

bridgebio

hope through
rigorous science

PROPEL2 topline results

March 6th, 2023



Forward-looking statements

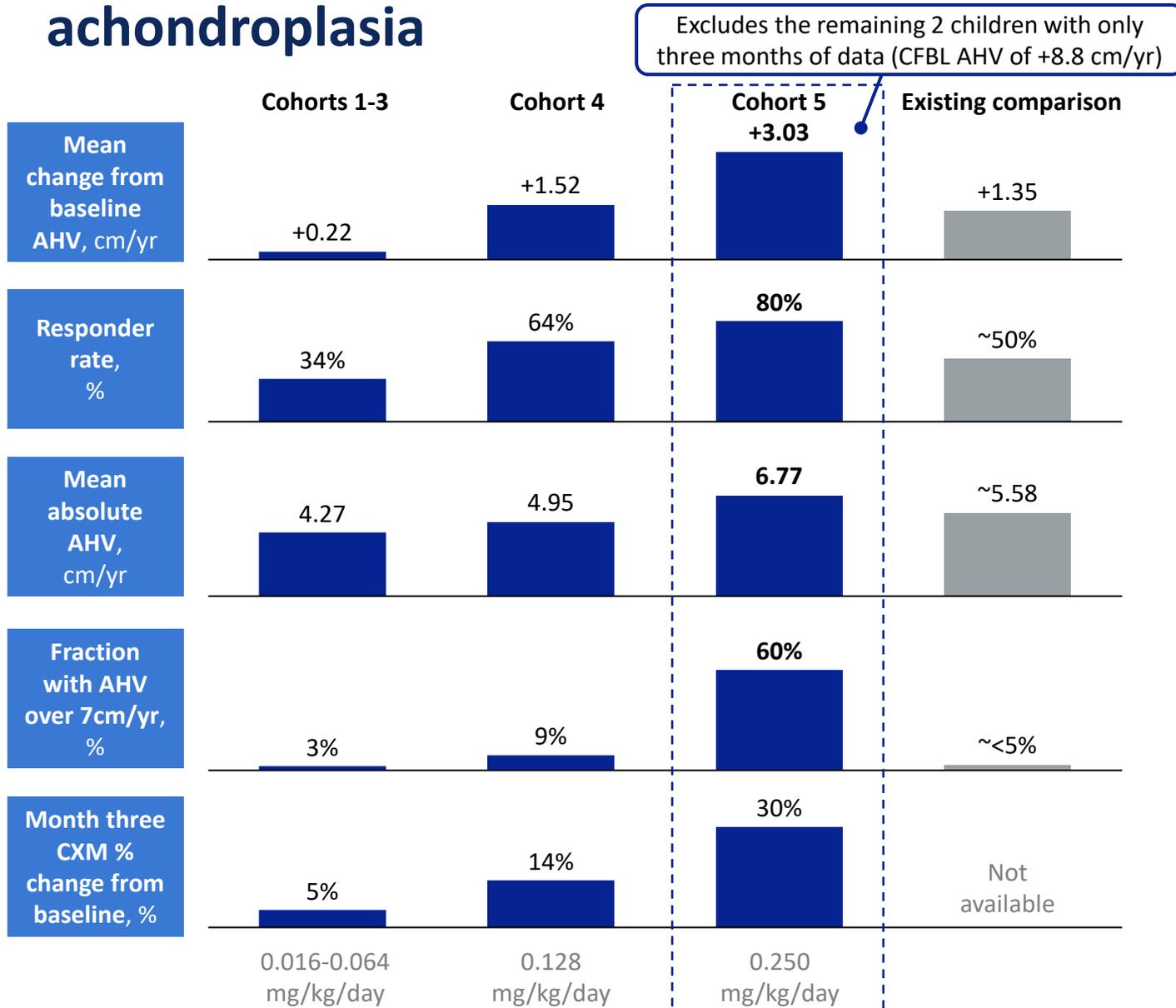
This presentation contains forward-looking statements. Statements in this presentation may include statements that are not historical facts and are considered forward-looking within the meaning of Section 27A of the Securities Act of 1933, as amended (the Securities Act), and Section 21E of the Securities Exchange Act of 1934, as amended (the Exchange Act), which are usually identified by the use of words such as “anticipates,” “believes,” “estimates,” “expects,” “intends,” “may,” “plans,” “projects,” “seeks,” “should,” “will,” and variations of such words or similar expressions. We intend these forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act and Section 21E of the Exchange Act. These forward-looking statements, including statements relating to the clinical, therapeutic and market potential of our programs and product candidates, including our clinical development program for infigratinib in achondroplasia, the timing and success of our clinical development programs, the progress of our ongoing and planned clinical trials of infigratinib in achondroplasia and in hypochondroplasia, including our plans to initiate a Phase 3 trial for infigratinib in achondroplasia and to initiate clinical development in hypochondroplasia, our planned interactions with regulatory authorities, the availability of data from our clinical trials of infigratinib, and the timing of these events, reflect our current views about our plans, intentions, expectations and strategies, which are based on the information currently available to us and on assumptions we have made. Although we believe that our plans, intentions, expectations and strategies as reflected in or suggested by those forward-looking statements are reasonable, we can give no assurance that the plans, intentions, expectations or strategies will be attained or achieved. Furthermore, actual results may differ materially from those described in the forward-looking statements and will be affected by a number of risks, uncertainties and assumptions, including, but not limited to, initial and ongoing data from our clinical trials not being indicative of final data, the design and success of ongoing and planned clinical trials, difficulties with enrollment in our clinical trials, adverse events that may be encountered in our clinical trials, the FDA or other regulatory agencies not agreeing with our regulatory approval strategies, components of our filings, such as clinical trial designs, conduct and methodologies, or the sufficiency of data submitted, potential adverse impacts due to the global COVID-19 pandemic such as delays in regulatory review, manufacturing and supply chain interruptions, adverse effects on healthcare systems and disruption of the global economy, the impacts of current macroeconomic and geopolitical events, including changing conditions from the COVID-19 pandemic, hostilities in Ukraine, increasing rates of inflation and rising interest rates, on our overall business operations and expectations, as well as those risks set forth in the Risk Factors section of our Annual Report on Form 10-K for the year ended December 31, 2022 and our other filings with the U.S. Securities and Exchange Commission. Moreover, we operate in a very competitive and rapidly changing environment in which new risks emerge from time to time. These forward-looking statements are based upon the current expectations and beliefs of our management as of the date of this presentation, and are subject to certain risks and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. Except as required by applicable law, we assume no obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

