Pharmaceutical overview for achondroplasia - July 2026

Purpose & Scope

This updated review (July 2026) is intended to provide clear, accessible information for LPA members and families as they learn about the evolving research and treatment landscape in achondroplasia. It is designed to support informed discussions and shared decision-making with qualified healthcare professionals; it is not medical advice. Information on treatments for other skeletal dysplasias, including hypochondroplasia, will be addressed in separate resources as the evidence base continues to evolve.

The review focuses primarily on pharmaceutical therapies that aim to influence the **biological pathways involved in bone growth in achondroplasia**, particularly those related to the **FGFR3 pathway or downstream signaling**.

LPA's Position

LPA recognizes the complexity and sensitivity of this topic for our community. As an organization, our role is to provide social support, advocacy, and access to accurate information. **This role does not mean that LPA is categorically opposed to medical research or treatment. Across skeletal dysplasias, we recognize the important role that medical advances can play in addressing serious health complications, reducing pain and healthcare burden, preserving function, and/or improving quality of life.**

We recognize that decisions about healthcare, including pharmaceutical therapies, are deeply personal and shaped by a wide range of values, experiences, and goals. There is not one approach or decision that is right for every individual or family. Some may pursue treatment, others may not, and many may continue to weigh evolving information over time. **LPA respects the choices of parents and individuals regarding their healthcare decisions and welcomes all individuals and families to be part of LPA, regardless of paths they choose.**

LPA aims to help provide accurate information to support truly informed decision making. Recognizing that these decisions can feel complex and, at times, overwhelming, LPA is committed to helping its members access clear, balanced, and accurate information.

LPA also advocates for research that reflects the priorities identified by our community and encourages an approach that focuses on healthcare outcomes beyond growth velocity. As a support organization, we believe that focusing on growth velocity is a pharmaceutical solution for a societal problem. We want to reframe these priorities in research to the most meaningful ones to our members, such as reducing spinal stenosis, sleep apnea, corrective surgeries, and other interventions that would improve

quality of life. **As medical science moves forward, we will continue to advocate that researchers are mindful of our commitment to the value of dwarf pride and its contributions to biological, social, and cultural diversity.** [1,2]

Executive Summary

Since our original 2021–2022 review, the treatment landscape for achondroplasia has evolved to include **two FDA-approved pharmaceutical treatments**, with additional therapies in late-stage clinical development.

In the United States, **Voxzogo (vosoritide)**[3] and **Yuviwel (navepegritide; developed as TransCon CNP)**[4] are both FDA-approved treatments intended to increase linear growth in individuals with achondroplasia who have open growth plates (often referred to as "open epiphyses"). Both therapies act through the C-type natriuretic peptide (CNP) pathway, which is involved in endochondral bone growth, but differ in molecular design, approved age ranges, dosing frequency, and the extent of available clinical and real-world evidence.

Both approvals are based on data that demonstrates improvements in **annualized growth velocity (AGV)**, a measure of how quickly an individual grows in linear height each year. These measures are considered **surrogate endpoints**, meaning they indicate treatment effect, but do not directly measure many of the health outcomes most relevant to individuals with achondroplasia and their families.[5]

Some studies have begun to report data on additional outcomes, including **body proportionality measures** (such as upper-to-lower body ratio and arm span), though many of these findings are still based on relatively small sample sizes. These findings contribute to a broader understanding of how these therapies may influence skeletal development.[6,7,8,9] However, **longer follow-up and additional studies are still needed** to determine whether treatment meaningfully affects outcomes across the lifespan such as:

- Sleep-disordered breathing
- Foramen magnum or spinal stenosis
- Pain
- Need for surgeries
- Functional independence
- Overall quality of life

Because data on many of these outcomes takes years to collect, they often require **longer observation periods** than current clinical trials have yet provided and it is unknown whether all of these will be fully answered. LPA is committed to advocating for

continued longitudinal research that examines not only growth-related outcomes, but long-term medical, functional, and quality-of-life impacts across the lifespan.

Key Updates

- **The clinical evidence base has expanded.** While early studies primarily focused on growth velocity, more recent trials have begun to report additional outcomes, including radiographic (e.g. X-ray, MRI) measures of skeletal development and patient- or caregiver-reported outcomes.[6,7,8,9]

