Supplementary Table 1. Details of the components of the primary composite endpoint

1. Death

The cause of death will be defined by the underlying cause, not the immediate mode of death. Death will be classified into two categories, Cardiovascular (CV) or Non-Cardiovascular (non-CV). All deaths will be assumed to be CV in nature unless a non-CV cause can be clearly identified (e.g. malignancy, suicide, accidental death). Death will be considered non-CV only if an unequivocal and documented non-CV cause can be established. Death will be classified into the following categories:

A. Cardiovascular Death:

- Myocardial infarction
- Heart Failure/Cardiogenic Shock
- Sudden death
  - Witnessed
  - Last seen ≥ 1 hr and < 24 hrs
  - Last seen ≥24 hrs
- Stroke
- CV Procedure
  - CABG
  - PCI/Stenting
  - Valvular
  - Other CV procedure
- Pulmonary embolism
- Other CV

B. Non-Cardiovascular Death:

Deaths will be considered non-cardiovascular only if an unequivocal and documented non-cardiovascular cause can be established. Examples of non-CV sub-classifications will include:

- Malignancy
- Chronic Pulmonary Disease
- Infection
- Hepatobilliary
- Gastrointestinal
- Non-CV Procedural
- Accidental/Trauma
- Suicide
- Other Non-CV
- Unknown

2. Myocardial Infarction

A. Acute MI

- Cardiac enzyme markers indicative of a MI (with a time-appropriate rise and fall), include any of the following:
  - Any combination of markers where Troponin result is ≥ 2x ULN or CKMB ≥ 2x ULN
  - If only a CK is drawn, serial changes of ≥ 2x ULN must be shown

And 1 of the following:

- ECG changes consistent with an infarction as defined by:
  - New significant Q waves (or R waves in V1-V2) in two contiguous leads in the absence of previous LVH or conduction abnormalities.
  - Evolving ST-segment to T-wave changes in two or more contiguous leads.
  - Development of new left bundle branch block.
  - ST segment elevation requiring thrombolytics or percutaneous coronary intervention

Or

- Ischemic symptoms of pain, dyspnea, pressure at rest or accelerated ischemic symptoms (either of which lasts ≥ 10 minutes) that the investigator determines is secondary to ischemia

B. For patients who undergo revascularization, an endpoint MI is as follows:

- Post – PCI MI: troponin or CK-MB cardiac marker ≥ 3 x ULN or persistent new pathological Q-waves or documented new non-septal wall motion abnormality

- Post – CABG MI: CK-MB cardiac marker ≥ 5 x ULN and increased by at least 50% over the last measurement or persistent new pathological Q-waves or Documented new non-septal wall motion abnormality

C. Recurrent MI:

- In order to make the determination whether there is evidence for a re-infarction, the subject must be clinically stable and symptom free for at least 12 hours since the previous event. In addition, the appropriate 'rise and fall' of cardiac markers should be present in order to provide evidence of a new MI.

D. Adjudication of acute MI in the presence of acute myocardial ischemia

- The worst-case event per calendar day will be adjudicated. For example, if hospitalization for unstable angina and an MI are reported during the same calendar day and the patient meets criteria for both, the endpoint adjudication committee will consider the unstable angina as an event that was evolving into a MI and therefore only positively adjudicate the MI

3. Hospitalization for Unstable Angina

The criteria for hospitalization will be met if the subject is 'admitted' to a hospital bed or observation unit and there is a change in the calendar day from hospital presentation to discharge.

The endpoint for acute myocardial ischemia is defined as:

- Hospitalization for unstable angina symptoms with either ischemic ECG changes or cardiac marker (troponin or CK-MB) greater than ULN but less than 2 x ULN

OR

- Hospitalization for unstable angina symptoms with either ischemic ECG changes or change in cardiac markers (CK) from below ULN to less than 2 x ULN

4. Heart Failure

Heart failure will be defined as any of the following:

- An unplanned presentation to an acute care setting (hospital or dialysis unit) with signs / symptoms of volume overload (see below) and the patient received mechanical fluid removal therapy (e.g., ultrafiltration or dialysis)

OR

- Acute exacerbation of HF with symptomatic pulmonary edema during an ongoing hospitalization for another condition in which HF becomes a major component of the hospitalization provided that the patient received a mechanical fluid removal (e.g., ultrafiltration or dialysis)

Signs / Symptoms of Volume Overload will be defined as:

