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BridgeBio Pharmaceuticals QED Therapeutics

Propel 3 Study: Infigratinib

(Data below compiled by Victoria Garcia, RN. The thoughts below are not mine and do not belong to me. This is only a summarization of data slides presented by BridgeBio. I am not a physician, the information in this document is intended to inform and educate. It is a description of my best understanding of medical/trial data presented by the researchers. I do not give permission for this document to be edited)

-Bridge bio is a biotechnology company dedicated to the development of novel, genetically targeted therapies for rare diseases

-QED Therapeutics is an affiliated company of BridgeBio Pharma Incorporation. Founded in January of 2018, with headquarters in San Francisco, California. QED employs 40 members focused on development of infigratinib for FGFR driven conditions like achondroplasia.

-Infigratinib targets FGFR. It is designed to decrease FGFR signaling inside a cell. Infigratinib is being developed as a mini tablet for potential treatment option in achondroplasia. The pill is approximately two millimeters in diameter, oral administration.

-Infigratinib could improve the balance between proliferation and differentiation of chondrocytes

-The PROPEL clinical program trial design consists of observational run-in, a dose finding phase, and long-term follow-up.

- **The observational run-in key inclusion criteria**

- children 2.5 to 17 years old

- clinical and molecular ACH diagnosis.

- The children were monitored for a minimum of six months to establish a baseline annualized growth velocity

- Primary endpoints for the observational run-in were change from baseline annualized growth velocity and safety/tolerability.

- **Phase2 was dose finding from 70 participants**

- dosing categories were (Cohort 1) 0.016 mg/kg, (Cohort 2) 0.032 mg/kg, (Cohort 3) 0.064 mg/kg, (Cohort 4) 0.128 mg/kg, and (Cohort 5) 0.25mg/kg

- **Open label extension exams long-term follow up**

- Follow up for long-term safety and efficacy to further explore the effect of infigratinib on overall health growth and possible medical complications.

- Evaluates safety and efficacy until closure of growth plates

- Key secondary endpoints for extension were change in upper body to lower body segment proportionality; Patient reported outcome measures such as PedsQoL, QoLISSY, Pain-NRS; and height-for-age z-score.

-PROPEL2 Cohort 5 data (0.25mg/kg/day)

- Number of children =12
- Female = 7
- Male = 5
- Median age = 7.17 years old
- 1 participant was aged three to five
- 7 participants were ages five to eight
- 4 participants were over eight years old
- Mean change from baseline in annualized growth velocity at month 6 was +3.03cm/yr.
- Data for cohort five were all children ages 5 and up.
- When looking at responder rate, (as defined as having a change from baseline annualized height velocity of 25% or greater), responders in Cohort 5 had a mean increase in annualized height velocity of +3.81 cm/yr.
- 80% of children in cohort 5 were considered responders, meaning they had a change from baseline in annualized height velocity of 25% or greater.

-Collagen X results: A marker for bone growth

-Cohort 5 exhibited a 30% increase in Collagen X Marker (CXM) levels compared to baseline after three months of therapy. This rise in CXM supports a dose-responsive relationship within cohort 5. Collagen X is produced and placed in hypertrophic zones of active growth plates. Upon endochondral ossification, collagen X is degraded and the NC1 domain, the maker designed as CXM, is released into the circulation in proportion to overall growth plate activity. **Circulating collagen X marker levels correlates with growth velocity in real time.

-Infigratinib Propel2 cohort 5 Safety Profile

-0 Severe adverse events

-0 Adverse events assessed as drug-related

-0 discontinuations due to adverse events

-No accelerated advancement of bone age or worsening of body proportions

-All TEAEs (treatment emergent adverse events) were grades 1 & 2 in severity and deemed not related to study drug. Grade 1 = 10, Grade 2 = 2. 92% of children presented at least one TEAE. Grade 1 AEs included fever, sore throat, GI disorder, (ie vomiting, abdominal pain), infections (ie ear infections, nasopharyngitis, rhinitis, croup), respiratory diseases (cough, Nasal congestion), blood triglycerides increased, hepatic enzyme increased. Grade 2 AEs were ear infection and viral infection.