- **Changes in the development pipeline.** Some earlier investigational programs have ended, while others have progressed.
    - **Voxzogo (vosoritide)**
        - FDA accelerated approval in **2021** for children **≥5 years old** with achondroplasia and open growth plates.
        - Approval expanded in **October 2023** to include **all children with open growth plates**, including infants.[3]
        - Supplemental application submitted April 2026 to the FDA seeking full approval based on additional long-term follow-up data.
    - **Yuviwel (navepegritide; TransCon CNP)**
        - FDA accelerated approval in **February 2026** for children **≥2 years old** with achondroplasia and open growth plates.[4]
        - Phase 2 COACH trial of navepegritide + lonapegsomatropin (CNP + growth hormone)
    - **Infigratinib (PROPEL clinical program)**
        - Not FDA approved for achondroplasia as of **July 2026**.
        - The Phase 3 **PROPEL-3** trial met it's primary endpoint, demonstrating a **statistically significant improvement in AGV compared with placebo at Week 52.**[9,10]
        - If development continues successfully, regulatory submission and potential approval could occur **around 2027**.
    - **Dabogratinib (TYRA-300)**
        - Currently being evaluated in the Phase 2 BEACH301 trial in children with achondroplasia
        - The study is assessing safety, tolerability, annualized growth velocity, & other exploratory outcomes. Clinical efficacy results have not been reported.[11]

Achondroplasia Medical Overview[12,13]

Achondroplasia is the most common form of skeletal dysplasia causing short stature or dwarfism. It is caused by a genetic change (mutation) in the fibroblast growth factor receptor 3 (*FGFR3*) gene. Everyone has the *FGFR3* gene, which helps regulate endochondral bone growth by acting like a brake on the growth and development of cartilage cells within the growth plate. In people with achondroplasia, FGFR3 signaling is overactive, causing this brake to be applied too strongly and slowing bone growth.

Achondroplasia is estimated to occur in approximately 1 in 15,000–25,000 live births worldwide. About 80% of cases occur spontaneously (*de novo*), meaning the child is born to average-height parents with no prior family history of dwarfism.

Most individuals with achondroplasia are diagnosed through clinical evaluation, including physical examination and imaging such as prenatal ultrasound or postnatal X-rays. Genetic testing can also be performed to confirm the diagnosis.

Every person with achondroplasia is unique. A person may have some or many of the physical features associated with achondroplasia. Common physical characteristics include disproportionate short stature, including an average-size torso with shortened long bones, most noticeable in upper arms (humerus) and legs (femur), larger head size (macrocephaly), prominent forehead (frontal bossing), and a flattened nasal bridge (midface hypoplasia). **Importantly, most individuals with achondroplasia live independent and productive lives, with diverse careers, families, and community involvement.**

The health considerations associated with achondroplasia can vary widely among individuals. Regardless if an individual is on a pharmaceutical therapy for achondroplasia, ongoing care by a provider experienced in caring for individuals with achondroplasia is important. Clinical guidance commonly highlights several potential complications that require monitoring, including, but not limited to:

- **Foramen magnum (FM) stenosis:** The FM is an opening in the skull where the brain connects to the spinal cord. Sometimes this opening is too small and can press on the spinal cord causing pauses in breathing (central sleep apnea) and other health concerns. The highest risk for FM stenosis occurs during infancy and early childhood.
- **Hydrocephalus:** Individuals with achondroplasia have larger heads when compared to their average-height peers. Head size should be tracked using an achondroplasia-specific head circumference chart. A rapid increase in head size could be a sign of hydrocephalus. This is caused by a slow build-up of fluid in the

brain. Although it is uncommon, it most often presents during infancy and early childhood.

- **Recurrent ear infections (otitis media):** Because of differences in the ear structure, children with achondroplasia may have frequent or long-lasting ear infections, or fluid in the ear that does not go away. If ear fluid is not treated, it may impact hearing and speech development.
- **Sleep-disordered breathing:** Changes of the midface can increase the chance that a child with achondroplasia has obstructive sleep apnea. Individuals with achondroplasia are also at risk for central sleep apnea as described above.
- **Spinal stenosis:** Narrowing of other parts of the spinal vertebrae or canal may lead to symptoms such as pain, numbness or weakness. If present, they typically develop later in life.
- **Genu varum:** Also known as bowing of the legs, is common and typically corrected if it causes pain or impacts activity. 20-30% of people with achondroplasia will require surgical intervention.

Lived Experience Perspective

Many individuals and families do not experience achondroplasia solely through a medical lens, but within a broader framework that includes identity, culture, community, and the interaction between dwarf bodies and the built and social environment. Disability rights frameworks, including the Social Model of Disability, emphasize that many barriers arise not inherently from short stature itself, but from environments, systems, and societal attitudes that were not designed with people with dwarfism in mind. Inaccessible spaces, standardized design, stigma, and social assumptions can significantly shape day-to-day experiences and quality of life.

Lived experience is highly variable and shaped by individual, familial, cultural, and environmental factors. Qualitative research highlights differences based on age, developmental stage, family composition, access to support, and whether other family members also have achondroplasia. Individuals may encounter practical challenges related to reach, mobility, transportation, or navigating public spaces, while also developing adaptive strategies, strong independence, humor, disability pride, and meaningful community connection over time. Social experiences may include unwanted attention, infantilization, assumptions, or discrimination, alongside strong cultural identity and connection within dwarf and broader disability communities. Importantly, many individuals do not view achondroplasia solely as a condition to be “treated,” but as an integral part of who they are.

