	3 (27.3)	1 (11.1)	2 (25.0)	1 (11.1)	1 (16.7)	5 (15.6)
Non-calcium phosphorus binders						
Lanthanum carbonate	1 (9.1)	0 (0.0)	1 (12.5)	0 (0.0)	0 (0.0)	1 (3.1)
Sevelamer	4 (36.4)	2 (22.2)	1 (12.5)	5 (55.6)	2 (33.3)	10 (31.3)
Sevelamer carbonate	6 (54.5)	4 (44.4)	3 (37.5)	1 (11.1)	2 (33.3)	10 (31.3)

Patients, n (%)	REN-002						
	Sotatercept Administration Route and Dose						
	IV 0.1 mg/kg n=7	IV 0.2 mg/kg n=9	IV 0.1–0.4 mg/kg n=12	SC 0.13 mg/kg n=7	SC 0.26 mg/kg n=9	SC 0.4–0.5 mg/kg n=6	All Sotatercept N=50
Calcium-based phosphorus binders							
Calcium acetate	2 (28.6)	1 (11.1)	4 (33.3)	3 (42.9)	5 (55.6)	2 (33.3)	17 (34.0)
Calcium carbonate	1 (14.3)	1 (11.1)	1 (8.3)	0 (0.0)	1 (11.1)	0 (0.0)	4 (8.0)
Calcium acetate/magnesium carbonate	0 (0.0)	0 (0.0)	1 (8.3)	2 (28.6)	0 (0.0)	0 (0.0)	3 (6.0)
Non-calcium phosphorus binders							
Lanthanum carbonate	1 (14.3)	4 (44.4)	2 (16.7)	0 (0.0)	1 (11.1)	1(16.7)	9 (18.0)
Sevelamer	1 (14.3)	2 (22.2)	3 (25.0)	1 (14.3)	0 (0.0)	1 (16.7)	8 (16.0)
Sevelamer carbonate	2 (28.6)	0 (0.0)	1 (8.3)	0 (0.0)	1 (11.1)	1 (16.7)	5 (10.0)

Table S3. Vascular calcification and bone modeling outcomes

	REN-001							
	Sotatercept dose							
	0.3 mg/kg n=9		0.5 mg/kg n=8		0.7 mg/kg n=9		0.7/0.4 mg/kg n=6	
	Baseline	Day 225	Baseline	Day 225	Baseline	Day 225	Baseline	Day 225
Total hip cortical BMD, median (min, max)	669.6 (602.3, 712.6)	667.6 (593.8, 693.8)	654.1 (604.7, 671.0)	663.3 (611.2, 675.4)	670.5 (604.3, 709.4)	654.5 (607.6, 699.0)	735.0 (646.0, 771.5)	712.6 (631.9, 769.4)
Femoral neck cortical BMD, median (min, max)	685.5 (552.7, 714.3)	670.9 (540.7, 731.8)	584.8 (523.3, 657.5)	600.2 (550.9, 651.4)	637.7 (565.5, 663.4)	622.6 (582.5, 679.6)	706.1 (630.5, 863.8)	690.8 (612.7, 848.3)
Lumbar spine BMD (mg/cm^3), median (min, max)	118.8 (53.9, 222.8)	124.2 (61.1, 212.2)	141.2 (106.1, 229.7)	141.0 (107.0, 226.2)	111.1 (71.0, 176.4)	123.6 (85.5, 168.6)	110.2 (62.8, 282.3)	132.4 (82.8, 288.1)
Agatston score, median (min, max)	2454.6 (0.0, 44,356.1)	2669.4 (0.0, 94,678.6)	83.7 (1.1, 9822.7)	90.9 (1.8, 10,299.7)	3767.5 (129.4, 8983.7)	4145.6 (141.2, 9352.2)	3317.2 (684.2, 14,177.6)	4742.2 (590.0, 14,859.0)

