PROPEL Program: Oral Infigratinib for Achondroplasia

MAT-US-INFI-0019

Disclaimers

The safety and efficacy of infigratinib in skeletal dysplasias have not been demonstrated and infigratinib has not been approved by any regulatory agency for the use described here.

To the children, families, advocates, and physicians who have been a part of this program:

THANK YOU!

Developing new treatment options relies entirely on your guidance, dedication, and effort.

QED is part of the BridgeBio family of companies

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

Our mission:

To **discover, create, test** and **deliver** transformative medicines to treat people who live with genetic conditions and cancers with clear genetic drivers

Our purpose:

Providing **hope** through **rigorous science**

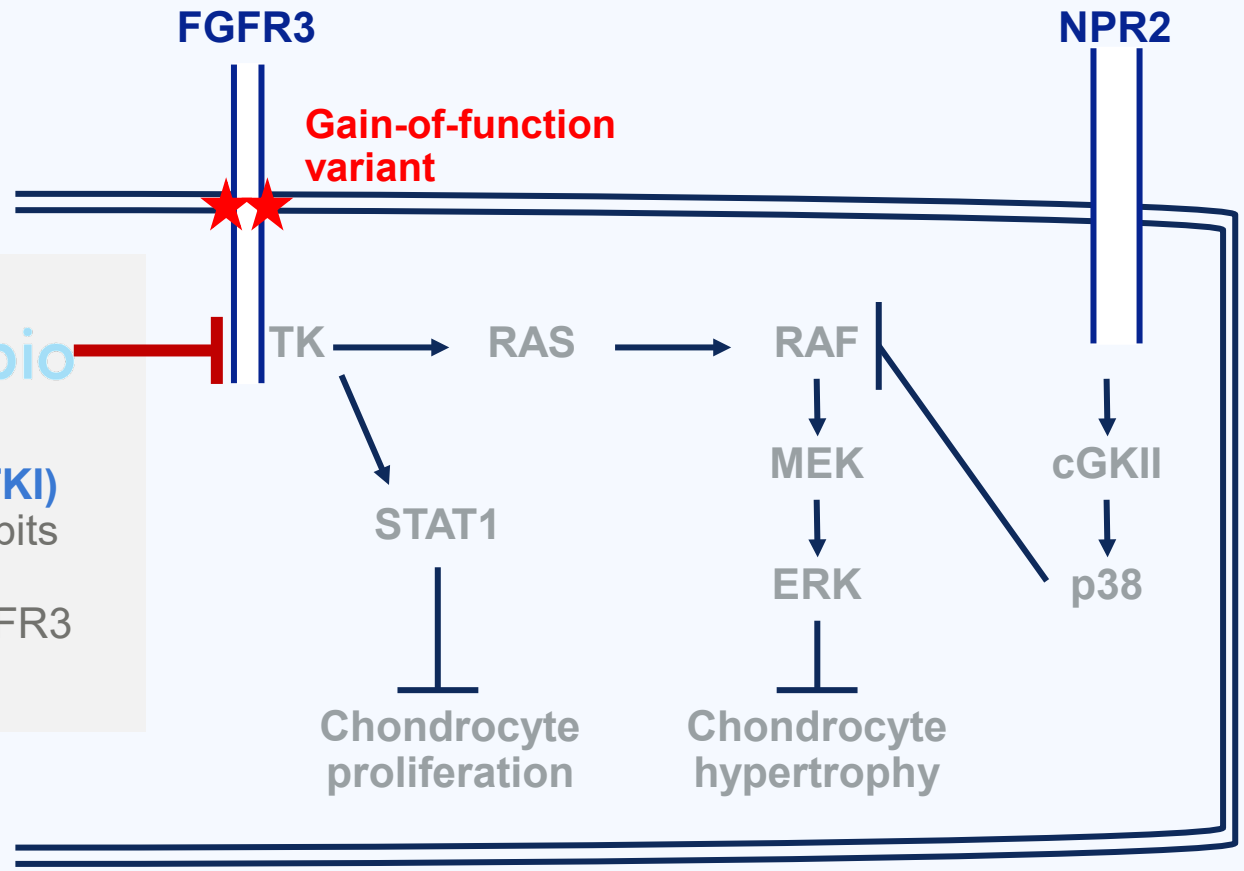
About QED Therapeutics:
We are solely focused on skeletal dysplasias

QED Therapeutics

- Affiliate Company of BridgeBio Pharma Inc
- Founded in January 2018
- Headquarters in San Francisco, CA
- ~80 employees
- **Solely focused** on development of infigratinib for FGFR-driven skeletal dysplasias, e.g. achondroplasia and hypochondroplasia

What is Infigratinib?