Research exploring identity and lived experience in achondroplasia remains more limited than the clinical literature, but available qualitative studies highlight the limitations of one-size-fits-all narratives. Perspectives within the community are diverse and evolving. Some individuals strongly identify with dwarf pride, some connect more broadly with disability rights identity, some embrace both, and others may not identify with either framework. These perspectives are not contradictory, but reflect the complexity and fluidity of identity across different life stages, environments, and experiences. The rapid expansion of pharmaceutical treatment options has also introduced new conversations within the dwarfism community around identity, belonging, visibility, and the future of dwarf culture and representation.

Family and caregiver perspectives further illustrate this complexity. Parents often describe navigating healthcare, education, accessibility, and social systems while supporting their child's autonomy, confidence, and sense of self. As new therapies emerge, these conversations become increasingly nuanced. Decisions about whether to pursue treatment may be influenced by personal values, cultural and disability identity, expectations for outcomes, treatment burden, access, financial considerations, and comfort with long-term unknowns. For some families, treatment may feel aligned with their goals around specific medical or functional concerns. For others, hesitation may reflect concerns about medicalization, societal pressure, long-term impacts, or the broader implications of framing dwarfism primarily through a treatment-focused lens.

A balanced approach recognizes that achondroplasia encompasses medical, social, cultural, and identity-based dimensions. Incorporating lived experience into clinical care, research, and policy discussions can help ensure that decision-making reflects what matters most to individuals and families themselves. This includes meaningfully involving individuals with achondroplasia, particularly as they mature, in decisions affecting their health, bodies, and lives, while respecting the wide range of perspectives that exist within the community.

Medical Management Across the Lifespan[12,13,14,15,16]

Medical care for individuals with achondroplasia focuses on monitoring for potential complications, identifying concerns early, and addressing medical needs as they arise, while also supporting overall health, independence, positive self-esteem, and mental well-being. Clinical experiences can vary widely among individuals with achondroplasia and may change throughout different stages of life.

Some individuals experience relatively few medical complications and require minimal medical intervention, while others may need more extensive management. In some

cases, this can include surgical or procedural interventions such as spinal decompression, leg straightening surgery, spinal fusion, or placement of ear tubes.

The types of health considerations associated with achondroplasia may also change across the lifespan. In infancy, clinicians often monitor for issues such as foramen magnum stenosis (narrowing at the base of the skull that can affect the spinal cord) and breathing concerns. During childhood and adulthood, individuals may experience other complications including recurrent ear infections, sleep-disordered breathing (such as obstructive sleep apnea), obesity, orthopedic concerns, and spinal stenosis.

Until recently, no pharmaceutical therapies were approved specifically for achondroplasia. Human growth hormone has been studied in an attempt to increase height, but its effects were generally modest and it has not been shown to address the underlying biology of achondroplasia or reduce associated medical complications.

More recently, researchers have developed therapies designed to target the biological pathways involved in bone growth in achondroplasia. These therapies do not all work in the same way. The currently approved therapies act through the C-type natriuretic peptide (CNP) pathway, which helps counteract part of the overactive FGFR3 signal, while other therapies in development are designed to act more directly on FGFR3 or at other points in the broader pathway. Differences in where or how a therapy acts do not, by themselves, establish that one approach will produce better outcomes than another.

In November 2021, Voxzogo (vosoritide) became the first FDA-approved therapy for achondroplasia. It is currently approved to increase linear growth in pediatric patients with achondroplasia and open growth plates.[3] In February 2026, Yuviwel (navepegritide) became the second FDA-approved therapy and is approved for children two years of age and older with achondroplasia and open growth plates.[4]

The introduction of these therapies has begun to expand clinical guidance beyond monitoring complications alone to include practical considerations for the use of targeted treatments. **Decisions about whether to pursue these therapies remain individualized and should be made collaboratively among patients, families, and their healthcare professionals, with appropriate involvement of the individual based on their age and ability to participate in decision-making. These decisions are best informed by each person's specific medical circumstances, as well as their values, preferences, and goals.**

The following sections summarizes the **scientific research, clinical trial evidence, and therapies currently approved or in development** for achondroplasia.

How Drug Development and Accelerated Approvals Work[5,17]

New medicines are typically developed through a multi-step process that includes discovery and laboratory research, preclinical testing, clinical trials in people, regulatory review, and ongoing monitoring after approval. A more thorough overview of these stages is provided by the FDA.

During clinical trials, researchers evaluate whether a therapy is safe and effective. These studies often compare the investigational treatment to a placebo (an inactive treatment) or to existing care. Trials are typically conducted in phases and measure specific outcomes known as endpoints, predefined measurements used to determine whether a treatment is having the intended effect.