**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



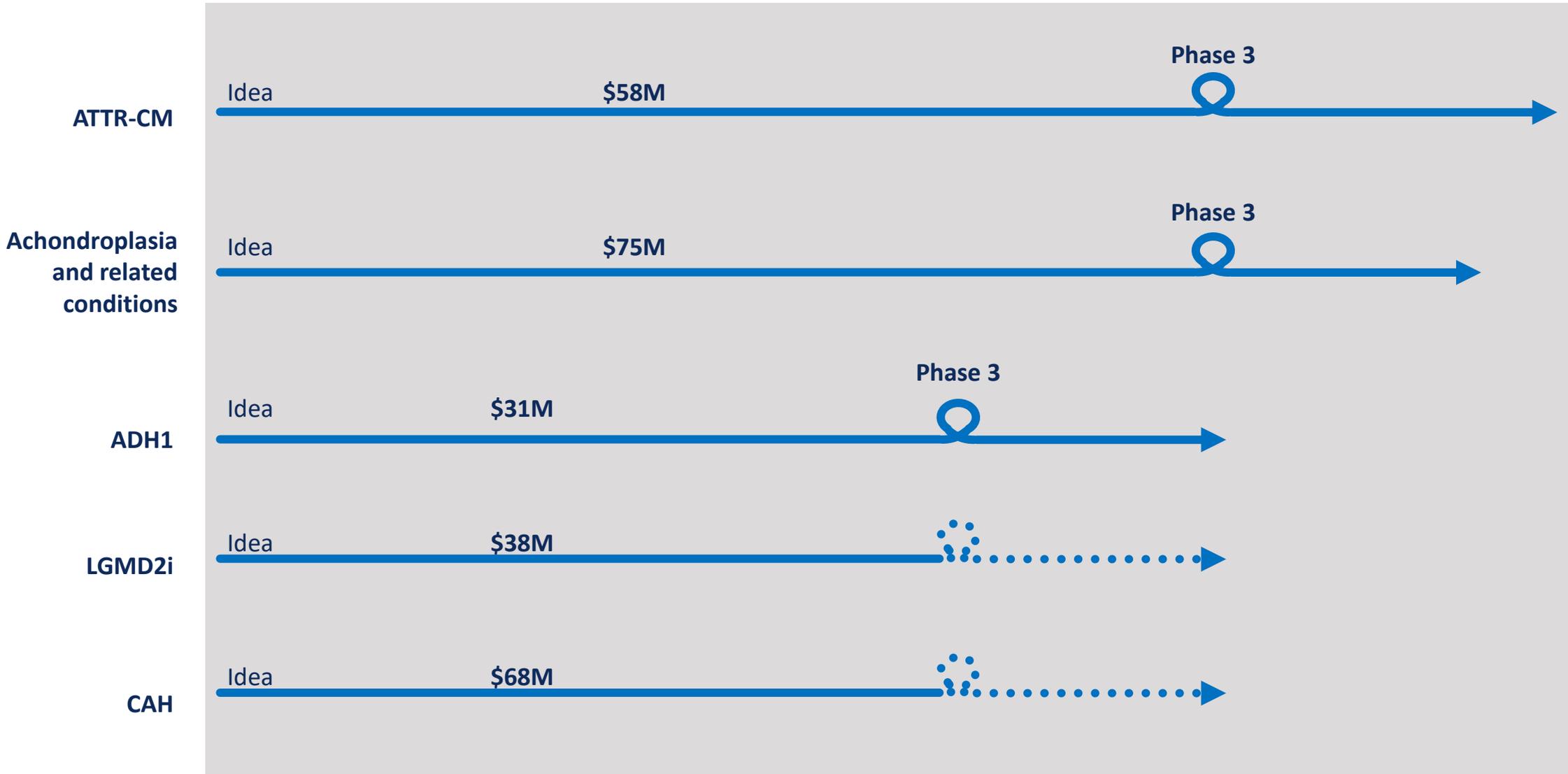
Infigratinib in cohort 5 has the strongest efficacy profile yet demonstrated in achondroplasia



- Cohort 5 has demonstrated a well-tolerated safety profile, with:
 - 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

- Changes in AHV indicate impact on bone growth, which may lead to impacts on medical complications, functionality, and proportionality, which we will continue to measure
- Based on these results **we have begun enrollment for a pivotal trial**
- BridgeBio is committed to delivering the value of infigratinib in all FGFR-driven skeletal dysplasias, and plans to **begin development in hypochondroplasia**

Program context



Note: Costs represent total BBIO investment from Inception to POC/P3 Initiation. CAH POC expected in 2H 2023

We are developing infigratinib as a treatment option for children with achondroplasia based on three key principles

Objectives

- ✓ **Maximize efficacy**
For all the manifestations of ACH—not just height— which matter for families and physicians
- ✓ **Demonstrate safety**
Avoiding hypotension & injection site reactions with no hyperphosphatemia or ocular effects
- ✓ **Avoid injections**
For children and families, to reduce burden and pain of treatment



Design principles

Target the condition directly at the source (FGFR3)