Infigratinib is designed to directly target the underlying cause of achondroplasia and hypochondroplasia: FGFR3 overactivity



Infigratinib (FGFR1-3 TKI)
Directly inhibits the gain-of-function FGFR3 receptor

- Infigratinib targets achondroplasia and hypochondroplasia **directly at the source**: FGFR3 overactivity
- Infigratinib **inhibits both downstream pathways** responsible for the clinical phenotype associated with achondroplasia

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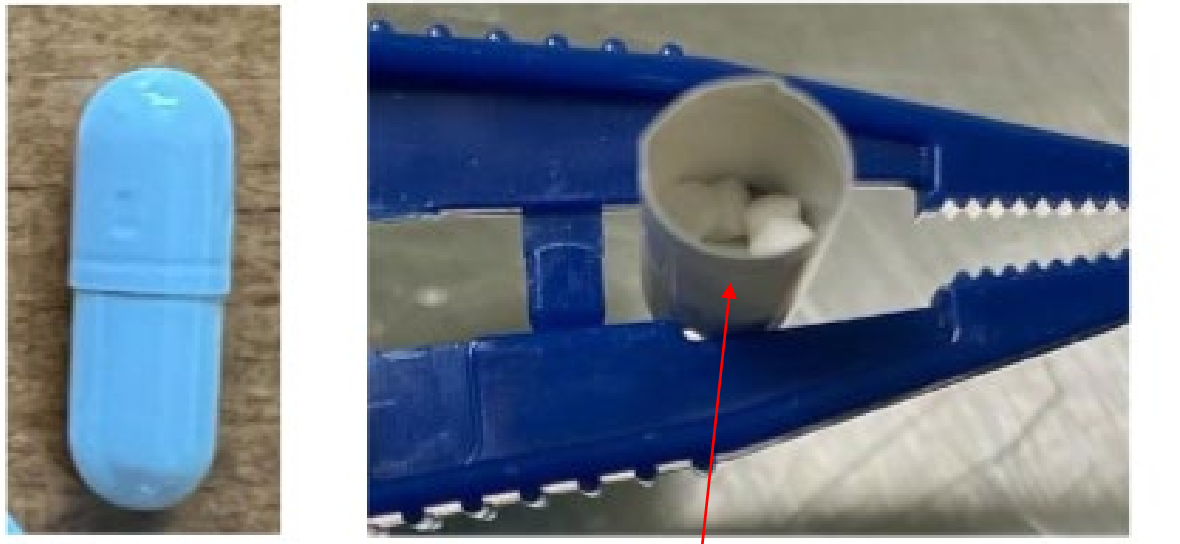
1. Savarirayan R. et al. Ther Adv Musculoskelet Dis. 2022; 14: 1759720X221084848. 2. Sabir A. H. et al. Am J Med Genet. 2021;185A:73–82

Infigratinib is an investigational medicine that targets FGFR

- Infigratinib is designed to decrease FGFR signaling inside a cell[1]
- Infigratinib is being developed for oral administration as a sprinkle capsule with minitablets (~2mm in diameter) for potential treatment option in achondroplasia and hypochondroplasia with oral administration
- The different strengths of the sprinkle capsules depend on the number of minitablets encapsulated per capsule.
- The sprinkle capsule strength for each child is based on the weight.
- The capsules can be taken either directly intact or the contents can be sprinkled on soft food.



Minitablets inside a sprinkle capsule

SOURCE: 1: Komla-Ebri et al. J Clin Invest. 2016

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What is the PROPEL Program?

The PROPEL Program in Achondroplasia

PROPEL

Observational Run-in (N ≈ 250)

Participants: Children and adolescents (2.5 to <17 years) with achondroplasia

1° endpoint: AHV

Duration: ≤2 years (≥6 months required for PROPEL interventional studies)

PROPEL2

Phase 2 Open-Label Dose-Escalation and Dose-Expansion (N ≈ 108)

Participants: Children (3–11 years) who complete ≥6 months in PROPEL

1° endpoints: TEAEs, CFB in AHV, and PK parameters

Duration: ≤18 months

PROPEL3

Phase 3 Randomized, Double-Blinded, and Placebo-Controlled (N ≈ 110)

Participants: Children and adolescents (3 to <18 years) who complete ≥6 months in PROPEL and have growth potential

1° endpoint: CFB in AHV

Key 2° endpoints: CFB in height Z-score (on ACH growth charts) and upper to lower body segment ratio.