Clinical Trials Summary

Clinical Trial Phase	Key Priority	Population Studied	Goal
Phase 1	Safety	Healthy individuals that do not have the condition.	To ensure the drug is safe and reasonable to continue to the next phase of development. No efficacy measures are assessed.
Phase 2	Safety & Dosing	A small group of people with the condition.	To continue to assess the safety of drug as well as the best (balancing safety & efficacy) dose to continue development.
Phase 3	Safety & Efficacy	A larger group of people with the condition	Larger-scale data collection about treatment effectiveness and safety.

For some conditions, it can take many years to measure whether a therapy improves long-term health outcomes. In achondroplasia, outcomes that are most important to individuals and families, such as lifetime surgical burden, spinal stenosis, or other complications, may take many years or decades to fully understand. Because of this, regulators may allow approval based on earlier measurable indicators that are expected to predict longer-term benefit.

One regulatory mechanism designed for this situation is the FDA's Accelerated Approval Program. Under this pathway, a therapy may be approved based on a surrogate endpoint, which is a measurable outcome that is considered reasonably likely to predict clinical benefit. When accelerated approval is granted, companies are required to conduct post-approval (confirmatory) studies to determine whether the treatment ultimately demonstrates meaningful clinical benefit. If those confirmatory trials fail to verify benefit, or if they are not completed in a timely manner, the FDA has the authority to withdraw the approval.

Both currently FDA-approved therapies for achondroplasia initially received FDA accelerated approval based primarily on improvements in annualized growth velocity (AGV), which reflects the rate of height gain over time. AGV is considered a surrogate endpoint because it does not directly measure many of the health outcomes most important to individuals with achondroplasia, such as pain, functional independence, or the need for medical interventions.

The FDA determined that AGV was reasonably likely to predict clinical benefit and therefore could support accelerated approval while additional evidence was collected. As part of this pathway, manufacturers are expected to conduct follow-up studies to determine whether treatment results in meaningful clinical benefits beyond growth velocity. Although additional evidence continues to emerge, important questions remain about how these treatments affect skeletal development and long-term health outcomes.[5]

Current Approved Pharmacologic Therapies

Reminder: *Data comparisons across clinical trials should be interpreted with caution. Differences in study design, patient populations, age at treatment initiation, and endpoints can meaningfully influence results, making comparisons between therapies difficult. Ongoing and longer-term studies will be important to better understand the durability of treatment effects and their impact on outcomes that matter most to individuals and families.*

VOXZOGO (vosoritide) - BioMarin Pharmaceutical Inc.

Regulatory status and eligible ages: As noted, the FDA granted accelerated approval for Voxzogo in November 2021, with a label expansion in 2023. It is currently indicated to increase linear growth in all pediatric patients with achondroplasia who have open epiphyses.

The updated label also includes additional safety data from a randomized study in younger children (approximately 4.4 months to <5 years of age), supporting use across the broader population of children with open growth plates.[3] In April 2026, BioMarin submitted a supplemental application to the FDA seeking full approval based on additional long-term follow-up data.

Mechanism: Voxzogo is a C-type natriuretic peptide (CNP) analog intended to counterbalance downstream signaling effects of overactive FGFR3 through NPR-B signaling.[3]

Administration: Voxzogo is given as a **once-daily injection under the skin** (subcutaneous injection). The dose is based on the child's weight and will range between 0.096mg and 0.8mg. Because the medication can cause a temporary drop in blood pressure, it's recommended that children **eat and drink before each dose** to help reduce this risk.[3]

Safety & adverse events: The most commonly reported side effects include injection site reactions (such as redness, swelling, or discomfort at the injection site) and vomiting.

Voxzogo can also cause temporary decreases in blood pressure (hypotension). In clinical trials, these events occurred more frequently in children receiving Voxzogo compared with placebo, although they were generally short-lived. Symptoms of low blood pressure may include dizziness, fatigue, or feeling faint, particularly around the time of dosing. Having adequate food and fluids before administration may help reduce this risk. Some families and healthcare professionals also find that administering the dose in the evening makes temporary symptoms easier to manage, although treatment timing should be discussed with the individual's healthcare professional.

As with any therapy, families and healthcare providers should regularly monitor safety and tolerability over time, and discuss any side effects or concerns to determine what is most appropriate for the individual.Voxzogo has accumulated more than a decade of clinical-trial and real-world experience, while additional safety information continues to emerge through longer-term follow-up and real-world use.[3]

Efficacy evidence: In the pivotal placebo-controlled study in children aged 5–15 years, the FDA label reports a treatment difference in the change from baseline annualized growth velocity of 1.57 cm/year at Week 52. Children receiving vosoritide also moved closer to the average height expected for their age and sex compared with those receiving placebo (height Z-score).