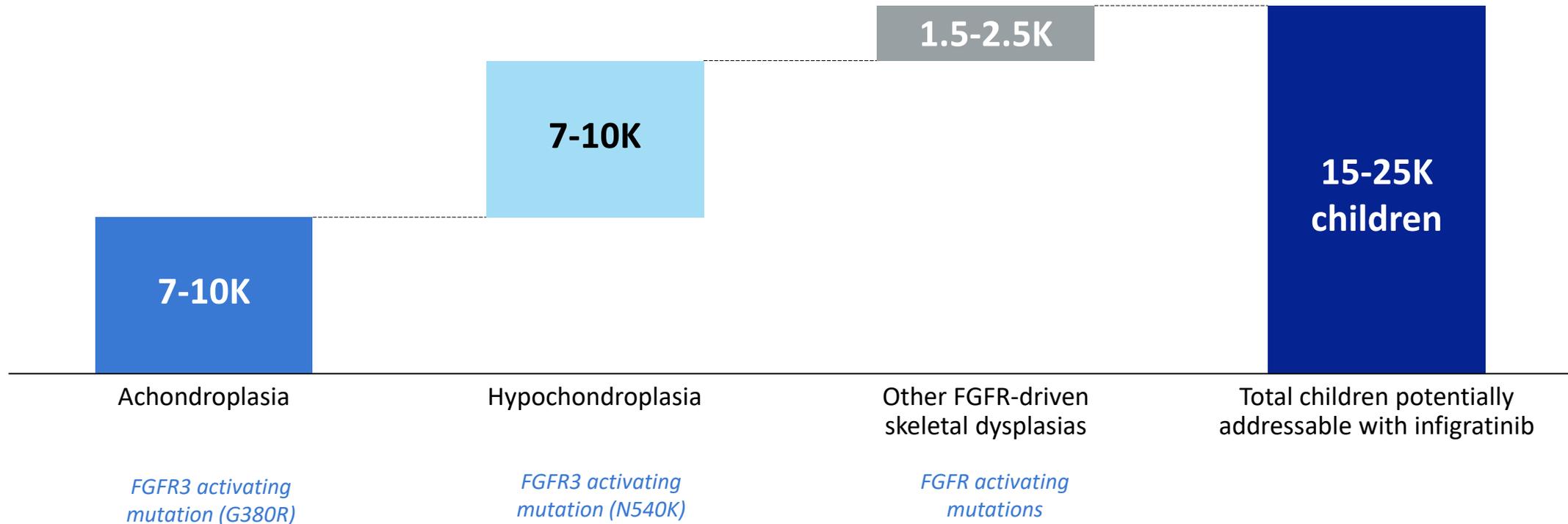
Use low doses to ensure safety

Provide an oral treatment option

Infigratinib is the only treatment option in development that could incorporate all of these features

Achondroplasia and related FGFR-driven skeletal dysplasias represent a large unmet medical need

Children eligible for FGFR inhibitor treatment in the US and Europe



BridgeBio is committed to developing a treatment option for children with FGFR-driven conditions

Achondroplasia comes with risk of serious medical complications

Life-threatening

- Sudden death (SIDS-like relative risk 50-fold in first 5 years)
- Foramen magnum stenosis with compression of the spinal cord
- Hydrocephalus

Spinal and orthopedic

- Thoracolumbar kyphosis
- Spinal stenosis
- Orthopaedic limb deformity

Functioning and general health

- Sleep apnea
- ENT, including recurrent ear infections with consequent hearing impairment
- Dental complications
- Obesity
- Challenges with activities of daily living due to short stature
- Pain (impact on function)

These medical complications represent a severe unmet need for people living with achondroplasia

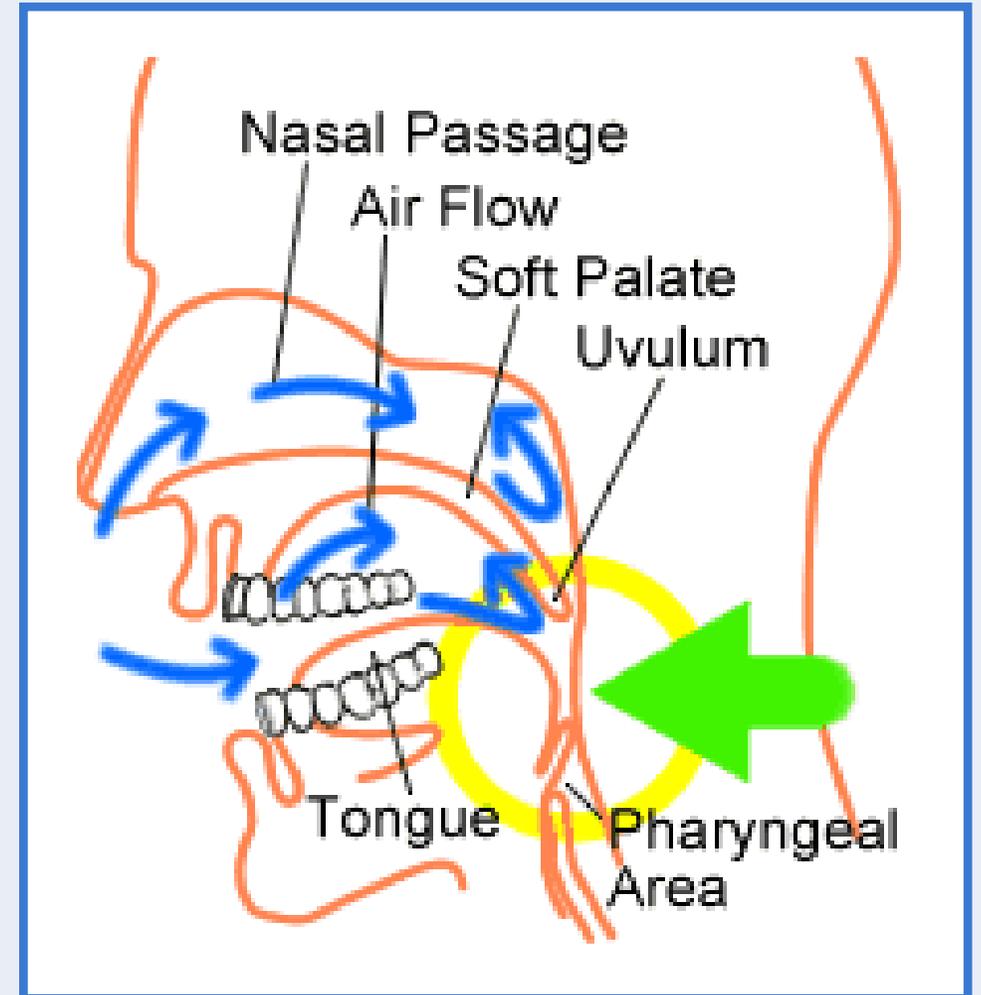
Stenosis of the foramen magnum is of particular concern

- The foramen magnum (FM) is the opening at the base of the skull which connects the brain with the spinal cord
- Stenosis of the FM can lead to compression in cervicomedullary structures, resulting in sleep-disordered breathing, hypotonia, hydrocephalus, and even sudden infant death
- FM compression is the cause of 50-fold higher infant mortality
- There is no consensus on evaluation and management, or markers
- Guidelines have been developed, but there is a major need for treatments which can address compression of the FM (White....Savarirayan, 2015, Am J Med Genet)



