UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported):March 6, 2023

BridgeBio Pharma, Inc.
(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-38959**	**84-1850815**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

3160 Porter Dr., Suite 250 **Palo Alto, CA**	**94304**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (650) 391-9740

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	BBIO	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On March 6, 2023, BridgeBio Pharma, Inc. (the "Company") issued a press release announcing positive topline Phase 2 Cohort 5 data from its PROPEL2 clinical trial of the investigational therapy infigratinib in children with achondroplasia, a copy of which is furnished herewith as Exhibit 99.1 to this Current Report on Form 8-K. The Company intends to host a conference call and live webcast to discuss the interim clinical data on March 6, 2023 at 7:30 a.m. E.T. The Company has made available a slide presentation to accompany the call, a copy of which is being furnished as Exhibit 99.2 to this Current Report on Form 8-K. The Company undertakes no obligation to update, supplement or amend the materials attached hereto as Exhibit 99.2.

The information in this Item 7.01, including Exhibit 99.1 and Exhibit 99.2 attached hereto, is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended (the "Securities Act"), or the Exchange Act, except as expressly set forth by specific reference in such filing.

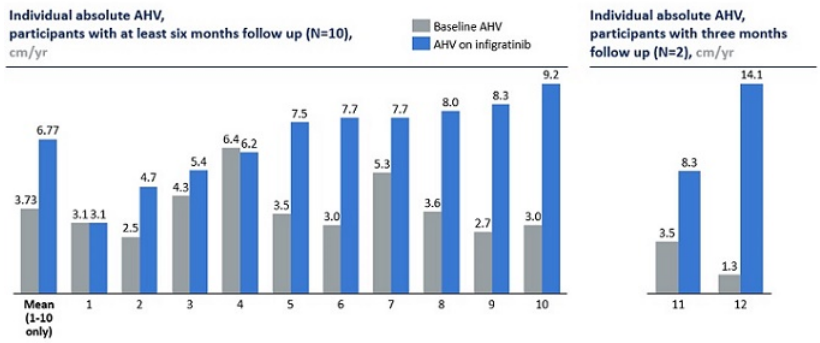
Item 8.01 Other Events.

On March 6, 2023, the Company announced positive topline results from PROPEL2, its Phase 2 clinical trial of infigratinib in children with achondroplasia. In the highest dose level (Cohort 5, 0.25mg/kg once daily), the mean change from baseline in annualized height velocity ("AHV") at six months was +3.03 cm/yr ($p = 0.0022$) for the first ten children with at least six months of follow-up in Cohort 5 as of the data cutoff date. The two remaining children who did not yet have six months of follow-up had a mean change from baseline in AHV of +8.8 cm/yr at three months. Infigratinib demonstrated clear dose-responsiveness when given as a single daily oral dose and was well-tolerated with no treatment-related adverse events (AEs) assessed in Cohort 5.

Key results from the clinical trial include:

- At the highest dose level evaluated to date (Cohort 5, 0.25 mg/kg once daily), the mean increase from baseline in AHV for the ten children that had six-month visits was +3.03 cm/yr ($p = 0.0022$). Individual data can be found in Figure 1 below.
- The baseline AHV for the ten children with six-month visits was in the expected range for children with achondroplasia at 3.73 cm/yr, increasing to 6.77 cm/yr after treatment.
- The two remaining children who did not yet have six months of follow-up had a mean change from baseline in AHV of +8.8 cm/yr at three months. The mean age for Cohort 5 was 7.24 years.
- 80% of the 10 children with six-month visits were responders, with an observed change from baseline AHV of at least 25%. Among the responders, the average change from baseline in AHV was +3.81 cm/yr.
- Preliminary analysis of Collagen X (CXM) levels also showed a statistically significant increase from baseline in Cohort 5 ($p=.03$). CXM is a widely accepted biomarker of chondrocyte-driven growth and further validates the response to infigratinib.
- Combined with the previously reported Cohort 4 change from baseline in AHV value of +1.52 cm/yr, the Cohort 5 data demonstrated a strong dose response for infigratinib.
- Median follow-up across all cohorts was 71.1 weeks. As of the cutoff date, infigratinib has shown a well-tolerated safety profile, with no study drug-related treatment emergent adverse events (TEAEs) in Cohort 5. No serious adverse events (SAEs) or discontinuations due to AEs were reported in any cohort.

Figure 1



Based on the positive results to date, the Company has started enrolling children in the run-in for a Phase 3 trial. Additionally, the Company expects to initiate clinical development for infigratinib in hypochondroplasia, a skeletal dysplasia closely related to achondroplasia and similarly driven by FGFR3 gain-of-function variants. The Company previously presented preclinical data for hypochondroplasia at the ENDO 2022 Annual Conference and the American Society of Human Genetics 2022 Annual Meeting.