	Sotatercept dose										
	0.3 mg/kg n=9			0.5 mg/kg n=8			0.7 mg/kg n=9			0.7/0.4 mg/kg n=6	
	Day 1	Day 15	Day 29	Day 1	Day 15	Day 29	Day 1	Day 15	Day 29	Day 1	Day 15
Intact PTH (pg/mL), median (min, max)											
Dose cycle 1	282.0 (118.0, 629.0)	—	—	342.5 (97.0, 1152.0)	—	—	240.0 (166.0, 650.0)	—	—	223.0 (30.0, 517.0)	
Serum calcium (ng/dL), median (min, max)											
Dose cycle 1	8.7 (8.5, 9.8)	8.6 (8.3, 10.2)	8.7 (7.7, 9.6)	8.8 (8.0 9.9)	8.8 (8.3, 9.9)	8.8 (8.1, 10.1)	9.1 (7.7, 10.0)	8.7 (8.0, 9.6)	8.1 (7.4, 9.3)	9.5 (8.1, 9.7)	7.8 (7.8, 7.8)
Dose cycle 2	8.8 (7.0, 9.4)	—	8.0 (7.4, 8.5)	8.8 (8.2 10.3)	—	8.6 (8.3, 10.0)	8.6 (7.4, 9.3)	—	8.6 (8.0, 9.2)	8.8 (7.7, 9.8)	7.5 (7.5, 7.5)
Dose cycle 3	8.8 (7.6, 9.8)	—	9.0 (8.1, 9.7)	9.4 (8.3, 10.1)	—	8.4 (8.2, 8.7)	9.0 (7.2, 9.3)	—	8.5 (7.7, 9.3)	8.9 (8.7, 9.4)	—
Dose cycle 4	9.0 (7.4, 9.9)	—	8.6 (7.4, 9.7)	8.6 (8.0, 10.4)	—	8.3 (7.7, 8.8)	8.8 (7.7, 9.4)	—	8.8 (7.9, 9.3)	8.5 (7.3, 10.8)	—
Dose cycle 5	8.7 (7.6, 9.7)	—	8.6 (8.4, 9.2)	8.9 (8.3, 10.6)	—	8.5 (8.5, 8.5)	8.8 (8.0, 9.2)	—	8.6 (7.5, 9.1)	8.5 (7.7, 10.9)	8.4 (8.2, 8.5)
Dose cycle 6	8.6 (7.7, 9.8)	—	8.9 (8.0, 9.7)	8.6 (8.3, 10.5)	—	8.2 (7.8, 8.6)	8.8 (7.8, 9.3)	—	9.3 (8.8, 9.8)	8.4 (8.3, 9.8)	—

	Sotatercept dose										
	0.3 mg/kg n=9			0.5 mg/kg n=8			0.7 mg/kg n=9			0.7/0.4 mg/kg n=6	
	Day 1	Day 15	Day 29	Day 1	Day 15	Day 29	Day 1	Day 15	Day 29	Day 1	Day 15
Dose cycle 7	8.7 (7.8, 9.8)	—	9.2 (8.7, 9.7)	9.9 (8.3, 10.0)	—	NA	8.6 (7.4, 9.3)	—	9.0 (8.6, 9.3)	8.7 (8.4, 9.8)	—
Dose cycle 8	9.0 (7.9, 9.9)	NA	9.7 (9.7, 9.7)	9.3 (8.6, 9.9)	8.4 (8.4, 8.4)	9.6 (9.6, 9.6)	9.0 (7.7, 9.7)	NA	8.9 (8.3, 9.3)	8.2 (7.9, 10.0)	—
Dose cycle 9	—	—	—	—	—	—	—	—	—	8.8 (7.4, 10.2)	8.9 (8.8, 8.9)
Dose cycle 10	—	—	—	—	—	—	—	—	—	9.0 (8.1, 9.6)	—
Dose cycle 11	—	—	—	—	—	—	—	—	—	8.4 (7.7, 9.2)	—
Dose cycle 12	—	—	—	—	—	—	—	—	—	8.6 (7.2, 9.1)	—
Dose cycle 13	—	—	—	—	—	—	—	—	—	8.8 (7.9, 9.4)	8.8 (8.2, 9.4)
Dose cycle 14	—	—	—	—	—	—	—	—	—	8.2 (7.9, 8.8)	—
Dose cycle 15	—	—	—	—	—	—	—	—	—	9.2 (8.2, 9.6)	9.2 (9.2, 9.2)
Serum phosphate (mmol/L), median (min, max)											
Dose cycle 1	1.3 (1.0, 2.4)	1.2 (0.7, 2.1)	1.8 (1.2, 2.3)	1.5 (1.2, 2.5)	1.6 (1.3, 2.1)	1.6 (0.9, 2.3)	1.8 (1.2, 2.8)	1.6 (1.4, 2.9)	2.2 (1.6, 2.3)	1.6 (1.0, 2.1)	1.6 (1.6, 1.6)
Dose cycle 2	1.6 (1.1, 2.2)	—	1.7 (1.6, 1.8)	1.6 (1.3, 2.1)	—	1.5 (0.7, 1.7)	1.9 (1.3, 2.1)	—	1.7 (1.4, 1.8)	1.5 (1.2, 1.7)	2.2 (2.2, 2.2)
Dose cycle 3	1.3 (1.0, 2.6)	—	1.4 (1.0, 1.9)	1.6 (0.7, 3.1)	—	1.4 (1.4, 1.7)	1.5 (1.2, 1.8)	—	1.4 (1.4, 1.5)	1.4 (0.8, 2.7)	—
Dose cycle 4	1.4 (0.8, 2.9)	—	1.6 (1.5, 1.7)	1.6 (0.9, 2.1)	—	1.4 (1.3, 1.6)	1.5 (0.7, 2.3)	—	1.5 (1.0, 1.9)	1.6 (1.1, 2.6)	—
Dose cycle 5	1.6 (1.0, 3.2)	—	1.4 (1.1, 2.3)	1.7 (1.1, 2.0)	—	1.5 (1.5, 1.5)	1.5 (1.1, 2.1)	—	2.0 (1.7, 2.4)	1.7 (1.2, 2.0)	1.9 (1.1, 2.7)
Dose cycle 6	1.7 (1.3, 2.5)	—	1.1 (0.9, 1,4)	1.6 (1.2, 1.8)	—	1.1 (1.0, 1.2)	1.7 (0.7, 2.5)	—	2.0 (1.8, 2.3)	1.4 (1.0, 2.4)	—
Dose cycle 7	1.4 (0.9, 2.6)	—	1.3 (1.3, 1.4)	1.9 (1.2, 2.4)	—	NA	1.6 (0.7, 2.3)	—	1.6 (0.9, 2.3)	1.5 (1.2, 2.5)	—
Dose cycle 8	1.7 (0.9, 2.4)	NA	1.5 (1.5, 1.5)	1.4 (1.3, 2.5)	1.3 (1.3, 1.3)	2.5 (2.5, 2.5)	1.5 (1.0, 2.3)	NA	1.3 (0.7, 2.2)	1.4 (0.8, 2.2)	—