Increased risk of sleep apnea is another medical complication of achondroplasia with unmet need

- There is high prevalence of sleep apnea in children and adults living with achondroplasia
- It is best to use sleep labs/sleep studies
- Can present as obstructive versus central versus combined
- Relationship to symptoms

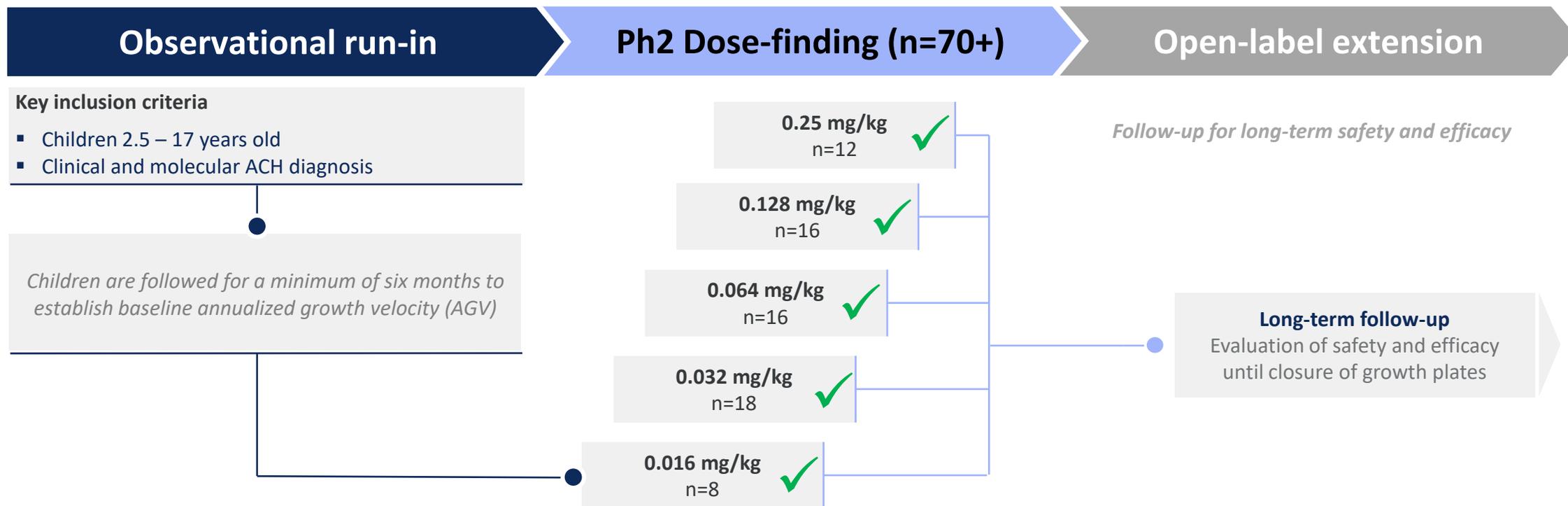


Children and adults living with achondroplasia have increased risk of debilitating spinal complications which require expert monitoring & treatment

- Thoraco-lumbar kyphosis
- Spinal stenosis (all levels)
- Chronic back pain
- Monitoring
- Assessment
- Treatment/management



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



Primary endpoints

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

Key secondary endpoints

- Change in upper body to lower body segment proportionality
- Patient-reported outcome measures
- Height-for-age z-score

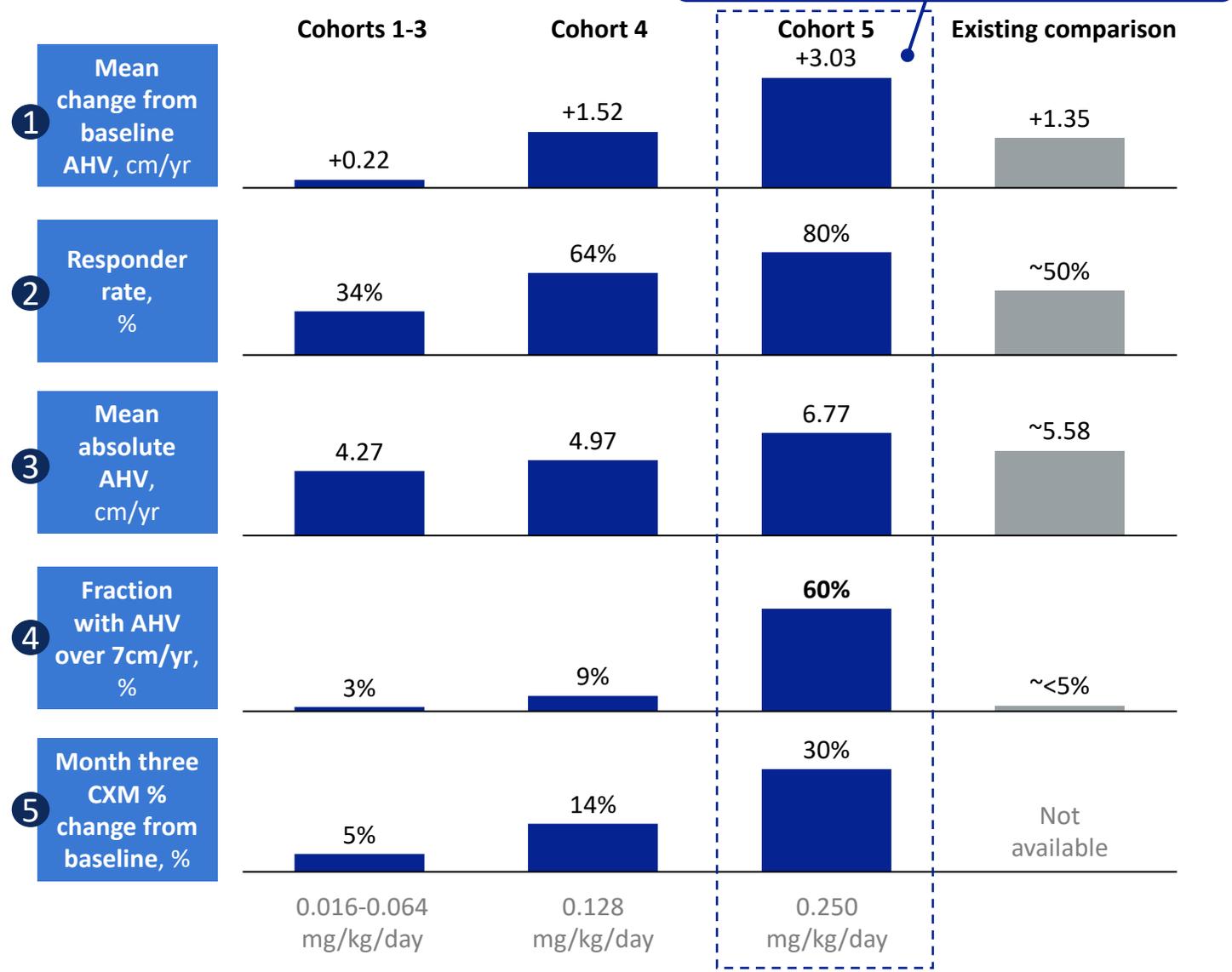
PROPEL2 cohort 5 participant demographics