Other 2° endpoints: Changes in physical functioning, HRQoL, cognitive function, participant and caregiver evaluation of treatment benefit

Duration: 12 months

PROPEL Open Label Extension

Open-label Extension (N ≈ 280)

Participants: Children and adolescents (3 to <18 years) who complete a prior PROPEL study and have growth potential

1° endpoints: TEAEs; changes in height Z-score (on ACH and non-ACH growth charts)

2° endpoints: Changes in upper body to lower body segment ratio; changes in HRQoL, overall body pain, functional abilities, cognitive function, and complications associated with ACH

Duration: 10 years*

ACH, achondroplasia; AHV, annual height velocity; CFB, change from baseline; HRQoL, health-related quality of life; PK, pharmacokinetics; TEAE, treatment-emergent adverse event. *Infigratinib given until final or near-final height reached.

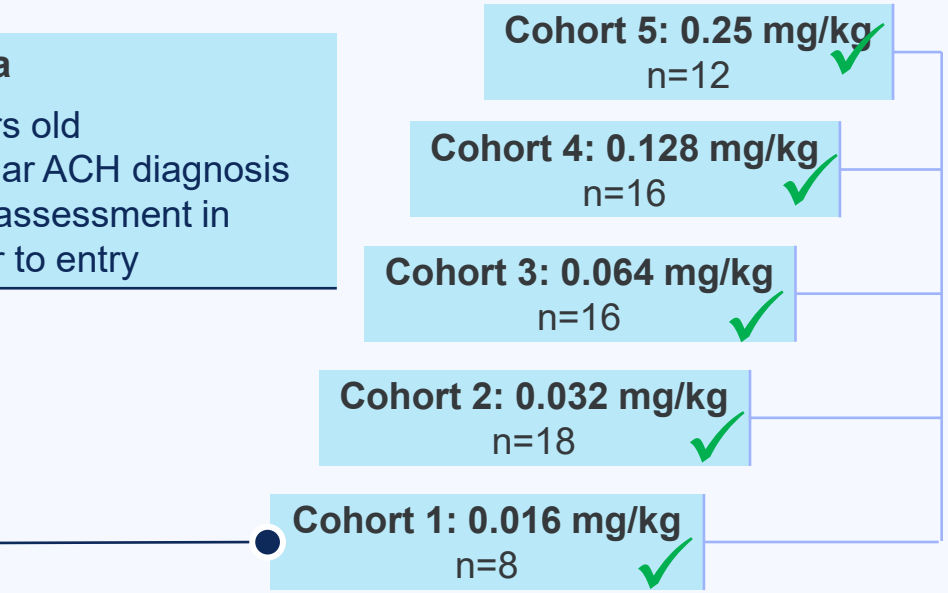
Source: NCT04265651, NCT06164951, NCT05145010

PROPEL2 Clinical Program Design

Phase 2 Open-Label Dose-Escalation and Dose-Expansion (N ≈ 108)

Key inclusion criteria

- Children 3 – 11 years old
- Clinical and molecular ACH diagnosis
- At least 6-month of assessment in PROPEL study prior to entry



Primary endpoints

- Change from baseline annualized height velocity (AHV)
- Safety and tolerability

Main secondary endpoints

- Change in upper body to lower body segment proportionality
- Patient-reported outcome measures: PedsQoL, QoLISSY, Pain-NRS
- Height-for-age z-score

Note: cohort sizes represent number of children who have completed or are anticipated to complete a month six visit. The planned interim analysis for Cohort 5 was when M6 data for 10 children was available. M6 AHV data is only available from the first 10 with the remaining 2 having six month visits shortly
Source: Savarirayan et al 2022 Ther Adv Musculoskelet Dis

PROPEL 2 :
Month 12 and Month 18 Results

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PROPEL 2 Safety Summary

- **In Cohort 5 (the highest dose escalation level of 0.25 mg/kg):**
  - No serious adverse events (SAEs)
  - No adverse events (AEs) that required treatment discontinuation
  - Most treatment-emergent adverse events (TEAEs) were grade 1 in severity and none of the TEAEs were assessed as related to study drug
  - 0 subjects with grade 3 TEAEs
  - 0 ocular adverse events
  - 0 hyperphosphatemia events
  - No accelerated progression of the bone age
- **Cohorts 1-4:** no new hyperphosphatemia events, ocular events, or SAEs

Infigratinib in PROPEL 2 cohort 5 is well-tolerated with no safety signals identified through month 18

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[1]Insert source / footnote

AEs across all cohorts

AEs occurring in ≥10% of study participants	Total (%) N = 72
Nasopharyngitis	29 (40.3%)
COVID-19	24 (33.3%)
Headache	24 (33.3%)
Vomiting	22 (30.6%)
Pain in extremity	20 (27.8%)
Ear infection	19 (26.4%)
Pyrexia	18 (25.0%)
Abdominal pain	11 (15.3%)
Cough	11 (15.3%)
Diarrhea	11 (15.3%)
Rhinitis	11 (15.3%)
Viral infection	11 (15.3%)
Upper respiratory tract infection	10 (13.9%)
Abdominal pain upper	8 (11.1%)
Ear pain	8 (11.1%)
Nausea	8 (11.1%)
Oropharyngeal pain	8 (11.1%)
Otitis media	8 (11.1%)

These reported AEs are common in the pediatric population.