Cautionary Note Regarding Forward Looking Statements

This Current Report on Form 8-K and certain of the materials filed herewith contain forward-looking statements. Statements in this Current Report on Form 8-K or the materials furnished or filed herewith may include statements that are not historical facts and are considered forward-looking within the meaning of Section 27A of the Securities Act, and Section 21E of 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. The Company intends 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 the Company's programs and product candidates, including its clinical development program for infigratinib in achondroplasia, the timing and success of its clinical development programs, the progress of its ongoing and planned clinical trials of infigratinib in achondroplasia and in hypochondroplasia, including its enrollment of patients in, and plans to initiate conduct, a Phase 3 trial for infigratinib in achondroplasia and to initiate clinical development of infigratinib in hypochondroplasia, its planned interactions with regulatory authorities, the availability of data from its clinical trials of infigratinib, the duration of the intellectual property protection available for infigratinib, and the timing of these events, reflect the Company's current views about its plans, intentions, expectations and strategies, which are based on the information currently available to the Company and on assumptions it has made. Although the Company believes that its plans, intentions, expectations and strategies as reflected in or suggested by those forward-looking statements are reasonable, it 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 the Company's clinical trials not being indicative of final data, the design and success of ongoing and planned clinical trials, difficulties with enrollment in its clinical trials, adverse events that may be encountered in its clinical trials, the FDA or other regulatory agencies not agreeing with its regulatory approval strategies, components of its 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 its overall business operations and expectations, as well as those risks set forth in the Risk Factors section of its Annual Report on Form 10-K for the year ended December 31, 2022 and its other filings with the U.S. Securities and Exchange Commission. Moreover, the Company operates 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 the Company's management as of the date of this Current Report on Form 8-K, 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, the Company assumes no obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

Item 9.01 Financial Statements and Exhibits.

99.1	Press release issued by BridgeBio Pharma, Inc. on March 6, 2023, furnished herewith.
99.2	Corporate presentation, dated March 6, 2023, furnished herewith.
104	Cover Page Interactive Data File (embedded within Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

BRIDGEBIO PHARMA, INC.

Date: March 6, 2023

By: /s/ Brian C. Stephenson
Brian C. Stephenson
Chief Financial Officer

Exhibit 99.1

BridgeBio Announces Positive Phase 2 Cohort 5 Results of Infigratinib in Achondroplasia Demonstrating Mean Increase in Annualized Height Velocity of 3.03 cm/year with No Treatment-related Adverse Events

- In the highest dose level (Cohort 5, 0.25 mg/kg once daily), the mean change from baseline in annualized height velocity (AHV) at six months was +3.03 cm/yr (p = 0.0022) for the first 10 children with at least six months of follow-up in Cohort 5. The two remaining children who have not yet had six months of follow-up have a mean change from baseline in AHV of +8.8 cm/yr based on three months data

- 80% of children at six months were responders, as defined by an increase from baseline AHV of at least 25%. The mean change from baseline in AHV of responders was 3.81 cm/yr

- As a result of treatment, the median absolute AHV reached 7.6 cm/yr, which is beyond the 99th percentile of growth for children living with achondroplasia

- Infigratinib demonstrated clear dose-responsiveness as a single daily oral therapy and was well-tolerated with no adverse events (AEs) assessed as treatment-related in Cohort 5

- Based on the positive Phase 2 results, BridgeBio has started to enroll children for a pivotal Phase 3 trial

- BridgeBio expects to initiate clinical development of infigratinib for hypochondroplasia, a skeletal dysplasia closely related to achondroplasia and driven by fibroblast growth factor receptor 3 (FGFR3) gain-of-function variants, and will continue to explore the impact on the medical and functional complications of achondroplasia in future studies of infigratinib

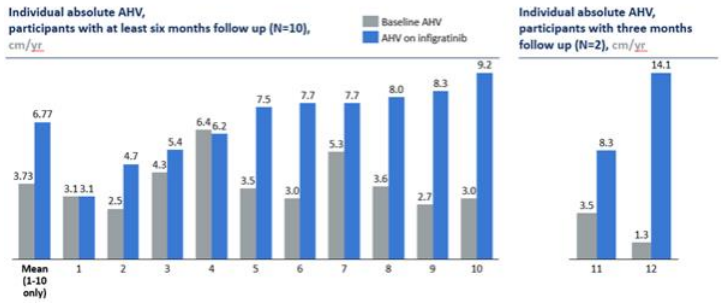
PALO ALTO, CA – March 6, 2023 — BridgeBio Pharma, Inc. (Nasdaq: BBIO) (BridgeBio), a commercial-stage biopharmaceutical company focused on genetic diseases and cancers, today announced positive results from PROPEL2, a Phase 2 trial of the investigational therapy infigratinib in children with achondroplasia, demonstrating potential best-in-class efficacy and a clean safety profile. Infigratinib is an oral small molecule designed to inhibit FGFR3 and target achondroplasia at its source. BridgeBio will also host an investor call on March 6, 2023, at 7:30 am ET to discuss the results from the Phase 2 study.

