A Multicenter, Phase 2, Dose-Escalation/Dose-Expansion Study of Dabogratinib (Formerly TYRA-300) in Children With Achondroplasia With Open Growth Plates: BEACH301

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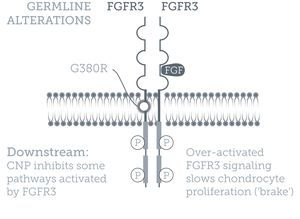
BACKGROUND

- Achondroplasia is the most common form of heritable skeletal dysplasia, affecting approximately 250,000 people worldwide[1,2]
- Achondroplasia is caused by a gain of function mutation in the *FGFR3* gene (most commonly G380R) leading to overactivation of FGFR3 signaling[1–4]
- Aberrant FGFR3 signaling inhibits chondrocyte proliferation and differentiation, resulting in impaired endochondral ossification and abnormal skeletal development (Figure 1)[2,3,5]
- Individuals with achondroplasia can experience lifelong morbidity, with early-life complications including foramen magnum stenosis, recurrent otitis media, sleep-disordered breathing, and ongoing impact across childhood and adulthood including obesity, skeletal complications, chronic pain, surgeries, and effects on function and psychosocial well-being[1,3,6,7]
- Inhibiting FGFR3 may benefit children with achondroplasia. Approved CNP analogs indirectly modulate this pathway,[2,8,9] while pan-FGFR inhibition has demonstrated encouraging safety and efficacy, supporting direct FGFR inhibition[10]
  - Dabogratinib is an oral, highly selective FGFR3 inhibitor designed to directly target the underlying driver of achondroplasia while minimizing off-target effects[11]
  - By avoiding the toxicities associated with inhibition of FGFR1, FGFR2, and FGFR4, dabogratinib may provide greater efficacy with a larger therapeutic window than non-isoform selective FGFR inhibitors[12]
  - Dabogratinib is being evaluated in children with achondroplasia in the phase 2 BEACH301 study (NCT06842355)[13]

Figure 1. Aberrant FGFR3 Signaling in Achondroplasia

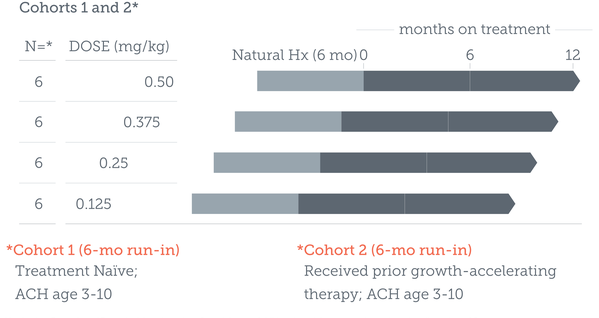


Gain-of-function *FGFR3* mutations (eg, G380R) lead to overactivation of FGFR3 signaling (via an increase in steady-state levels of receptor),[4] inhibiting chondrocyte proliferation and impairing endochondral bone growth.

METHODS

- BEACH301 (NCT06842355) is a phase 2, multicenter, open-label, dose-escalation/dose-expansion study to evaluate the safety, tolerability, and potentially effective dose(s) of oral dabogratinib QD in children aged 3 to 10 years with achondroplasia with open growth plates[13]
- Dabogratinib is administered at weight-based dose levels (0.125-0.50 mg/kg), with dose escalation per protocol-defined criteria
- The study includes 3 cohorts (Figure 2)
  - Sentinel Safety Cohort
  - Cohort 1: Treatment-naïve
  - Cohort 2: Received prior growth-accelerating therapy

Figure 2. Study Design of BEACH301



✓ Indicates that the dose level has been cleared by an independent Data Safety Monitoring Committee. *Dose decisions based on 6 participants. Additional participants may be assigned at discretion of Sponsor. Schematic representation of the study design, illustrating cohort structure and weight-based dabogratinib dosing.