	Sotatercept dose										
	0.3 mg/kg n=9			0.3 mg/kg n=9			0.3 mg/kg n=9			0.3 mg/kg n=9	
	Day 1	Day 1	Day 1	Day 1	Day 1	Day 1	Day 1	Day 1	Day 1	Day 1	Day 1
Dose cycle 9	—	—	—	—	—	—	—	—	—	1.4 (1.1, 2.4)	2.0 (1.5, 2.5)
Dose cycle 10	—	—	—	—	—	—	—	—	—	1.5 (0.8, 1.8)	—
Dose cycle 11	—	—	—	—	—	—	—	—	—	1.6 (1.2, 2.1)	—
Dose cycle 12	—	—	—	—	—	—	—	—	—	1.8 (0.7, 2.2)	—
Dose cycle 13	—	—	—	—	—	—	—	—	—	1.5 (1.4, 2.2)	2.0 (1.0, 2.6)
Dose cycle 14	—	—	—	—	—	—	—	—	—	2.0 (1.0, 2.4)	—
Dose cycle 15	—	—	—	—	—	—	—	—	—	1.7 (0.6, 2.2)	1.8 (1.8, 1.8)

The n values represent number of patients randomized to treatment at baseline. The summary statistics for each parameter, treatment group, and visit are based on patients with non-missing data.

Table S4. Summary of patients who developed anti-sotatercept antibodies

	REN-001			
	Sotatercept dose			
Patients, n (%)	0.3 mg/kg n=9	0.5 mg/kg n=8	0.7 mg/kg n=9	0.7/0.4 mg/kg n=6
Anti-sotatercept antibodies detected	0 (0.0)	0 (0.0)	1 (11.1)	2 (33.3)

	REN-002					
	Sotatercept route of administration and dose					
Patients, n (%)	IV 0.1 mg/kg n=7	IV 0.2 mg/kg n=9	IV 0.1−0.4 mg/kg n=12	SC 0.13 mg/kg n=7	SC 0.26 mg/kg n=9	SC 0.13−0.5 mg/kg n=6
Anti-sotatercept antibodies detected	1 (14.3)	3 (33.3)	1 (8.3)	2 (28.6)	0 (0.0)	0 (0.0)

IV, intravenous; SC, subcutaneous.

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2
Background and objectives	2a	Scientific background and explanation of rationale	4
	2b	Specific objectives or hypotheses	5
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	5-6, Figure 1
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	NA
Participants	4a	Eligibility criteria for participants	5
	4b	Settings and locations where the data were collected	
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	5-6, Figure 1
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	9-10
	6b	Any changes to trial outcomes after the trial commenced, with reasons	NA
Sample size	7a	How sample size was determined	
	7b	When applicable, explanation of any interim analyses and stopping guidelines	9-10, Figure 1
Randomisation: Sequence	8a	Method used to generate the random allocation sequence	5-6

generation	8b	Type of randomisation; details of any restriction (such as blocking and block size)	6
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	6
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	5-6
	11b	If relevant, description of the similarity of interventions	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	9-10
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	10-11, Figure 2
	13b	For each group, losses and exclusions after randomisation, together with reasons	Figure 2
Recruitment	14a	Dates defining the periods of recruitment and follow-up	
	14b	Why the trial ended or was stopped	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Tables S1 & S2
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Tables S1 & S2
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Table 1, Figure 3
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Figure 3
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	Table 2
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	20
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	21
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other	21

		relevant evidence	
Other information			
Registration	23	Registration number and name of trial registry	5, 6
Protocol	24	Where the full trial protocol can be accessed, if available	
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	1, 21

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.