To date, key results from the clinical trial include:

- At the highest dose level evaluated to date (Cohort 5, 0.25 mg/kg once daily), the mean increase from baseline in annualized height velocity (AHV) for the 10 children that have had six-month visits was +3.03 cm/yr (p = 0.0022). Individual data can be found in Figure 1 below
- The baseline AHV for the 10 children with six-month visits was in the expected range for children with achondroplasia at 3.73 cm/yr, rising to 6.77 cm/yr after treatment

- The two remaining children who have not yet had six months of follow-up have a mean change from baseline in AHV of +8.8 cm/yr at three months. The mean age for the cohort was 7.24 years
- 80% of the 10 children with six-month visits were responders, with a change from baseline AHV of at least 25%. Among the responders, the average change from baseline in AHV was +3.81 cm/yr
- Preliminary analysis of Collagen X (CXM) levels also saw a statistically significant increase from baseline in Cohort 5 (p=.03). CXM is the gold-standard biomarker of chondrocyte-driven growth and further validates the robust response to infigratinib
- Combined with the previously reported Cohort 4 change from baseline in AHV value of +1.52 cm/yr, the Cohort 5 data demonstrate a strong dose response for infigratinib
- Median follow-up across all cohorts is 71.1 weeks. To date, the study has shown a well-tolerated safety profile, with no study drug related treatment emergent adverse events (TEAEs) in Cohort 5. No serious adverse events (SAEs) or discontinuations due to AEs were reported in any cohort

Figure 1



"The data from Cohort 5 has shown a major impact on annualized height velocity for children with achondroplasia and an excellent safety profile to date. We are thrilled to see these promising results and consider that AHV increases of this magnitude will translate to improvements in the medical and functional complications of achondroplasia. We are excited about taking the next steps towards initiating a Phase 3, pivotal clinical trial," said Professor Ravi Savarirayan, M.D., Ph.D., clinical geneticist and group leader of molecular therapies research at the Murdoch Children's Research Institute in Australia, the lead investigator for PROPEL2.

“I am encouraged by these efficacy and safety results and thankful for our partnership with the physicians, community advocates, children, and families in this study. These results reach a new tier of efficacy, and coupled with our differentiated safety and convenience profile, provide us the opportunity to serve children with achondroplasia and other skeletal dysplasias. We look forward to exploring the potential of infigratinib on the wider medical and functional impacts of achondroplasia, hypochondroplasia and other skeletal dysplasias, which hold significant unmet needs for families,” said Neil Kumar, Ph.D., founder and CEO of BridgeBio.

Based on the positive results to date, BridgeBio has started enrolling children in the run-in for a Phase 3 trial. Additionally, BridgeBio expects to initiate clinical development for infigratinib in hypochondroplasia, a skeletal dysplasia closely related to achondroplasia and similarly driven by FGFR3 gain-of-function variants. BridgeBio has previously presented promising preclinical data for hypochondroplasia at ENDO 2022 and ASHG 2022.

“Achondroplasia can have broad impact that affects the whole person. People can experience a range of medical complications, including foramen magnum stenosis, spinal stenosis, cardiovascular complications, sleep-disordered breathing, obesity, and sometimes, individuals may need surgical intervention. In addition to the potential medical and physical complications, people with achondroplasia may also experience social and emotional impacts as a result of living with the condition. We are encouraged by BridgeBio’s mission to develop a therapy with the potential to address this as a whole-person condition that affects the overall health, independent function, and quality of life of those with achondroplasia,” said Dianne Kremidas, executive director of The MAGIC Foundation.

Infigratinib has IP protection out to at least 2041.

Webcast Information

BridgeBio will host an investor call and simultaneous webcast to discuss the Phase 2 data from Cohort 5 of infigratinib in children with achondroplasia on March 6, 2023 at 7:30 am ET. A link to the webcast may be accessed from the event calendar page of BridgeBio’s website at https://investor.bridgebio.com/. A replay of the conference call and webcast will be archived on the Company’s website and will be available for at least 30 days following the event.

About Achondroplasia

Achondroplasia is the most common cause of disproportionate short stature, affecting approximately 55,000 people in the United States (US) and European Union (EU), including up to 10,000 children and adolescents with open growth plates. Achondroplasia impacts overall health and quality of life, leading to medical complications such as obstructive sleep apnea, middle ear dysfunction, kyphosis, and spinal stenosis. The condition is uniformly caused by an activating mutation in FGFR3.

About BridgeBio Pharma, Inc.

BridgeBio Pharma (BridgeBio) is a commercial-stage biopharmaceutical company founded to discover, create, test and deliver transformative medicines to treat patients who suffer from genetic diseases and cancers with clear genetic drivers. BridgeBio’s pipeline of development programs ranges from early science to advanced clinical trials. BridgeBio was founded in 2015 and its team of experienced drug discoverers, developers and innovators are committed to applying advances in genetic medicine to help patients as quickly as possible. For more information visit **bridgebio.com** and follow us on **LinkedIn** and **Twitter**.

BridgeBio Pharma, Inc. Forward-Looking Statements

This press release contains forward-looking statements. Statements in this press release 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 press release, 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.