Longer-term follow-up data extend to six years and suggest that the increased growth effect is sustained over time. In an analysis using an external untreated comparison

group, children receiving vosoritide gained approximately 5.75 cm more height over 3 years. An improvement in upper-to-lower body-segment ratio was observed among younger participants included in that analysis. Because these longer-term comparisons used external rather than randomized controls, the findings should be interpreted with appropriate caution.[3, 6, 7, 22]

Real-world evidence for Voxzogo continues to expand. Multiple observational studies have generally reported increases in annualized growth velocity and height Z-scores that are consistent with the growth effects observed in clinical trials.

Some studies have also begun to explore outcomes beyond linear growth, but findings remain early and mixed. One 12-month retrospective study reported improvement in the 6-minute walk test but no significant change in sitting-height-to-height ratio. Other small observational studies and case series have evaluated proportionality, muscle function, and functional independence, but these designs cannot reliably determine whether observed changes were caused by treatment rather than growth, maturation, adaptation, or other factors.[7, 20]

Ongoing studies continue to evaluate how these observed effects may translate into longer-term outcomes, including skeletal health, function, and quality of life.

YUVIWEL (navepegritide) - Ascendis Pharma

Regulatory status and eligible ages: In February 2026, the FDA granted accelerated approval to Yuviwel (navepegritide) to increase linear growth in pediatric patients 2 years of age and older with achondroplasia who have open epiphyses. As with Voxzogo, approval is based on improvements in annualized growth velocity (AGV), and continued approval may depend on confirmatory studies demonstrating clinical benefit.[4]

Mechanism: Yuviwel is a CNP analog, similar to vosoritide, but is designed as a prodrug that allows for more sustained exposure to CNP over time. This supports a longer duration of action, enabling once-weekly dosing.[4]

Administration: Yuviwel is administered as a once-weekly injection under the skin (subcutaneous injection). The dose is based on the child's weight and will range between 0.88mg and 8.8mg For individuals transitioning from a daily CNP therapy (such as vosoritide), the prescribing information recommends starting Yuviwel the day after the last daily dose.

Safety and adverse events: The most commonly reported side effects include vomiting, injection site reactions (such as redness or swelling), pain in the arms or legs, and nausea. As with other therapies in this class, effects related to blood pressure may occur, and monitoring is recommended as part of routine care. Families should watch

for symptoms such as dizziness, fatigue, or feeling faint, particularly around the time of dosing. Yuviwel is not recommended for individuals with moderate to severe kidney impairment (defined as an eGFR <60 mL/min/1.73 m²).

As with any therapy, ongoing communication with healthcare providers is important to monitor safety, manage side effects, and determine what is most appropriate for the individual over time.[4,8]

Efficacy evidence: In a 52-week randomized, placebo-controlled trial (ApproaCH), children receiving navepegritide grew faster than those receiving placebo, with a treatment difference of 1.5 cm per year in annualized growth velocity.

In addition to growth, the study prospectively evaluated skeletal development outcomes. These included measures of body proportionality (such as upper-to-lower body segment ratio), lower limb alignment including tibiofemoral angle (TFA), mechanical axis deviation (MAD), and radiographic measures of bone growth in the lower limbs. At 52 weeks, navepegritide was associated with statistically significant improvements in several lower-limb measures compared with placebo, including leg alignment and the relative lengths of the fibula and tibia. The average placebo-adjusted differences included approximately 1.8 degrees in tibial-femoral angle and 2.8 mm in mechanical-axis deviation. A small directional change was also observed in upper-to-lower body-segment ratio, although the difference compared with placebo was not statistically significant.

These findings suggest potential effects beyond linear height; however, the magnitude of change at 1 year is modest, and it is not yet known whether these differences will translate into clinically meaningful outcomes over time, such as reduced need for surgery, improved mobility, or decreased pain.

Emerging combination data (investigational): In addition to monotherapy studies, navepegritide has been evaluated in combination with a long-acting growth hormone (TransCon hGH) in the ongoing Phase 2 COACH trial. Early 52-week data suggest that combination therapy may further increase growth velocity and show larger changes in measures such as arm span, spinal canal dimensions, and lower limb alignment compared with navepegritide alone.[18]

However, these findings are from a small, open-label, early-phase study and should be interpreted with caution. The combination of navepegritide and growth hormone is **not FDA approved for achondroplasia**, and additional studies are needed to better understand its safety, durability, and potential impact on long-term clinical outcomes.