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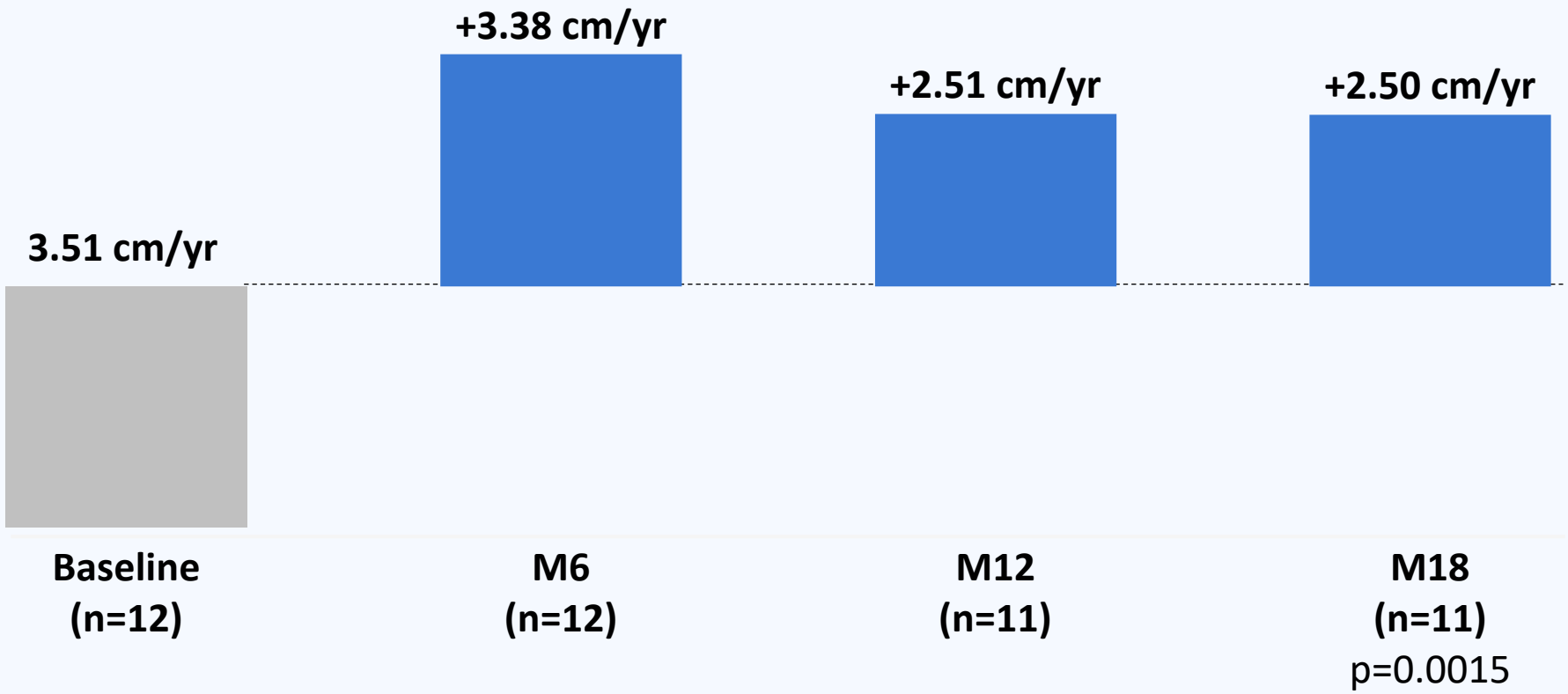
Source: Data on file

Cohort 5: Change from baseline in AHV

Mean change from baseline in annualized height velocity (AHV)