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(650)-789-8220

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(415)-694-0979

Exhibit 99.

bridgebio

hope through
rigorous science

PROPEL2 topline results

March 6th, 2023

Forward-looking statements

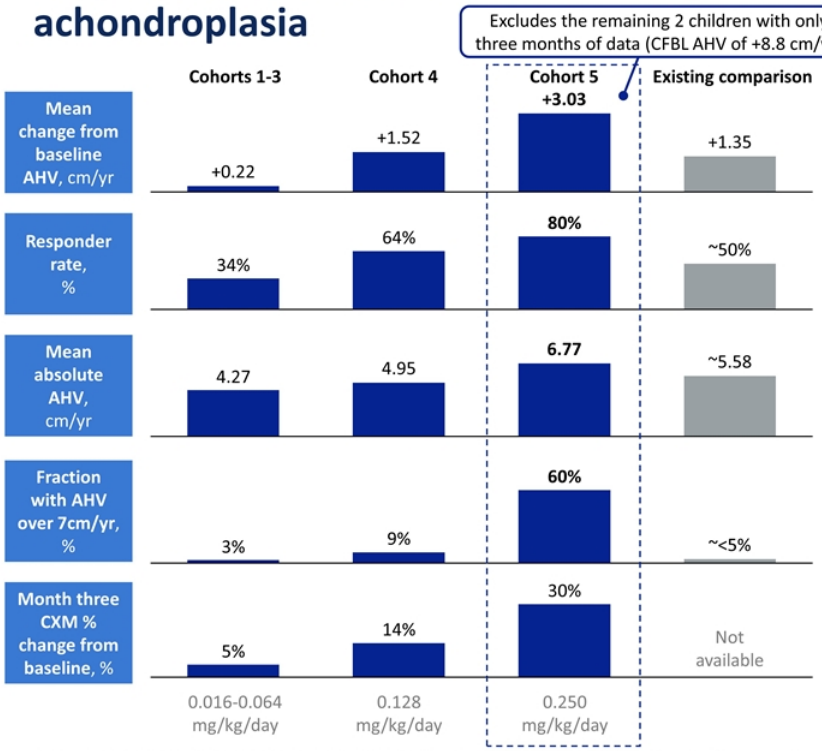
This presentation contains forward-looking statements. Statements in this presentation may include statements that are not historical facts and are considered forward-looking within the meaning of Section 27A of the Securities Act of 1933, as amended (the Securities Act), and Section 21E of the Securities 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

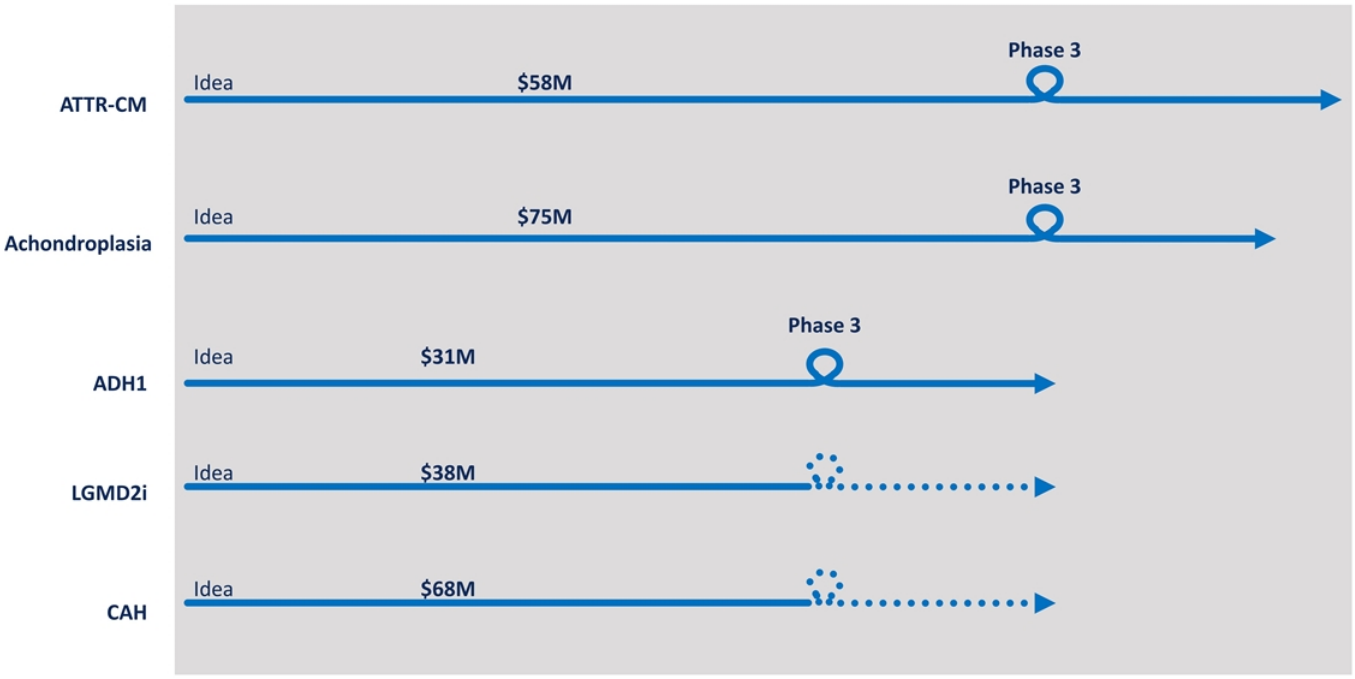


- **Cohort 5 has demonstrated a well-tolerated safety profile**, with:
  - 0 severe adverse events
  - 0 adverse events assessed as drug-related
  - 0 discontinuations due to adverse events
  - No accelerated advancement of bone age or worsening of body proportions

- 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**

Note: All cohorts are restricted to children ages 5 and greater – cohort 5 includes one child who turned 5 between screening and dosing. Responders are defined as having at least a 25% increase from baseline in AHV. Month six CXM results are still pending
Source: Data on file; Savarirayan et al 2019 NEJM; Savarirayan et al 2020 Lancet; Vosoritide M12 data from summary basis of approval

