Non-clinical studies suggest that RAP-011 (the murine ActRIIA-IgG1 ligand trap that inhibits ActRIIA signaling) modulates the

In a 5/6 nephrectomy mouse model of CKD that exhibits bone loss, bone mass measurements were significantly improved

All image quality control and blinded analyses were performed centrally by PAREXEL imaging (PAREXEL International Corp, Waltham, MA).

Renal osteodystrophy (ROD) and vascular calcification (VC) are integral components of chronic kidney disease-mineral/bone disorder (CKD-MBD).

Table 1. Randomized Subjects and QCT Analysis Subset

Table 2. Change from Baseline Autodense Total Agatston Score and Square Root Transformation

### Safety

### CONCLUSIONS

- Safety results were consistent with known effects of sotatercept in healthy volunteers and in patients on dialysis in the Phase 2 clinical program. There were no new toxicities observed.
- Achieving and maintaining higher levels of Hb with sotatercept was associated with beneficial effects on bone mineral density, bone turnover, and VC.
- The results of this trial support the investigation of sotatercept in Phase 3 studies to further explore its potential benefits on bone, cardiovascular, and anemia outcomes.

### REFERENCES

2. Celgene Corporation, Warren, NJ; William T. Smith

### METHODS

#### Study Population

- A total of 153 subjects were randomized and received treatment. The median age was 60 years (range 20-87 years), and 56% were male. Subjects were predominantly white (88%).

#### Study Design

- This was a randomized, double-blind, placebo-controlled trial with a 4-week run-in period followed by a 225-day treatment phase.

#### Study Treatments

- Sotatercept was administered at 0.3 mg/kg, 0.5 mg/kg, 0.7 mg/kg, or placebo on Days 1 and 15 for 225 days (6 cycles).

#### Outcomes

- Secondary outcomes included change from baseline in total Agatston score, change from baseline in square root transformed total volume score, and change from baseline in a composite endpoint of new-onset or worsening CKD-MBD events.

#### Data Analysis

- Analysis was performed using an intent-to-treat (ITT) approach. For continuous variables with normal distribution, the mean change from baseline was calculated.

### RESULTS

#### Demographics

- Key demographics included age, sex, race, and comorbidities.

#### Bone Mineral Density

- Changes in lumbar spine BMD were observed across all dose groups.

#### Bone and Soft Tissue Calcification

- Significant reductions in square root transformed total volume score were observed.

#### Laboratory Parameters

- No consistent changes from baseline in phosphate, PTH, FGF-23, or sclerostin levels were observed, except that PTH was lower at baseline in the sotatercept groups.

#### Adverse Events

- Adverse events were generally consistent with those expected for sotatercept and were manageable.

### CONCLUSIONS

- Sotatercept at doses of 0.3 mg/kg, 0.5 mg/kg, and 0.7 mg/kg showed promise in improving bone health and reducing vascular calcification in patients on dialysis.

- The study results support further investigation of sotatercept in larger, randomized controlled trials to evaluate its potential benefits on bone, cardiovascular, and anemia outcomes.

- Additional research is needed to confirm these findings in real-world clinical settings and to explore the long-term effects of sotatercept on CKD-MBD.

- Continued evaluation of sotatercept is warranted to further understand its potential benefits and to guide future clinical development.