- Dyspnea with at least 2 of the following:
  - Bilateral basilar rales on physical exam
  - Raised jugular venous pressure (JVP) or *
  - Interstitial edema findings on Chest Xray
  - Increased upper pulmonary vessel diameter noted on Chest Xray
  - Elevated left ventricular end diastolic pressure (LVEDP) or pulmonary capillary wedge pressure (PCWP) (by swanz ganz catheter)

** If bibasilar rales are noted on exam and data about other criteria are not available or were not collected then, a heart failure event may be adjudicated based on preponderance of clinical and laboratory evidence using bibasilar rales as the only supporting physical exam sign.*

5. Peripheral Vascular Event

Any of these three events:

- Lower limb amputation (meta-tarsal and higher) for peripheral vascular disease (PVD)*
- Revascularization procedure (bypass, stent, thrombectomy) for PVD *
  Note: procedures involving vascular access for dialysis are not included.
- Hospitalization for ischemic rest pain with documented gangrene/tissue necrosis

** PVD will be defined by presence of any of the following:*

a. *diminished peripheral pulse*
b. *lower extremity pallor or hairlessness*
c. *rest pain*
d. *non-healing ulcer or gangrene*
e. *non-invasive measurements of vascular insufficiency*

Supplementary Table 2. Exposure and Adherence to Study Drug by Age Group				
	< 65 years (N=2860)		**≥ 65 years (N=1001)**	
	Placebo (N_1=1451)	**Cinacalcet (N_1=1409)**	**Placebo (N_1=472)**	**Cinacalcet (N_1=529)**
Duration of exposure months, median (p10, p90)	18 (3,52)	23 (3,53)	15 (2,50)	16 (2,49)
Daily dose, mg/day, median (p10, p90)	127 (46,162)	58 (29,136)	119 (34,160)	46 (26,109)
Maximum dose (180 mg) achieved n (%)	1181 (81)	599 (43)	358 (76)	143 (27)
Adherence %, median (p10, p90)	92 (73,99)	87 (61,98)	92 (68,99)	85 (59,98)

Percentages are based on N_1
Adherence was defined as the proportion of time patient took study drug during the time they were exposed to study drug.
Only patients who received at least one dose of study drug (3861 of 3883 randomized) were included in analyses of adherence.

Supplementary Table 3. Reasons for Discontinuation by Age Group						
	< 65 years			**≥ 65 years**		
	Placebo (N_1=1460)	**Cinacalcet (N_1=1418)**	**Total (N_1=2878)**	**Placebo (N_1=475)**	**Cinacalcet (N_1=530)**	**Total (N_1=1005)**
Dead n (%)	151 (10.3)	161 (11.4)	312 (10.8)	115 (24.2)	85 (16.0)	200 (19.9)
Permanently discontinued – n (%)	1065 (72.9)	932 (65.7)	1997 (69.4)	300 (63.2)	368 (69.4)	668 (66.5)
Adverse event	148 (10.1)	187 (13.2)	335 (11.6)	81 (17.1)	121 (22.8)	202 (20.1)
Parathyroidectomy	136 (9.3)	42 (3.0)	178 (6.2)	12 (2.5)	5 (0.9)	17 (1.7)
Kidney transplant	210 (14.4)	236 (16.6)	446 (15.5)	20 (4.2)	24 (4.5)	44 (4.4)
Low PTH	5 (0.3)	60 (4,2)	65 (2.3)	3 (0.6)	41 (7.7)	44 (4.4)
Administrative decision	223 (15.3)	89 (6.3)	312 (10.8)	64 (13.5)	41 (7.7)	105 (10.4)
Subject request	225 (15.4)	189 (13.3)	414 (14.4)	83 (17.5)	83 (15.7)	166 (16.5)

Percentages are based on N_1

Only patients who received at least one dose of study drug (3861 of 3883 randomized) were included in analyses of discontinuation.

Supplementary Table 4. Concomitant medications to manage MBD over time by randomized group and by age group.