	Cohort 5 0.25 mg/kg/day
N	12
Sex	
• Female	7 (58.3%)
• Male	5 (41.7%)
Age in years (Mean)	
• Mean ± Std Dev	7.24 ± 1.9
• Median (Range)	7.17 (4.9-11.3)
• 3 - <5	1 (8.3%)
• 5 - <8 years	7 (58.3%)
• ≥8 years	4 (33.3%)

	Cohort 5 0.25 mg/kg/day
Racial background	
• White	6 (50%)
• Black or African American	1 (8.3%)
• Asian	2 (16.7%)
• Multiple	1 (8.3%)
• Other	0
• Not reported	2 (16.7%)

Infigratinib in cohort 5 has the strongest efficacy profile yet demonstrated in achondroplasia

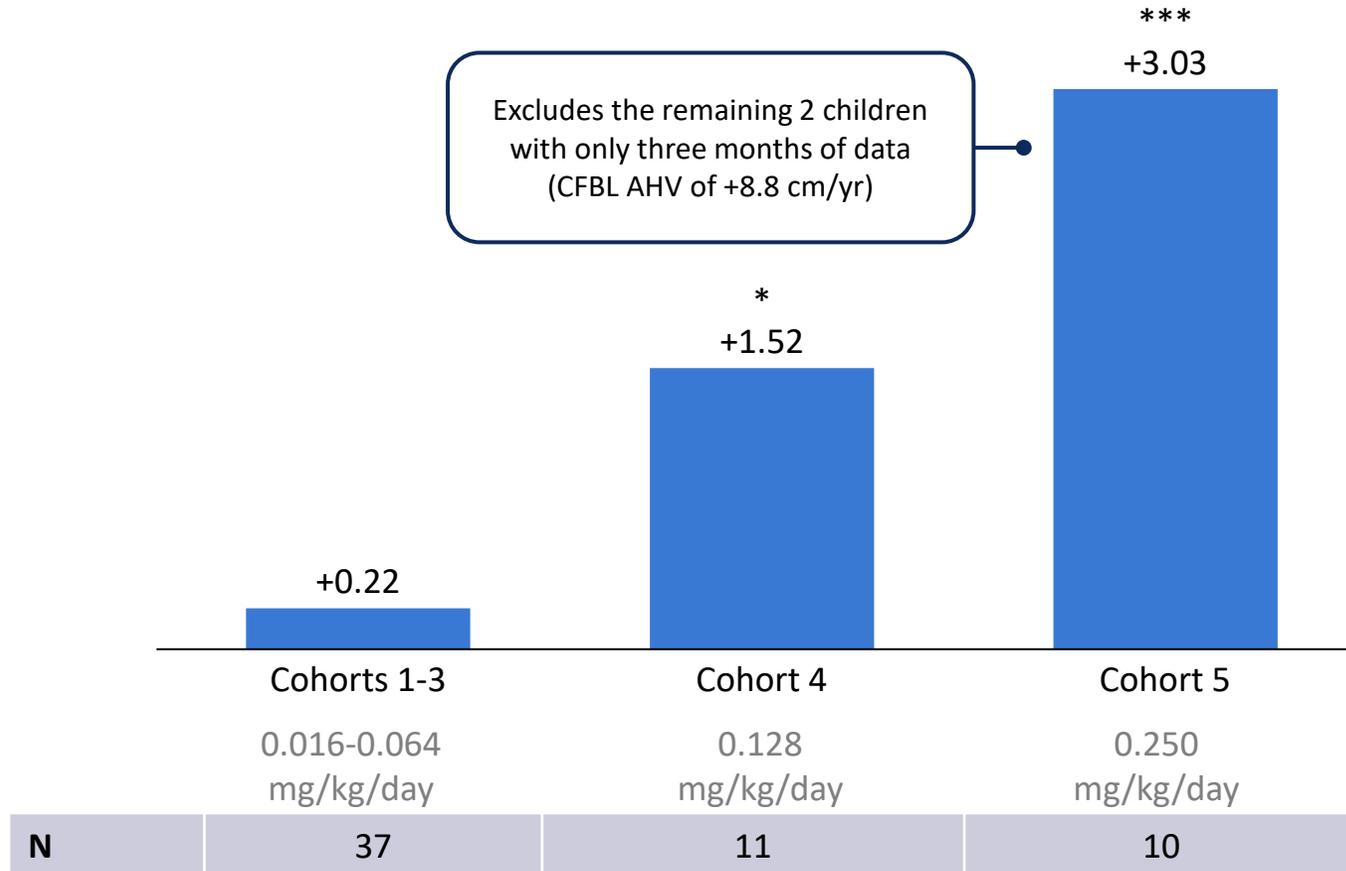
Excludes the remaining 2 children with only three months of data (CFBL AHV of +8.8 cm/yr)



