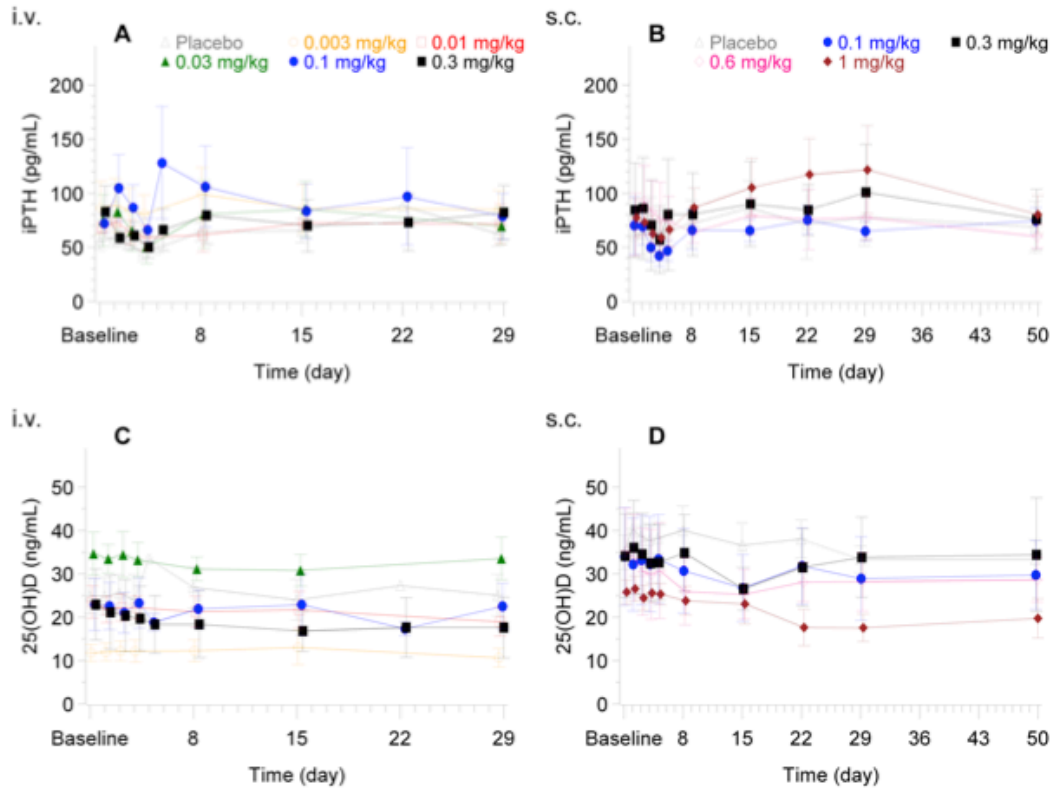
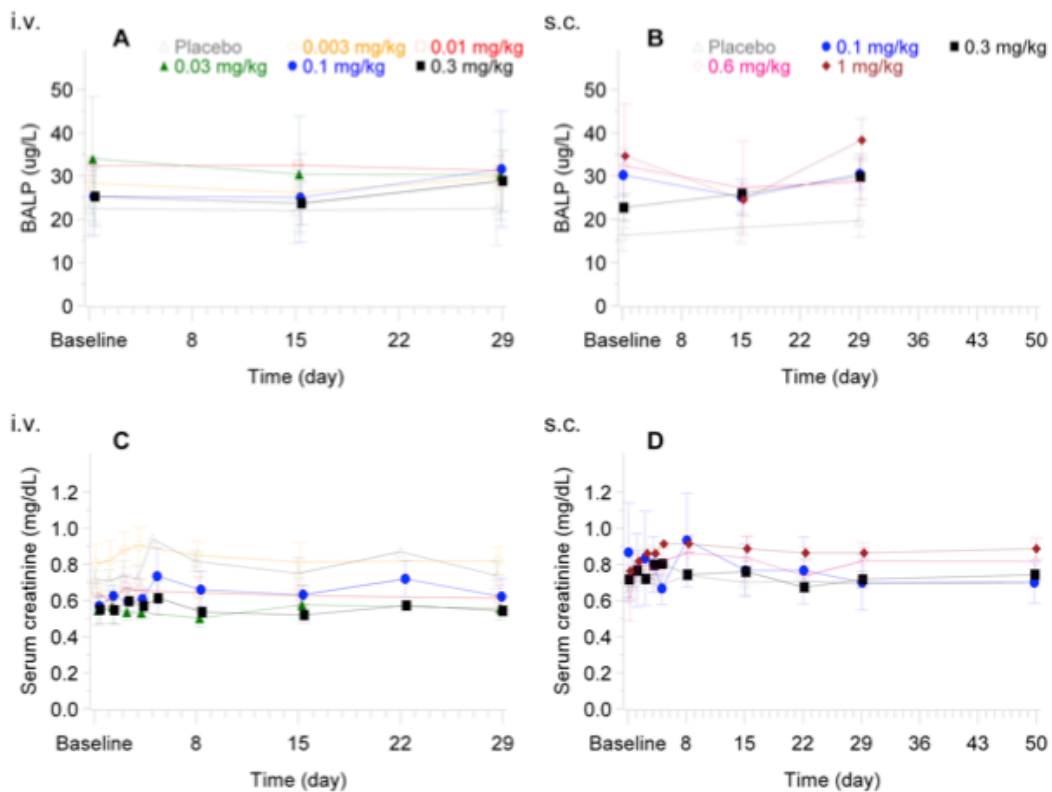


Supplementary Figure 1.



