Persistent and Stable Growth Promoting Effects of Vosoritide in Children with Achondroplasia for up to 2 Years: Results From the Ongoing Phase 3 Extension Study

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Objectives: Vosoritide is a potent stimulator of endochondral bone growth and is in development for the treatment of achondroplasia, the most common form of disproportionate short stature. We previously reported on a 52-week, phase 3, pivotal study that demonstrated a highly statistically significant improvement in annualized growth velocity (AGV) when vosoritide was compared to placebo in children with achondroplasia aged 5-18 years (Savarirayan et al, Lancet, 2020). This is an analysis of data after an additional 52 weeks of treatment in the ongoing phase 3 extension study.

Methods: After completion of the phase 3 placebo-controlled study, 119 children were enrolled into the extension study, where they all receive open label 15 µg/kg/day vosoritide. AGV, height Z-score and body proportion ratio were analyzed to assess efficacy of vosoritide in children who were treated with vosoritide for up to 2 years. Fifty-eight continued treatment with vosoritide and 61 switched from placebo to vosoritide. Two participants on continuous vosoritide treatment discontinued before the Week 52 timepoint. Four participants on continuous vosoritide treatment and 7 participants who switched from placebo to vosoritide missed the Week 52 assessment due to COVID-19.

Results: In children randomized to receive daily vosoritide, baseline mean (SD) AGV was 4.26 (1.53) cm/year. After the first 52 weeks of treatment, mean (SD) AGV was 5.67 (0.98) cm/year. Mean (SD) AGV over the second year was 5.57 (1.10) cm/year. Mean (SD) change from baseline in height Z-score improved by +0.24 (0.31) at Week 52 in the pivotal study and +0.45 (0.56) at Week 52 in the extension study. Mean (SD) upper-to-lower body segment ratio improved with a change from baseline of -0.03 (0.11) at Week 52 in the pivotal study and -0.09 (0.11) at Week 52 in the extension study. In children who switched from placebo to vosoritide after 52 weeks, baseline AGV was 4.06 (1.20) cm/year and 3.94 (1.07) cm/year after 52 weeks on placebo. In the second year, after receiving 52 weeks of vosoritide, mean AGV was 5.65 (1.47) cm/year, the mean (SD) change in height Z-score was +0.24 (0.34), and the change in upper-to-lower body segment ratio was -0.03 (0.08). No new adverse events associated with vosoritide treatment were detected with up to 2 years of continuous daily, subcutaneous treatment. Most adverse events were mild and no serious adverse events were attributed to vosoritide. The most common adverse event remains mild and transient injection site reactions.

Conclusions: The effect of vosoritide administration on growth as measured through AGV and height Z-score was maintained for up to 2-years in children with achondroplasia aged 5 to 18 years, with an improvement of body proportions.