- Infigratinib shows a **clear dose response** in change from baseline of AHV – the cohort 5 increase of **+3.03** in AHV is the largest ever published to our knowledge
 - Cohort 5 had a **broad impact**, with **80%** of children responding (Mean change from baseline AHV is **+3.81 cm/yr** among responders)
 - Cohort 5 also demonstrated a **strong effect**, with **60% of the children at an AHV over 7 cm/yr**, which is above the 99th percentile growth rate for children with achondroplasia of comparable age
 - Infigratinib also demonstrates a robust dose-response in absolute AHV, although we believe change from baseline AHV is a better measure that accounts for inter-patient variability
 - Collagen X marker, a biomarker of skeletal growth, further supports the robust dose-dependent response to infigratinib
-
- Cohort 5 has demonstrated a well-tolerated safety profile, with:
 - 0 severe adverse events
 - 0 adverse events assessed as drug-related
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 - No accelerated advancement of bone age or worsening of body proportions

1 Infigratinib demonstrates significant, dose-responsive increases in annualized height velocity compared to baseline

Mean change from baseline in annualized height velocity at M6, cm/yr



Cohort 5 (Children w/ M6 visits) N=10	
Female:Male ratio	6:4
Mean age (yr)	7.12
<5	10%
5 - <8	60%
8 - <11	20%
>=11	10%
Mean BL AHV (cm/yr)	3.73
<3.5	50%
3.5 to <4.5	30%
≥4.5	20%
Month 6 AHV	
Mean (SD)	6.77 (1.89)
Median	7.58

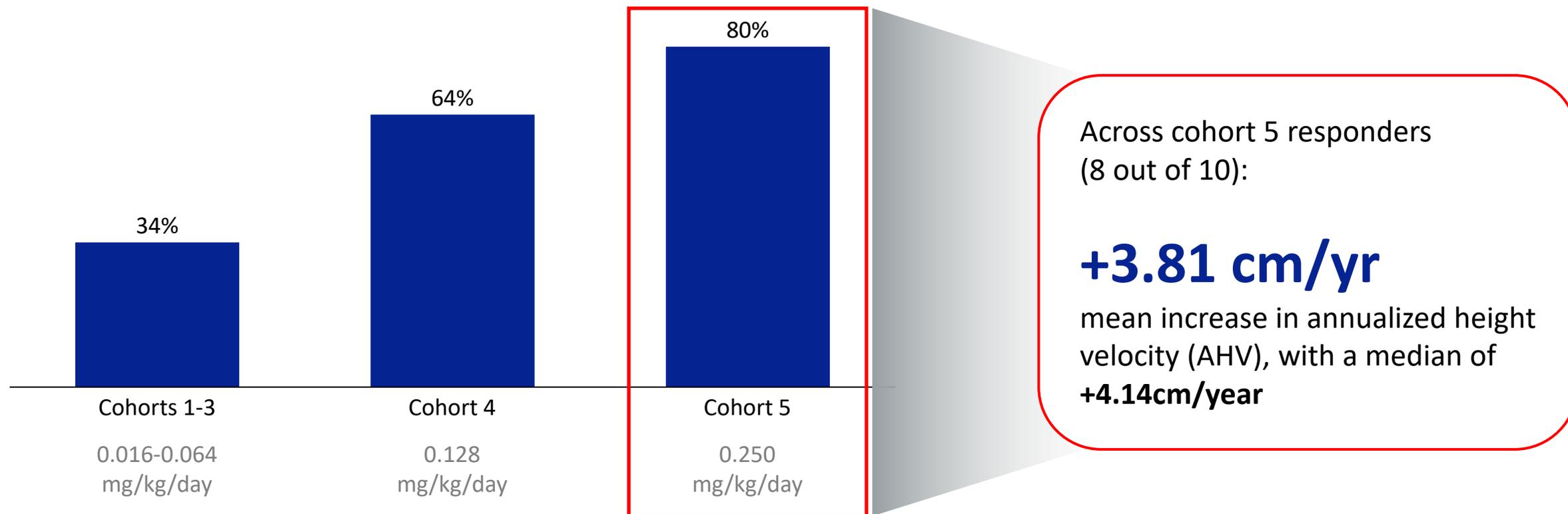
Note: Data shown is restricted to children ages 5 and greater – cohort 5 includes one child who turned 5 between screening and dosing. The remaining 2 children in cohort 5 have not yet reached their month six visit and are excluded from this analysis.

Source: Data on file

② 80% of children in cohort 5 responded to infigratinib, and responders had a mean AHV change from baseline of 3.81 cm/yr

