Reviewer’s report

**Title:** Cathepsin K inhibitors increase distal femoral bone mineral density in rapidly growing rabbits

**Version:** 1  **Date:** 15 August 2013

**Reviewer:** Rosaria Guzzo

**Reviewer’s report:**

The authors described the limitations of existing animal models for evaluation of the in vivo potencies of anti-resportive compounds. This was a well written manuscript providing clearly stated aims and well designed experiments. The authors provided strong rationale for developing a short-term, cost-effective and reliable in vivo screening of bone resorption inhibitors in rapidly growing rabbits. As the authors discussed, the rabbit Schenk assay may be a useful, cost-effective screen for providing a rank-order potency of inhibitors prior to evaluation in an estrogen deficiency-related bone loss model. Importantly, use of cathepsinK inhibitors, specifically L-006, 235 and odanacatib, in rapid growing rabbits indicated a similar outcome as in estrogen-deficiency induced bone loss in skeletally mature rabbits.

**Major Compulsory Revisions:**

1. Histological evidence demonstrating the potency of the CatK inhibitors in rapidly growing rabbits would be necessary to support the validity of this model as a reliable screen for the anti-absorptive effects of specific CatK inhibitors.

**Minor Essential Revisions:**

2. The authors provide evidence for increased bone mineral densities in response to their tested compounds. Inclusion of representative DXA images for all treatments and compounds should be provided.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.