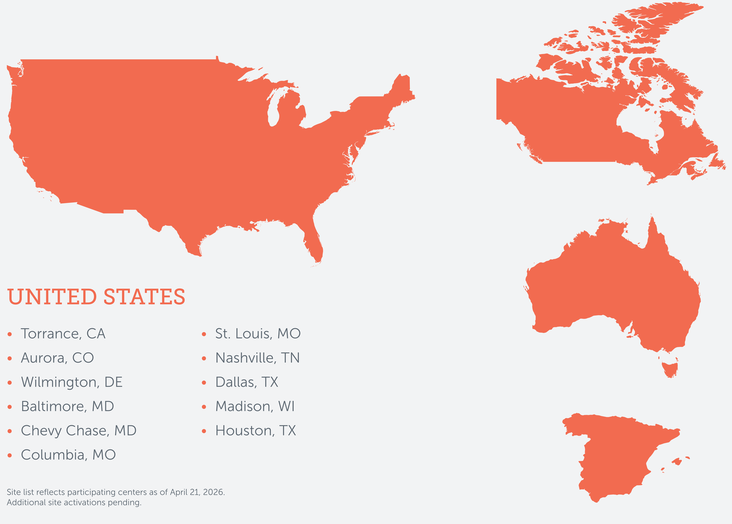
Participant Criteria[13]

Key Inclusion Criteria	Key Exclusion Criteria
• Children aged 3 to 10 years of age • Molecularly confirmed achondroplasia with *FGFR3* G380R mutation • Radiographically confirmed open growth plates by bone age X-ray • Ability to stand and ambulate independently • Sentinel Safety Cohort only: aged 5 to 10 years old (inclusive) • Cohort 1 only: aged 3 to 10 years old (inclusive) and are naïve to prior growth-accelerating therapy • Cohort 2 only: aged 3 to 10 years old (inclusive) and have received prior growth-accelerating therapy • Ability to take oral medication	• Presence or history of any concurrent disease or condition that would interfere with study participation, safety evaluations, or any uncontrolled or untreated condition that could impact pediatric growth • Endocrine condition that alters calcium/phosphate homeostasis • Prior limb lengthening surgery or planned or expected to have limb lengthening surgery while enrolled in the study • History or current evidence of corneal or retinal disorder/keratopathy • Presence of guided growth hardware (eg, 8 plates). Planned or anticipated orthopedic surgeries

Study Endpoints[13]

Primary Endpoints	Secondary Endpoints
• Incidence of treatment-emergent AEs • Change from baseline in AGV	• Change from baseline in height z-score • Comparison of single- and multiple-dose sparse pharmacokinetic parameters, including but not limited to C_{max}, T_{max}, $AUC_{0\text{-}last}$, AUC_{Tau}, $AUC_{0\text{-}\infty}$, Vd/F, CL/F, and $t_{½}$ • Change from baseline in anthropometric measurements, including but not limited to standing height, sitting height, upper arm length, lower arm length, tibial length, femur length, arm span proportionality (arm span/height ratio), and upper segment/lower segment ratio with dabogratinib

BEACH301 SITE LIST



UNITED STATES

- Torrance, CA
- Aurora, CO
- Wilmington, DE
- Baltimore, MD
- Chevy Chase, MD
- Columbia, MO
- St. Louis, MO
- Nashville, TN
- Dallas, TX
- Madison, WI
- Houston, TX

CANADA

- Toronto

AUSTRALIA

- Westmead
- Parkville

SPAIN

- Vitoria

Site list reflects participating centers as of April 21, 2026.
Additional site activations pending.

Abbreviations

ACH, achondroplasia; AE, adverse event; AGV, annualized growth velocity; $AUC_{0\text{-}last}$, area under the curve from time zero to the last measurable concentration; AUC_{Tau}, area under the curve from time zero to tau; $AUC_{0\text{-}\infty}$, area under the curve from time zero to infinity; CL/F, apparent clearance; C_{max}, maximum plasma concentration; CNP, C-type natriuretic peptide; FGFR, fibroblast growth factor receptor; Hx, history; mo, month; QD, once daily; $t_{½}$, half-life; T_{max}, time to maximum concentration; Vd/F, apparent volume of distribution.

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