Responder rate¹ at M6

% with an AHV increase of >25% from baseline

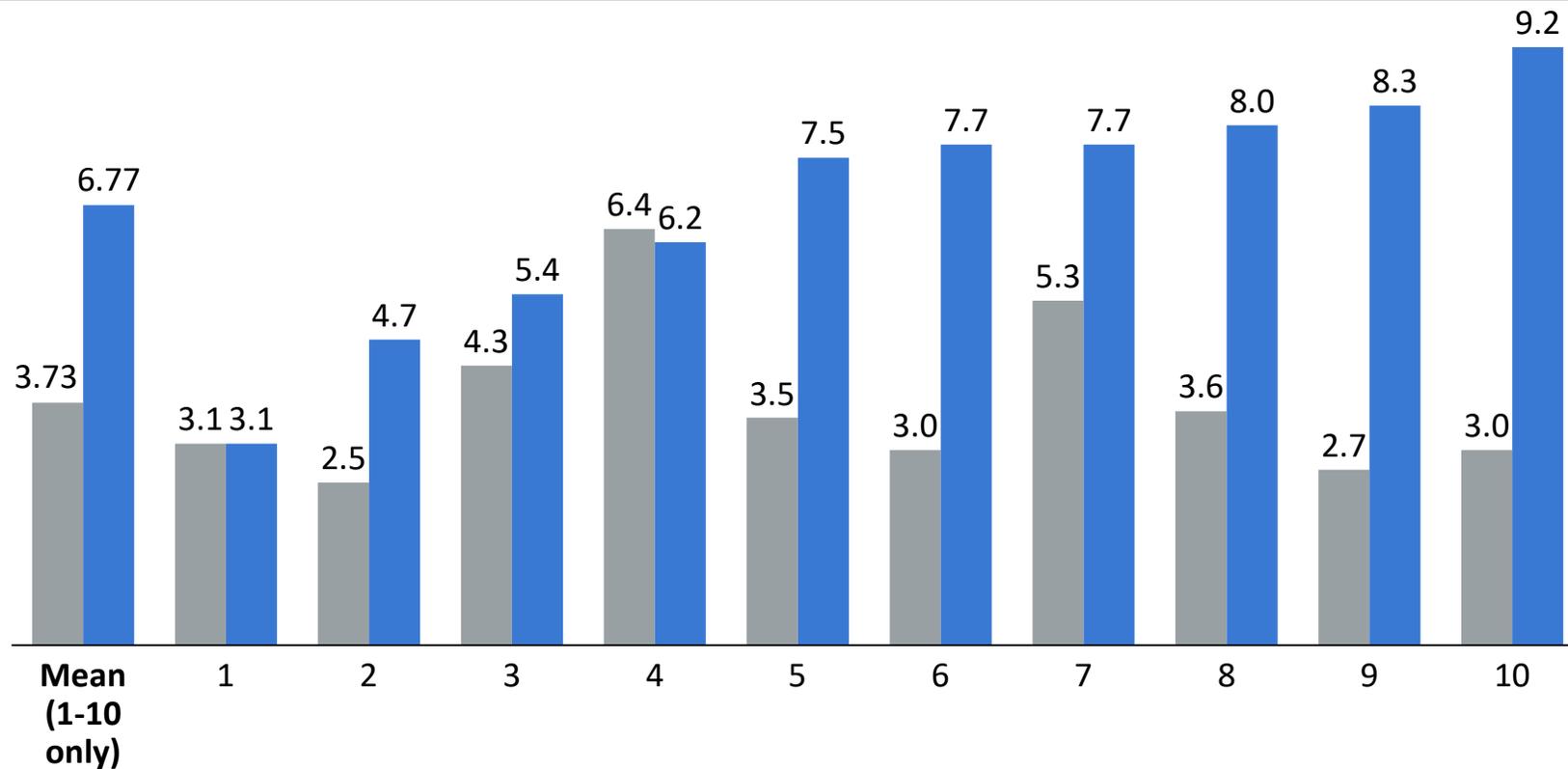


The response to treatment in cohort 5 is broad and robust

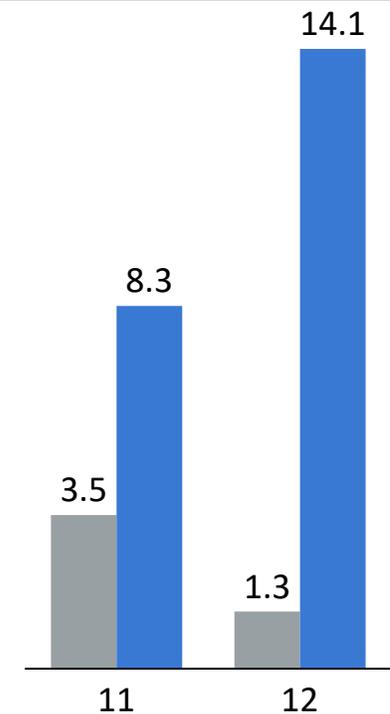
③ Individual-level data for cohort 5 participants shows the breadth and strength of the response; baseline AHV for the cohort is just under 4 cm/yr

Individual absolute AHV, participants with at least six months follow up (N=10), cm/yr

■ Baseline AHV
■ AHV on infiratinib

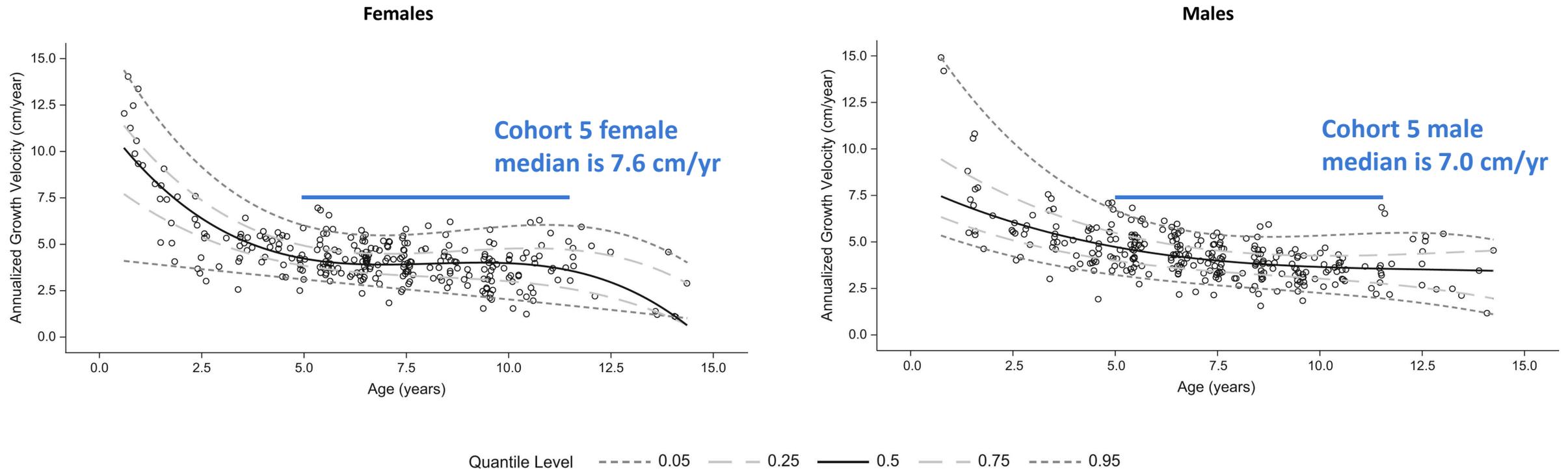


Individual absolute AHV, participants with three months follow up (N=2), cm/yr



④ The median AHV exceeds 7 cm/yr, which is above the 99th percentile growth rate for children of comparable age with achondroplasia