Investigational Therapies

Infigratinib - BridgeBio (formerly QED)

Regulatory status and eligible ages: As of July 2026, infigratinib is not FDA approved for achondroplasia. Results from the Phase 3 PROPEL-3 trial reported a statistically significant improvement in annualized growth velocity (AGV) compared with placebo at 52 weeks. A regulatory submission is anticipated in 2026, with potential approval as early as 2027 if development and review proceed as expected.[9, 21]

Mechanism: Infigratinib represents a different biological approach than CNP-based therapies and is classified as a tyrosine-kinase inhibitor (TKI). It is an oral medication that directly inhibits the FGFR3 receptor, which plays a central role in the FGFR3 signaling pathway that regulates bone growth.[9,10]

Administration: Infigratinib is being studied as an oral medication taken by mouth once daily. In clinical trials, dosing is weight-based and may be adjusted as children grow. The medication is being evaluated in a sprinkle-capsule formulation. The capsule may be swallowed whole or opened and the granules inside sprinkled onto a small amount of soft food (such as applesauce), which may help support administration in younger children. Specific dosing instructions and administration details continue to be evaluated in ongoing studies.

Safety and adverse events: In the Phase 2 clinical study, PROPEL 2, infigratinib was generally well tolerated, with most side effects or adverse events described as mild to moderate. The most commonly observed adverse events included gastrointestinal symptoms (such as diarrhea) and changes in laboratory values, particularly increases in phosphate levels, which are consistent with the mechanism of FGFR inhibition. These laboratory changes were typically managed with dose adjustments or supportive care.[9,10]

Results from the Phase 3 PROPEL-3 trial have reported no new or unexpected safety findings. Three cases of increased serum (blood) phosphate levels were observed. These changes in the blood phosphate level were transient (lasting a short period), asymptomatic (the child did not feel anything), and resolved without any specific treatment. No serious adverse events or treatment discontinuations were considered related to the study drug. As with any investigational therapy, longer-term safety data and larger studies will be important to better understand the full safety profile over time.[9, 21]

Efficacy evidence: In the Phase 3 PROPEL-3 trial, infigratinib demonstrated a statistically significant improvement in annualized growth velocity compared with placebo at 52 weeks, with an adjusted (least squares mean) treatment difference of approximately +1.74 cm/year. These findings indicate an increase in growth rate among treated children and are generally consistent with earlier Phase 2 results.[9]

In a pre-specified exploratory subgroup analysis, infigratinib demonstrated a statistically significant improvement in a measure of body proportionality (upper-to-lower body segment ratio) compared with placebo in children younger than 8 years of age (representing more than half of trial participants), with an LS mean treatment difference of approximately −0.05 ($p<0.05$). Infigratinib also demonstrated a statistically significant improvement in arm span relative to height compared with placebo, providing additional evidence of effects on skeletal growth. While these findings suggest potential effects beyond linear growth, they are based on subgroup and exploratory analyses and should be interpreted with caution.9

At this stage, publicly available data remain primarily focused on growth and selected skeletal measures. More detailed results, including broader effects on skeletal development, alignment, and physical function, have not yet been fully reported in peer-reviewed publications.

As with other therapies in achondroplasia, it remains unclear how treatment may affect longer-term outcomes, such as the need for surgery, spinal stenosis, pain, or functional independence, which typically require years of follow-up to fully assess.

Dabogratinib (TYRA-3000) – Tyra Biosciences

Regulatory status and eligible ages: As of July 2026, dabogratinib (TYRA-3000) is not FDA approved for achondroplasia. It is currently being evaluated in Phase 2 clinical trials in children with achondroplasia. Early results have been reported from ongoing studies, but the therapy remains investigational, and no regulatory submission timeline has been publicly confirmed.[11]

Mechanism: Dabogratinib is similar to infigratinib as an oral tyrosine-kinase inhibitor designed to selectively inhibit the FGFR3 receptor. It has been designed with the goal of increasing selectivity for FGFR3, which may help minimize off-target effects seen with less selective FGFR inhibitors; however, this remains an area of ongoing study.[19]

Administration: Dabogratinib is being studied as a once-daily oral medication (taken by mouth). In clinical trials, dosing is weight-based and may be adjusted over time. As with other investigational therapies, specific dosing schedules and administration details continue to be evaluated.[11,19]

Safety and adverse events: The safety profile of dabograitinib is not yet fully established. In early-phase studies, reported adverse events have generally been mild to moderate and have included gastrointestinal symptoms and changes in laboratory values, including phosphate levels, which are consistent with FGFR inhibition.

The degree to which increased selectivity for FGFR3 may influence tolerability compared with other agents in this class is not yet fully understood. As with any investigational therapy, longer-term safety data and larger studies will be important to better characterize potential risks over time.

Efficacy evidence: Early clinical data from Phase 2 studies have reported increases in AGV compared with baseline in children treated with dabogratinib, suggesting a potential effect on growth rate. At this stage, results are based on relatively small study populations and shorter durations of follow-up, and placebo-controlled data are still emerging.

Additional outcomes, including effects on skeletal development, proportionality, and physical function, have not yet been fully characterized in publicly available data. As with other therapies in achondroplasia, it remains unclear how treatment may affect longer-term outcomes, such as the need for surgery, spinal stenosis, pain, or functional independence, which typically require years of follow-up to fully assess.

