Effects of Burosumab (KRN23), a Fully Human Anti-FGF23 Monoclonal Antibody, on Functional Outcomes in Children with X-linked Hypophosphatemia (XLH): Final Results from a Randomized, 64-week, Open-label Phase 2 Study

Thomas Carpenter, MD, Erik Imler, MD, Agnieszka Bood, MD, Wolfgang Högler, MD, Raja Paddela, MD, William van’t Hof, MD, Anthony Portela, MD, Meng Mao, PhD, Alison Skinar, PhD, Javier San Martin, MP, Michael Whyte, MD*1

1. Yale University School of Medicine, New Haven, CT, USA; 2. University of Pittsburgh Medical School, Pittsburgh, PA, USA; 3. University of California, San Francisco, CA, USA; 4. Ultragenyx Pharmaceutical Inc., Hudson, MA, USA; 5. Birmingham Children’s Hospital, Birmingham, UK; 6. Royal Manchester Children’s Hospital, Manchester, UK; 7. Royal Children’s Hospital, Melbourne, VIC, Australia; 8. Texas Children’s Hospital, Houston, TX, USA

PURPOSE: To report the 64-week results of a Phase 2 randomized, double-blind, placebo-controlled, multicenter trial evaluating the efficacy and safety of subcutaneous (SC) and intravenous (IV) burosumab in children with X-linked hypophosphatemia (XLH) with functional impairment.

METHODS: In this trial, children aged 2–12 years with X-linked hypophosphatemia (XLH) with impaired function at baseline (PODNI-PODCI Global Functioning score <40) were randomized to receive placebo or burosumab (500 mg/m2 SC Q2W or 200 mg/m2 SC Q4W) for 64 weeks. The primary endpoint was improvement in the modular component of the Pediatric Outcomes Database for the Children’s Inpatient and Outpatient Rehabilitation (PODNI-PODCI) Global Functioning score. Secondary endpoints included measures of pain and comfort, physical function, and walking ability. Safety data were also collected.

RESULTS: A total of 52 children with XLH and baseline functional impairment were randomized (17 to Q2W or 26 to Q4W) and received at least 1 dose of study drug. At baseline, children with XLH presented with significant residual rickets, pain, and impaired function. At Week 64, improvements in PODNI-PODCI Global Functioning score were observed across all treatment groups. Burosumab subjects experienced greater improvements compared with placebo subjects. In the Q2W group, 32 of 34 subjects (94%) achieved a PODNI-PODCI Global Functioning score of 40 or greater at Week 64. Multiple additional endpoints, including pain and comfort, physical function, and walking ability, also improved over baseline.

CONCLUSIONS: Burosumab treatment demonstrated marked improvement in functional outcomes and safety in children with XLH, and should be considered for registry or clinical trial enrolment in the near future.