Big wheels keep on turning



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

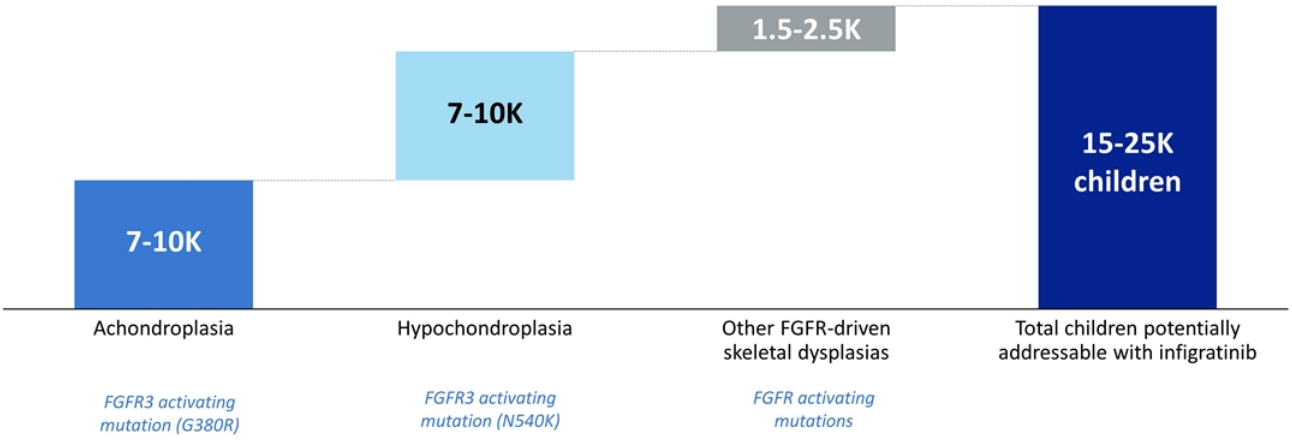
We are developing infigratinib as a treatment option for children with achondroplasia based on three key principles

Objectives		Design principles
✓ **Maximize efficacy** For all the manifestations of ACH—not just height– which matter for families and physicians	→	**Target the condition directly at the source (FGFR3)**
✓ **Demonstrate safety** Avoiding hypotension & injection site reactions with no hyperphosphatemia or ocular effects	→	**Use low doses to ensure safety**
✓ **Avoid injections** For children and families, to reduce burden and pain of treatment	→	**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

Source: CDC birth estimates; EU Eurostats birth estimates; Foreman et al 2020 Am J Med Genet; Bober et al 2020 Gene Reviews; Wenger et al 2020 Gene Reviews; Al-Namman et al 2019 J Oral Biol Craniofac Res

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

Source: Savarirayan et al. 2022 Nat Rev Endocrinol

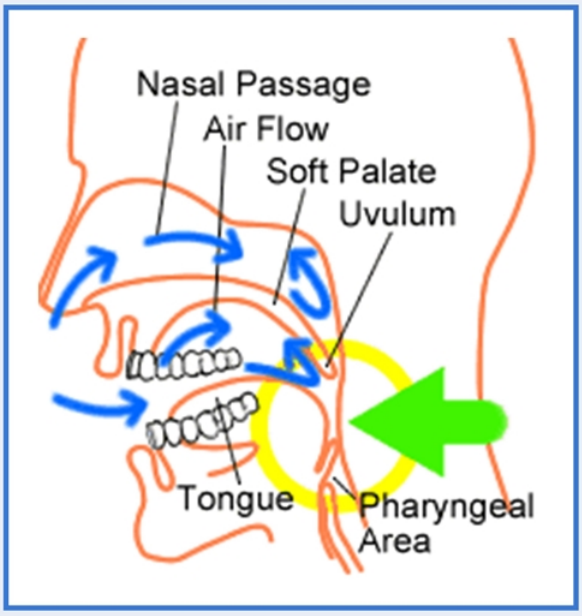
Stenosis of the foramen magnum is of particular concern

- 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)

Source: White….Savarirayan 2015 Am J Med Genet

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

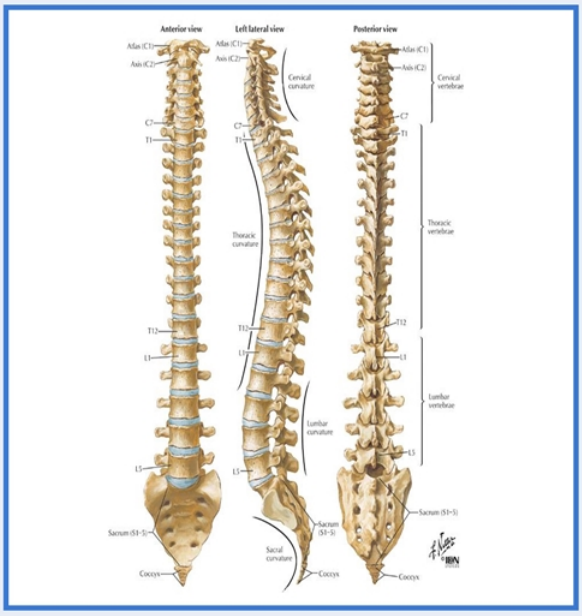
- There is high prevalence of sleep apnea in children and adults living with achondroplasia
- It is best to use sleep labs/sleep studies
- Can present as obstructive versus central versus combined
- Relationship to symptoms