Navepegritide + Lonapegsomatropin (Yuviwel + Skytrofa) – Ascendis Pharma

Regulatory status and eligible ages: As of July 2026, both Yuviwel (navepegritide) and Skytrofa (lonapegsomatropin) are FDA-approved medications, but they are approved for different indications and are not approved for use in combination. Navepegritide received FDA accelerated approval in February 2026 to increase linear growth in children 2 years of age and older with achondroplasia and open growth plates. Lonapegsomatropin is approved for pediatric growth hormone deficiency but is not approved for achondroplasia.

Ascendis Pharma is currently evaluating the combination of navepegritide and lonapegsomatropin in clinical trials for children with achondroplasia. Because the two therapies act through different biological pathways involved in growth and skeletal development, researchers are studying whether they may provide additive effects on growth. However, the combination remains investigational and has not been approved by the FDA or other major regulatory agencies.

Mechanism: Navepegritide is a long-acting C-type natriuretic peptide (CNP) prodrug designed to provide a predictable and sustained exposure to CNP and counteract

overactive FGFR3 signaling, the underlying pathway responsible for achondroplasia. Lonapegsomatropin is a long-acting prodrug of recombinant human growth hormone (rhGH) that works through a separate pathway than FGFR3. The rationale for combination therapy is that targeting two distinct growth pathways may improve skeletal development and increase growth beyond what either therapy can achieve alone, although the long-term biological effects of combining these mechanisms remain under study.

Administration: Both navepegritide and lonapegsomatropin are administered as once-weekly subcutaneous injections. In combination studies, participants receive both therapies weekly, with dosing based on body weight and adjusted as children grow.

Safety and adverse events: Navepegritide has generally been associated with mild to moderate adverse events in clinical studies, most commonly injection-site reactions. Because CNP-based therapies can affect blood pressure and vascular tone, cardiovascular monitoring remains an important component of treatment and ongoing research. Known risks associated with growth hormone therapy may include headache, edema, joint pain, insulin resistance, slipped capital femoral epiphysis (SCFE), worsening scoliosis, and intracranial hypertension.

In the Phase 2 COACH trial evaluating combination therapy, treatment was generally well tolerated through 52 weeks. Reported safety findings were consistent with the known safety profiles of navepegritide and lonapegsomatropin when used individually, with generally mild treatment-emergent adverse events and a low incidence of injection-site reactions. Bone age progression remained consistent with chronological age at 52 weeks, and all enrolled participants completed the first year of treatment and continued in the study. Long-term safety data regarding skeletal proportionality, orthopedic outcomes, metabolic effects, and potential interactions between therapies have not yet been fully established.

Efficacy evidence: The Phase 2 COACH trial evaluated the combination of navepegritide and lonapegsomatropin in children aged 2 to 11 years with achondroplasia. At 52 weeks, treatment-naïve children (kids who have never received any type of treatment for achondroplasia) receiving combination therapy achieved a mean AGV of 8.8 cm/year, compared with approximately 6 cm/year observed in matched children receiving navepegritide alone in the ApproaCH trial. Children previously treated with navepegritide also experienced increased acceleration in growth at week 52 of the COACH trial after the addition of lonapegsomatropin with an AGV of 8.4 cm/year. In addition to increased linear growth, children receiving combination therapy demonstrated improvements in body proportionality and arm span. While these findings are promising, important limitations remain. COACH was an open-label Phase

2 study involving a relatively small number of participants, and longer-term outcomes remain unknown. It is not yet established whether the observed improvements in growth, proportionality, and arm span will translate into meaningful changes in medical complications, functional independence, mobility, pain, need for surgery, quality of life, or adult height. These outcomes require substantially longer follow-up and may not correlate directly with short-term increases in growth velocity.

BMN 333 – BioMarin Pharmaceutical Inc.

Regulatory status and eligible ages: As of July 2026, BMN 333 is not FDA approved for achondroplasia. BMN 333 is BioMarin's investigational long-acting C-type natriuretic peptide (CNP) therapy and is currently being evaluated in the ASPEN Phase 2/3 registration-enabling study. The study is enrolling approximately 160 treatment-naïve children with achondroplasia ages 2 to 17 years and will compare BMN 333 directly against vosoritide (Voxzogo), the current standard-of-care CNP therapy.

Mechanism and formulation: BMN 333 is a long-acting CNP therapy designed to provide sustained exposure to CNP and counteract overactive FGFR3 signaling, the underlying molecular pathway responsible for achondroplasia. Like vosoritide, BMN 333 targets the CNP pathway but is intended to provide longer-lasting activity.

Administration: BMN 333 is being studied as a once-weekly subcutaneous injection therapy. The ongoing ASPEN study includes a dose-finding Phase 2 component followed by a Phase 3 comparison against vosoritide. The final dosing regimen that would be used commercially, if approved, has not yet been established.