Supplementary Figure 1. Effect of i.v. and s.c administration KRN23 on serum iPTH and 25(OH)D compared to placebo. **A and B:** serum iPTH; **C and D:** serum 25(OH)D. For i.v. cohorts, six profiles are shown for panels A and C [placebo (grey), 0.003 (yellow), 0.01 (red), 0.03 (green), 0.1 (blue) and 0.3 mg/kg (black)]. For s.c. cohorts, 5 profiles are shown for panels B and D [placebo (grey), 0.1 (blue), 0.3 (black), 0.6 (pink) and 1.0 mg/kg (brown)]. Data are presented as mean \pm SEM.

Supplementary Figure 2.



Supplementary Figure 2. Effect of i.v. and s.c administration KRN23 on serum BALP and creatinine compared to placebo. **A and B:** serum BALP; **C and D:** serum creatinine. For i.v. cohorts, six profiles are shown for panels A and C [placebo (grey), 0.003 (yellow), 0.01 (red), 0.03 (green), 0.1 (blue) and 0.3 mg/kg (black)]. For s.c. cohorts, 5 profiles are shown for panels B and D [placebo (grey), 0.1 (blue), 0.3 (black), 0.6 (pink) and 1.0 mg/kg (brown)]. Data are presented as mean \pm SEM.

Supplemental Table 1.

Summary of ANOVA for additional pharmacodynamic parameters following i.v. administration of KRN23

Parameters	Dose Level (mg/kg)	Treatment Response vs Placebo Response ^A	Lower Limit of 95% CI	Upper Limit of 95% CI	P-value (Pair-wise Comparison)
iPTH, pg/mL	0.003	4.3	-6.0	14.6	0.412
	0.01	-3.2	-13.5	7.1	0.537
	0.03	-2.1	-12.4	8.1	0.683
	0.1	13.2	4.5	21.8	0.003*
	0.3	-15.8	-25.6	-6.1	0.002*
25(OH)D, ng/mL	0.003	0.20	-1.07	1.47	0.76
	0.01	-2.08	-3.35	-0.81	0.001*
	0.03	-1.17	-2.44	0.10	0.070
	0.1	0.19	-0.88	1.26	0.727
	0.3	-2.87	-4.07	-1.66	<0.001*
BALP, µg/L	0.003	-0.16	-4.03	3.72	0.935
	0.01	-0.19	-4.07	3.68	0.922
	0.03	-2.27	-6.14	1.61	0.246
	0.1	2.17	-1.19	5.52	0.201
	0.3	0.82	-3.05	4.69	0.673
Serum creatinine, mg/dL	0.003	0.006	-0.030	0.041	0.757
	0.01	-0.038	-0.074	-0.003	0.032*
	0.03	-0.042	-0.077	-0.006	0.021*
	0.1	0.011	-0.018	0.041	0.452
	0.3	-0.045	-0.078	-0.011	0.009*

^A Least squares mean difference in change from baseline between active and placebo treatment calculated from ANOVA model with dose and visit as explanatory variables. * $P < 0.05$.

Supplemental Table 2.

Summary of ANOVA for additional pharmacodynamic parameters following s.c. administration of KRN23

Parameters	Dose Level (mg/kg)	Treatment Response vs Placebo Response^A	Lower Limit of 95% CI	Upper Limit of 95% CI	P-value (Pair-wise Comparison)
iPTH, pg/mL	0.1	-15.5	-23.8	-7.17	<0.001*
	0.3	-10.8	-19.1	-2.48	0.011*
	0.6	-0.45	-8.79	7.88	0.915
	1	-2.98	-11.3	5.36	0.482
25(OH)D, ng/mL	0.1	-4.70	-6.54	-2.87	<0.001*
	0.3	-2.54	-4.37	-0.71	0.007*
	0.6	-6.41	-8.24	-4.57	<0.001*
	1	-4.26	-6.10	-2.43	<0.001*
BALP, µg/L	0.1	-3.32	-8.24	1.60	0.181
	0.3	1.72	-3.21	6.64	0.486
	0.6	-4.56	-9.49	0.36	0.068
	1	-3.85	-8.78	1.07	0.122
Serum creatinine, mg/dL	0.1	-0.13	-0.19	-0.078	<0.001*
	0.3	-0.026	-0.082	0.031	0.366
	0.6	0.130	0.073	0.186	<0.001*
	1	0.030	-0.026	0.086	0.296

^A Least squares mean difference in change from baseline between active and placebo treatment calculated from ANOVA model with dose and visit as explanatory variables. * $P < 0.05$.