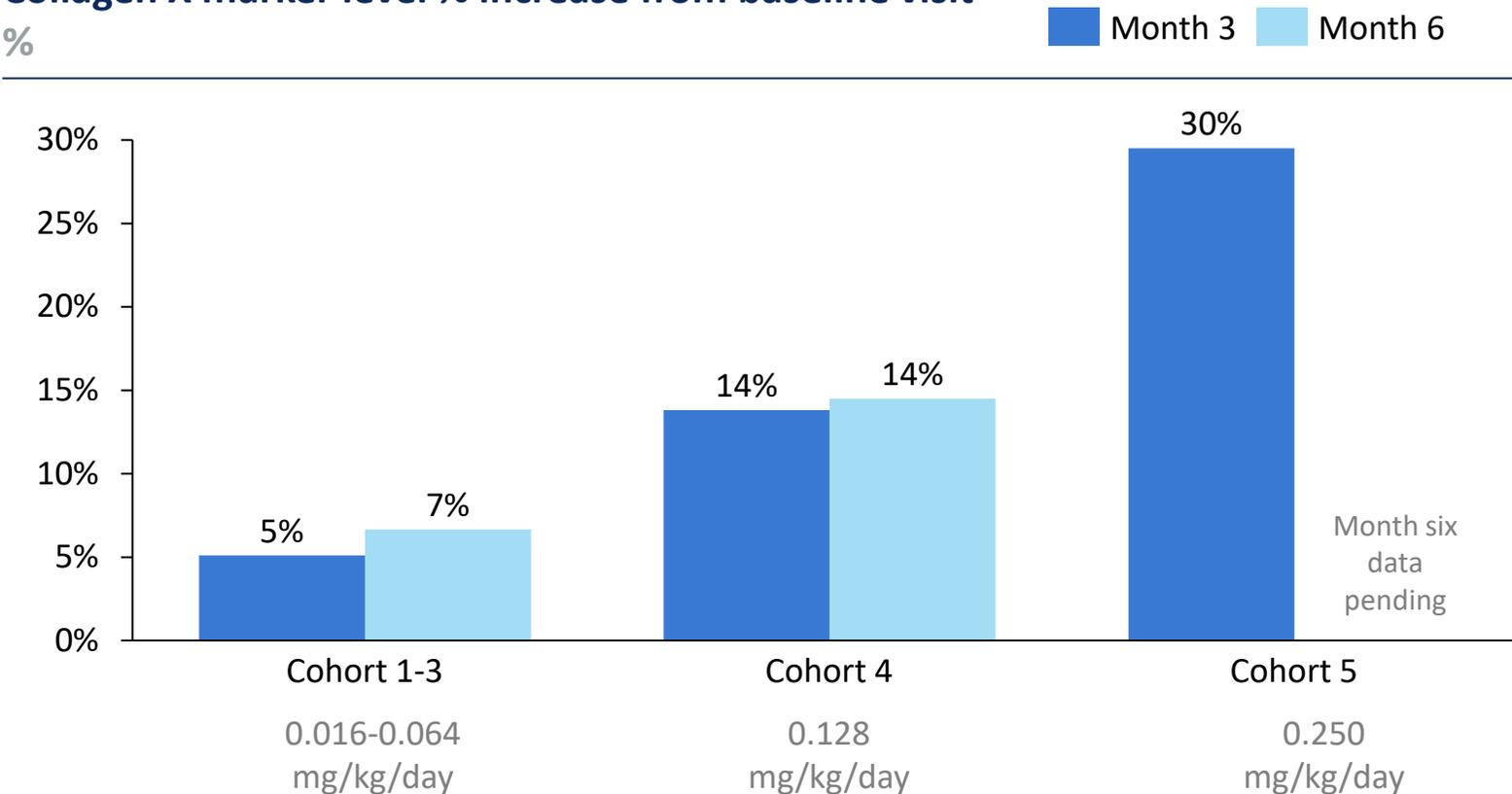
AHV of children living with achondroplasia, cm/yr



60% of children in cohort 5 had an AHV equal to or greater than 7 cm/yr. The median AHV overall was 7.6 cm/yr

⑤ Collagen X, a biomarker for growth in the long bone growth plates, supports the clinical results in suggesting a robust, dose-responsive effect

Collagen X marker level % increase from baseline visit
%



- Collagen X is synthesized and deposited in the hypertrophic zones of active growth plates
- Upon endochondral ossification, collagen X is degraded and the NC1 domain, the marker designated as CXM, is released into the circulation in proportion to overall growth plate activity
- Circulating CXM levels correlates well with growth velocity in real time

The increase in CXM also supports a dose-responsive relationship with cohort 5

Infigratinib was well-tolerated, with no study-drug related treatment-emergent adverse effects seen in cohort 5

Cohort 5 had a well-tolerated safety profile



- **0 serious adverse events (SAEs)**
- **0 subjects** experienced a treatment-emergent adverse event (TEAE) **assessed as related to study drug**
- 0 subjects had a **Grade 3 TEAE**
- 0 subjects presented a TEAE that led to **dose decrease**
- 0 subjects discontinued due to adverse events
- **0 ocular** adverse events
- **0 hyperphosphatemia** events
- No accelerated **bone age**
- No worsening of **body proportions**

With follow up out to 961 days, infigratinib continues to be well-tolerated, with no SAEs and no discontinuation due to AEs across all cohorts

Next steps



Enrollment for Phase 3 has started

- BridgeBio has begun enrolling children in the run-in for the Phase 3 pivotal trial, with 59 participant slots already requested



Regulatory interactions planned for mid-2023

- BridgeBio expects to complete an FDA End of Phase 2 meeting and an EMA scientific advice meeting in mid-2023



Committed to delivering the full potential of infigratinib

Building on the promising results in achondroplasia, BridgeBio has initiated plans to develop infigratinib in other FGFR-driven skeletal dysplasias, beginning with hypochondroplasia

- Hypochondroplasia has a similar prevalence to achondroplasia - the majority of cases are also due to gain-of-function variants in FGFR3
- Given the similarity of mechanism and physiology, development will be substantially de-risked

What do these results mean for the achondroplasia community and physicians?



Significant increase in growth and a broad response rate

The magnitude of effect we saw today could result in meaningful improvement in functional abilities



Well-tolerated safety profile

Seeing the lack of treatment-related adverse events of any kind in cohort 5 is very encouraging



Oral treatment option

The convenience, and child & family-friendliness of an oral medicine compared with an injection is very exciting



Optimistic about impacts on severe medical complications of achondroplasia

The impact on AHV seen today gives reason to be very optimistic about impacts on proportionality and severe medical complications, such as the impact on foramen magnum and spine which was seen for infigratinib in preclinical models. These impacts will be measured over time in the PROPEL studies.

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Thank you