Safety and adverse events: Publicly available safety data for BMN 333 in children with achondroplasia remain limited. BioMarin has reported Phase 1 pharmacokinetic data from healthy volunteers and has moved the program into a Phase 2/3 pediatric study. Because BMN 333 is still investigational, the safety profile in children with achondroplasia has not yet been fully established. Key areas to watch will likely include injection-site reactions, blood pressure or cardiovascular effects related to CNP biology, and any safety differences compared with vosoritide.

Efficacy evidence: As of July 2026, there are no publicly available peer-reviewed efficacy data on the impact of BMN 333 on AGV, proportionality, function, pain, surgery risk, spinal stenosis, or other longer-term outcomes in children with achondroplasia. The ongoing Phase 2/3 study is designed to evaluate BMN 333 against vosoritide, with growth as a major outcome. BioMarin has stated that its goal is for BMN 333 to demonstrate superiority to Voxzogo, but that remains a development goal rather than an established result.

Evidence Gaps, Community-Prioritized Outcomes, and Interpretation

What approvals do and do not yet establish

Both FDA-approved therapies (Voxzogo and Yuviwel) received accelerated approval, intended to allow earlier access to therapies when confirmatory evidence is still needed. Under this pathway, additional studies are required to verify and describe clinical benefit, and approvals may be withdrawn if confirmatory trials fail or are not completed with due diligence.

For the LPA community, the most important open question remains: **to what extent do these therapies reduce the frequency or severity of high-burden complications**, such as clinically significant stenosis, sleep-disordered breathing requiring intervention, pain over time, and the need for orthopedic or neurosurgical procedures, and how do they affect lived experience, independence, and participation over years, not months. The accelerated approval framework itself reflects this uncertainty, and FDA postmarketing requirements emphasize the need for longer-term outcomes, including adult height and complication monitoring.

Signals that begin to move beyond “growth velocity”

Voxzogo’s most mature data now include multi-year follow-up suggesting sustained growth effects and some improvement in proportionality in certain younger subgroups at 3 years, with a tolerable safety profile reported through up to 6 years in extension analyses. Observational real-world data suggest improvements in physical function testing (such as 6-minute walk distance) after 12 months; however, proportionality and quality-of-life findings remain variable, and longer follow-up is needed to better understand the long-term safety & efficacy outcomes.[3,6,7]

Navepegritide’s randomized trial is notable for prospectively assessing outcomes beyond linear growth, including radiographic measures of lower-limb alignment and an achondroplasia-specific measure of physical functioning. Statistically significant improvements were observed in several skeletal alignment measures at 52 weeks compared with placebo, along with improvements in physical functioning, particularly in younger subgroups. These endpoint choices begin to broaden the assessment beyond linear height and are more closely aligned with community priorities around function and orthopedic burden. However, the magnitude and consistency of these effects and whether they translate into meaningful long-term outcomes such as reduced need for

surgery, improved mobility, or decreased pain remain uncertain and require longer-term follow-up.[4,8]

Results from the Phase 3 PROPEL-3 trial of infigratinib have also reported early signals beyond growth, including a statistically significant improvement in a measure of body proportionality (upper-to-lower body segment ratio) in a pre-specified subgroup of children younger than 8 years of age. While these findings suggest potential effects on skeletal development, they are based on subgroup analyses, and full results, including broader effects on alignment, function, and long-term outcomes, are not yet available.[9, 21]

Practical questions that remain unanswered

Even with early signals beyond growth, several uncertainties remain highly relevant to individuals and families:

- Whether any pharmacologic therapy reduces the incidence or severity of complications such as foramen magnum stenosis, sleep-disordered breathing, or adult spinal stenosis remains a key evidence gap that will require long-term follow-up and registry data.
- The long-term safety profile of these therapies, including potential effects on bone quality, fracture risk, cardiovascular parameters, and other organ systems, remains incomplete, particularly with treatment beginning in early childhood and continuing over many years.
- Whether observed improvements in limb alignment, growth velocity, and other surrogate endpoints translate into fewer corrective surgeries, reduced pain, or improved mobility over time has not yet been confirmed in long-term controlled datasets.
- The impact of treatment on day-to-day functioning, independence, and overall quality of life remains uncertain, in part due to limitations in current measurement tools (i.e., QoLISSY, PEDsQL) and the variability of individual experiences.
- Practical considerations, including treatment & psychological burden, adherence, access, and cost, may also influence real-world outcomes and decision-making for individuals and families.
- Comparative effectiveness across therapies has not been established through head-to-head randomized trials. Cross-trial comparisons are limited by differences in study design, patient populations, and endpoints, and the use of accelerated approval and external controls in some analyses highlights these methodological constraints.

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