Source: White….Savarirayan 2015 Am J Med Genet

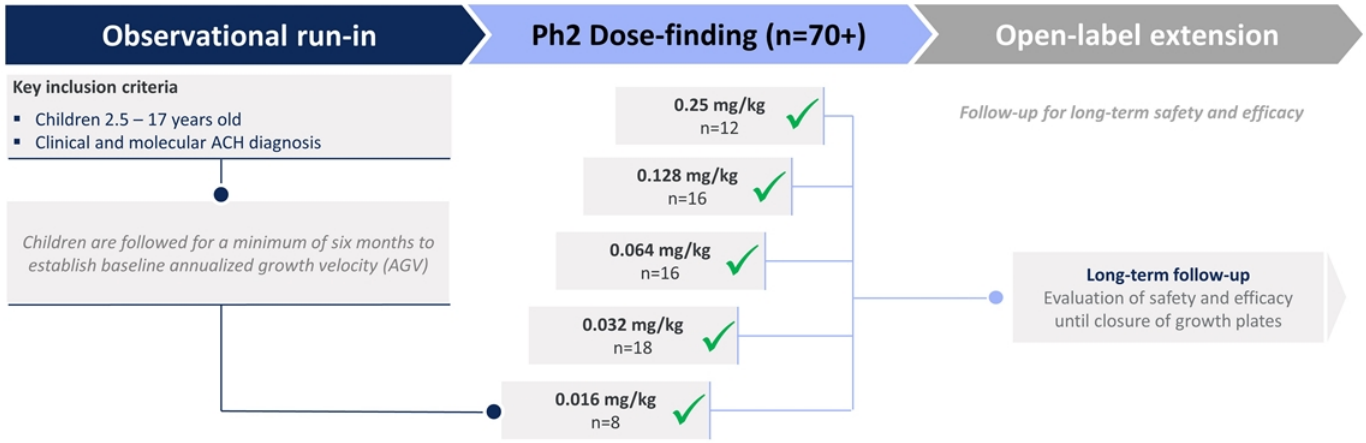
Children and adults living with achondroplasia have increased risk of debilitating spinal complications which require expert monitoring & treatment

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



Source: Fredwall et al 2021 Orphanet J Rare Dis

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

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

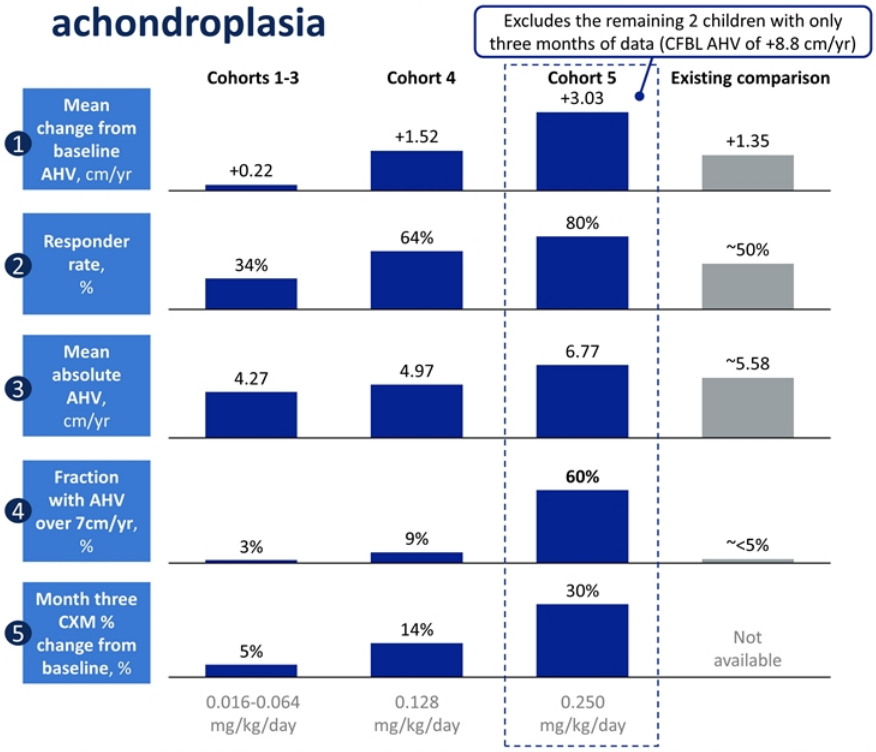
PROPEL2 cohort 5 participant demographics

	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%)

