GTP

• C-type natriuretic peptide (CNP) promotes chondrocyte development through inhibition of the FGFR3

• Achondroplasia (ACH) is the most common short limbed skeletal dysplasia. It is caused by a gain-of-overactive signalling resulting from both ligand-dependent and independent signalling through the achondroplasia. Due to its very short half-life (2–3 minutes), native CNP has historically not been a

• Type IIA, IIIA, and IIIA/IIIB phenotypes are associated with a normal or slightly reduced renal clearance and independent signaling through the mutated FGFR3 receptor causing ADPKD

• There are currently no approved treatments which address the underlying pathophysiology of achondroplasia. Due to its very short half-life, CNP is not effective. The CNP-38 antibody has been able to provide sustained exposure of CNP to the chondrocytes for up to 200 μg/kg/week. An Independent Data Monitoring Committee will review safety data prior to initiation of a higher dose cohort.

Figure 2. Achondroplasia Signaling Defect is Well Understood

Figure 3. TransCon CNP Design

Figure 4. Dose Proportional CNP Exposure For 1 Week

Figure 5. Change from Baseline in Plasma (A) and Urine (B) cGMP

Figure 6. Mean Resting Blood Pressure Unchanged from Predose+

Figure 7. TransCon CNP: Phase 1 Trial Design

BACKGROUND

• TransCon CNP is a sustained-release prodrug of CNP. CNP is transiently bound via the TransCon Carrier to a dosing device that delivers the CNP to the plasma, thereby reducing the risk of interfering

• The phase 2 ACcomplisH trial of TransCon CNP in children with achondroplasia will be conducted at approximately 20 sites worldwide.

METHODS

• The primary objective is to evaluate the safety and efficacy of once-weekly TransCon CNP compared to placebo at 12 months in prepubertal ACH children, aged 2–21 years old. Approximately 80 subjects will be randomized 3:1 to receive either weekly TransCon CNP or placebo.

• Following screening and verification of clinical ACH with genetic confirmation, patients will be randomized to receive TransCon CNP or placebo at 12 months in prepubertal ACH children, aged 2–21 years old. Approximately 80% of patients will be randomized 3:1 to receive either weekly TransCon CNP or placebo.

• No effective medicinal product is currently available for the treatment of ACH. CNP is targeted specifically to the underlying pathophysiology of ACH through inhibition of FGFR3.

CONCLUSIONS AND STUDY STATUS

• TransCon CNP is designed to provide sustained exposure of CNP

• The Phase 2 ACcomplisH trial is designed to assess the efficacy, safety, and PK of TransCon CNP by weekly administration compared to placebo. The trial is currently ongoing.