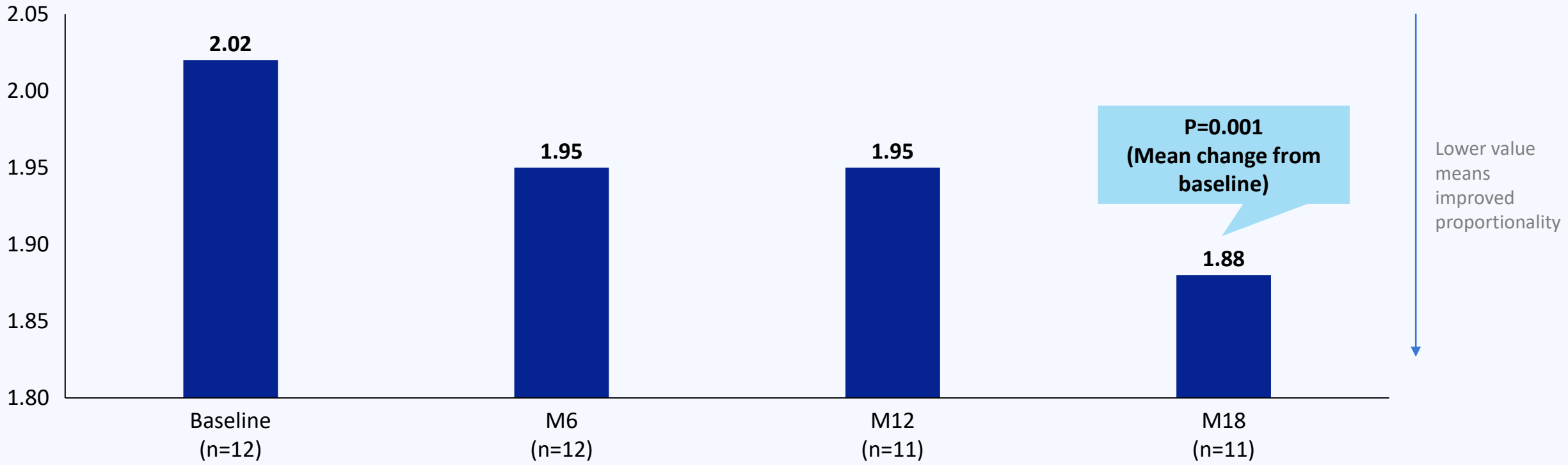
Baseline demographics	
Female:Male ratio	**7:5**
Mean age at screening (yr)	**7.24**
<5	8%
5 - <8	58%
8 - <11	25%
>=11	8%
Baseline AHV (cm/yr) Mean (SD)	**3.51 (1.3)**

The AHV increased from a baseline of ~3.5 cm/year to ~6.0 cm/year on infigratinib treatment at 18 months.

[1]Insert source / footnote

Cohort 5 presents a decrease in upper/lower body segment ratio

Upper body to lower body segment ratio



Statistically significant improvement in proportionality was observed at 18 months. For context, the upper/lower body segment ratio of those of average stature is 1.0.

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1 Insert source / footnote

PROPEL 3:
A Pivotal Phase 3, Randomized, Placebo-Controlled Double-Blinded Study

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PROPEL 3: Pivotal Phase 3, Randomized, Double-Blinded Study

PROPEL: Observational run-in → **PROPEL 3: Ph3 randomized, double-blinded pivotal trial (n=~110)** → **PROPEL OLE: Open-label extension**

Observational

Children are followed for a minimum of 6 months

2:1

- **0.25 mg/kg/day Infigratinib**
- **Placebo**

52-week duration

0.25 mg/kg/day Infigratinib

Followed on treatment until final adult height is reached

Key inclusion criteria

Children 3 – <18 years old with open growth plates

Primary endpoint:

Change from baseline in annualized height velocity at week 52

Key secondary endpoints:

Change from baseline in height z-score

Change from baseline in upper body:lower body segment ratio

Other secondary endpoints:

Change in physical functioning; HRQoL; cognitive function, participant and caregiver evaluation of treatment benefit (qualitative interview)

PROPEL 3 Site Locations

- Argentina
- Australia
- Canada
- France
- Germany
- Italy
- Norway
- Singapore
- Spain
- United Kingdom
- United States

Visit clinicaltrials.gov, NCT04035811 or contact PROPELstudyinfo@qedtx.com for more details.

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Summary

- In the PROPEL 2 study, the target dose of 0.25mg/kg/day of oral infigratinib was well-tolerated
- Infigratinib demonstrated a durable improvement in AHV at month 18 compared to baseline in PROPEL 2, with a statistically significant improvement in upper/lower body segment ratio
- PROPEL 3 pivotal study of infigratinib in achondroplasia is currently enrolling globally.
- Expansion of infigratinib in hypochondroplasia is initiated, with the ACCEL clinical trial open and first participant enrolled

Thank you

Contact medinfo@qedtx.com for any questions on the ongoing trials