Source: Data on file Note: race information was not collected in France

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



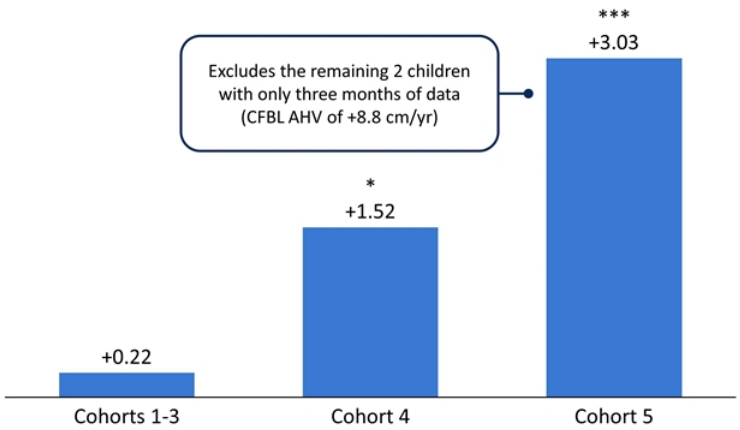
- Infigratinib shows a **clear dose response** in change from baseline of AHV – the cohort 5 increase of **+3.03** in AHV is the largest ever published to our knowledge
- Cohort 5 had a **broad impact**, with **80%** of children responding (Mean change from baseline AHV is **+3.81 cm/yr** among responders)
- 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
  - 0 discontinuations due to adverse events
  - No accelerated advancement of bone age or worsening of body proportions

Note: All cohorts are restricted to children ages 5 and greater – cohort 5 includes one child who turned 5 between screening and dosing. Responders are defined as having at least a 25% increase from baseline in AHV. Month six CXM results are still pending
Source: Data on file; Savarirayan et al 2019 NEJM; Savarirayan et al 2020 Lancet; Vosoritide summary basis of approval

❶ 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



	Cohorts 1-3 (0.016-0.064 mg/kg/day)	Cohort 4 (0.128 mg/kg/day)	Cohort 5 (0.250 mg/kg/day)
N	37	11	10

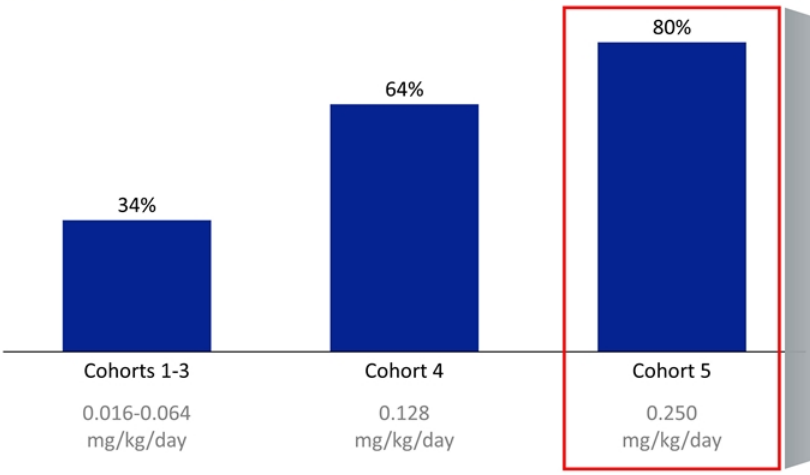
Cohort 5 (Children w/ M6 visits) N=10	
Female:Male ratio	**6:4**
Mean age (yr)	**7.12**
<5	10%
5 - <8	60%
8 - <11	20%
>=11	10%
Mean BL AHV (cm/yr)	**3.73**
<3.5	50%
3.5 to <4.5	30%
≥4.5	20%
Month 6 AHV	
Mean (SD)	**6.77 (1.89)**
Median	**7.58**

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

❷80% of children in cohort 5 responded to infigratinib, and responders had a mean AHV change from baseline of 3.81 cm/yr

Responder rate[1] at M6

% with an AHV increase of >25% from baseline



Across cohort 5 responders (8 out of 10):

+3.81 cm/yr

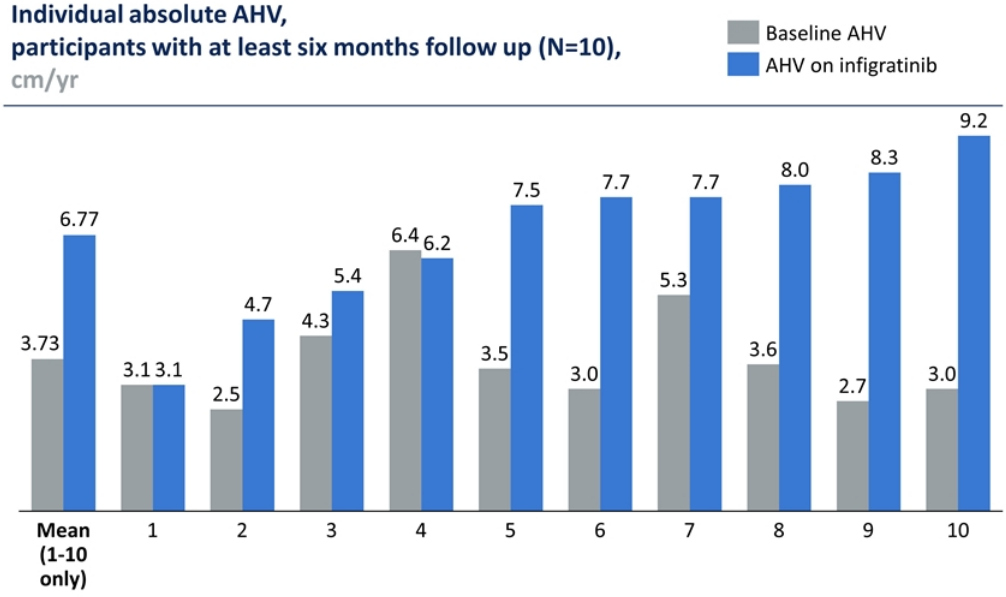
mean increase in annualized height velocity (AHV), with a median of **+4.14cm/year**