	< 65 years (N = 2878)		≥ 65 years (N = 1005)	
Baseline	**Placebo (N_1 = 1460)**	**Cinacalcet (N_1 = 1418)**	**Placebo (N_1 = 475)**	**Cinacalcet (N_1 = 530)**
Vitamin D sterol use, n (%)	812 (56)	810 (57)	312 (66)	326 (62)
Mean ± SD weekly IV paricalcitol-equivalent dose, µg/week	17.5 ± 14.8	17.1 ± 13.6	15.3 ± 13.1	15.7 ± 11.5
Phosphate binder use, n (%)	1309 (90)	1254 (88)	413 (87)	457 (86)
Calcium-containing phosphate binder use, n (%)	795 (55)	770 (54)	230 (48)	267 (50)
Year 1	**Placebo (N_1 = 1118)**	**Cinacalcet (N_1 = 1076)**	**Placebo (N_1 = 309)**	**Cinacalcet (N_1 = 393)**
Vitamin D sterol use, n (%)	705 (63)	592 (55)	226 (73)	219 (56)
Mean ± SD weekly IV paricalcitol-equivalent dose, µg/week	19.7 ± 17.5	16.1 ± 19.6	16.1 ± 11.4	13.0 ± 11.5
Phosphate binder use, n (%)	988 (88)	948 (88)	268 (87)	346 (88)
Calcium-containing phosphate binder use, n (%)	573 (51)	649 (60)	150 (49)	238 (61)
Year 2	**Placebo (N_1 = 865)**	**Cinacalcet (N_1 = 882)**	**Placebo (N_1 = 232)**	**Cinacalcet (N_1 = 299)**
Vitamin D sterol use, n (%)	556 (64)	455 (52)	170 (73)	160 (54)
Mean ± SD weekly IV paricalcitol- equivalent dose, µg/week	20.6 ± 21.4	16.0 ± 15.4	16.7 ± 23.2	14.4 ± 14.1
Phosphate binder use, n (%)	751 (87)	763 (87)	197 (85)	255 (85)
Calcium-containing phosphate binder use, n (%)	444 (51)	518 (59)	96 (41)	171 (57)
Year 3	**Placebo (N_1 = 707)**	**Cinacalcet (N_1 = 727)**	**Placebo (N_1 = 165)**	**Cinacalcet (N_1 = 220)**
Vitamin D sterol, n (%)	439 (62)	377 (52)	128 (78)	122 (56)
Mean ± SD IV paricalcitol-equivalent dose, µg/week	21.1 ± 29.3	16.3 ± 15.1	15.9 ± 16.4	14.2 ± 12.2
Phosphate binder use, n (%)	606 (86)	612 (84)	143 (87)	187 (85)
Calcium-containing phosphate binder use, n (%)	338 (48)	413 (57)	61 (37)	128 (58)

Percentages are based on N_1

Supplementary Table 5. Adverse Effects by age group in patients randomized to cinacalcet and placebo

< 65 years	**Cinacalcet (N=1409)**			**Placebo (N=1451)**		
	Number of Patients	**Exposure Adjusted Rate[a]**	**Crude Incidence[b]**	**Number of Patients**	**Exposure Adjusted Rate[a]**	**Crude Incidence[b]**
All adverse events	1295	277.2	91.9	1293	206.8	89.1
Nausea	428	18.4	30.4	225	8.9	15.5
Vomiting	378	15.5	26.8	200	7.8	13.8
Hypocalcemia	167	6.1	11.9	21	0.7	1.4
Serious adverse events	915	48.3	64.9	943	51.0	65.0
Treatment related events						
Adverse events	659	34.9	46.8	262	10.4	18.1
Serious adverse events	47	1.6	3.3	32	1.1	2.2
Neoplastic events	88	3.0	6.2	86	3.1	5.9
Calciphylaxis	6	0.2	0.4	16	.06	1.1
≥ 65 years	**Cinacalcet (N=529)**			**Placebo (N=472)**		
	Number of Patients	**Exposure Adjusted Rate[a]**	**Crude Incidence[b]**	**Number of Patients**	**Exposure Adjusted Rate[a]**	**Crude Incidence[b]**
All adverse events	511	264	96.6	455	256.5	96.4
Nausea	135	17.9	25.5	74	10.1	15.7
Vomiting	119	15.2	22.5	64	8.6	13.6
Hypocalcemia	50	5.7	9.5	6	.07	1.3
Serious adverse events	423	68.6	80.0	408	77.8	86.4
Treatment related events						
Adverse events	231	36.7	43.7	101	14.4	21.4
Serious adverse events	22	2.4	4.2	12	1.5	2.5
Neoplastic events	52	5.7	9.8	32	4.1	6.8
Calciphylaxis	0	0	0	2	0.2	0.4

The data that are listed are for patients who received at least 1 dose of study drug.

[a] The exposure-adjusted rate was calculated as 100 x (total number of patients who had first event/total patient-year of exposure).Exposure excludes gaps if there are more than 7 days between study drug stop and restart.

[b] The crude incidence was calculated as 100 x (total number of patients who had an event/total number of patients who received at least one dose of study drug