The response to treatment in cohort 5 is broad and robust

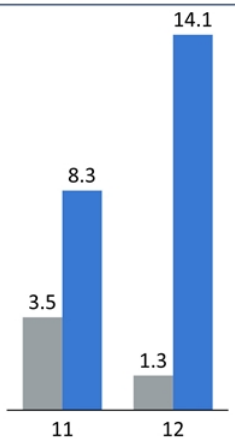
[1]Responder defined as having a change from baseline AHV of 25% or greater
Source: Data on file.

❸ 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



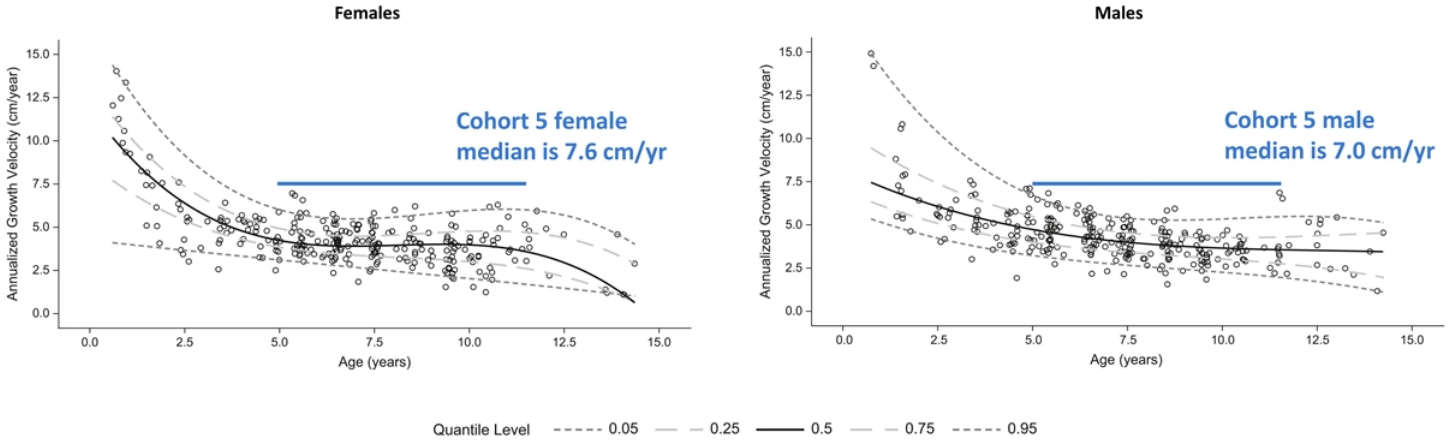
Individual absolute AHV, participants with three months follow up (N=2), cm/yr



Source: Data on file

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

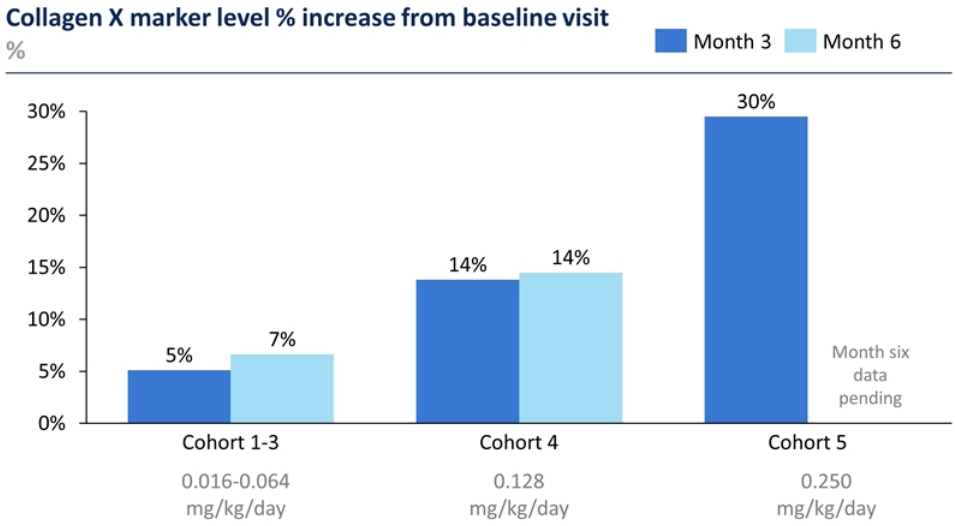
AHV of children living with achondroplasia, cm/yr



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

Source: Savarirayan et al, Genet Med 2022; cohort 5 data on file

❺ 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 is synthesized and deposited in the hypertrophic zones of active growth plates
- Upon endochondral ossification, collagen X is degraded and the NC1 domain, the maker 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

Source: Data on file; Coghlan et al 2017; Linsenmayer et al 1988

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

Source: Data on file

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.

bridgebio

hope through
rigorous science

Thank you