Sanofi Commitment to Rare Diseases

For over 30 years, Sanofi has pioneered the development and delivery of therapies for patients affected by rare diseases. Now, Sanofi is investigating a novel drug for treatment of Achondroplasia. We are dedicated to making a positive impact on the lives of the patients and families we serve.

Find information about clinical sites, go to **clinicaltrials.gov and search for Study ID NCT06067425**

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upreACH

ACHONDROPLASIA CLINICAL TRIAL

sanofi

Bone Growth in Achondroplasia

Growth and development are highly controlled processes in the body. In normal bone growth, cartilage (a type of bone tissue that has a rubbery texture) turns into bone. The chondrocyte is a special type of cell in cartilage that is present in the growth plate near the ends of long bones in children and teens. These cells and the growth plates determine the length and the shape of the bone when it is done growing. The chondrocytes are stacked in layers in the growth plate. At the top of the growth plate chondrocytes grow and divide. In the bottom layers, chondrocytes become larger, then mature, and finally are replaced by normal bone cells.

There are "small molecules" throughout the body that regulate how fast and where this process of bone growth occurs. Chondrocytes contain a small molecule called the FGFR3 receptor. Receptors are like sockets that other molecules "plug into" to transmit instructions to the cell. When another molecule called FGF plugs into the FGFR3 receptor, a signal is sent to tell the chondrocyte to stop growing. Normally, someone's body balances between turning this signal on and off, which helps to regulate the normal formation of the skeleton[1].

In achondroplasia, the FGFR3 receptor is different compared with individuals without achondroplasia; this is called a pathogenic variant. The variant causes the FGFR3 receptor to function abnormally interrupting the balance between "on" and "off" signals to the chondrocyte to direct normal bone growth. As a result, the bones don't grow normally leading to short stature, short limbs, and differences in the development of the skull, spine, and middle ear from what you would see in healthy people without achondroplasia.
These differences can lead to medical complications such as back pain, breathing problems and frequent ear infections.

Sanofi has performed preclinical studies in animals in the laboratory using a special molecule that plugs into the abnormal FGFR3 receptor. This molecule interrupts the abnormal FGFR3 signaling helping to restore the balance between "on" and "off" signals to growing bone. Sanofi is researching whether targeting the abnormal signal in people with achondroplasia improves bone growth, resulting in increased height, limb length, and skull growth, and decreases some of the medical complications associated with achondroplasia. The molecule Sanofi has developed is an investigational drug; how well it works has not been proven yet in humans.

[1]Pauli RM. Achondroplasia: a comprehensive clinical review. Orphanet J Rare Dis. 2019 Jan 3;14(1):1. doi: 10.1186/s13023-018-0972-6. PMID: 30606190; PMCID: PMC6318916.

Study Design

upreACH-2 is a clinical trial that will investigate two dose levels of the investigational drug in participants with achondroplasia. The primary purpose of this trial is to evaluate the safety and side effects of the investigational drug. The trial will also examine various growth measurements in pediatric participants receiving subcutaneous injections of the investigational drug. A subcutaneous injection is given by a needle that goes just under the skin and into the layer of fat that is above the muscle. Either the doctor's team or caregiver will administer the injection twice per week for at least a 52-week period (about one year).

Participants will return to the site for visits throughout the study, where the doctor's team will measure their growth, draw some blood, take X-rays, and ask them or their parents to complete some questionnaires. Depending on the age of the participant, the study doctor may need to obtain an MRI (a machine that takes picture of the inside of the body) of the brain and/or neck.

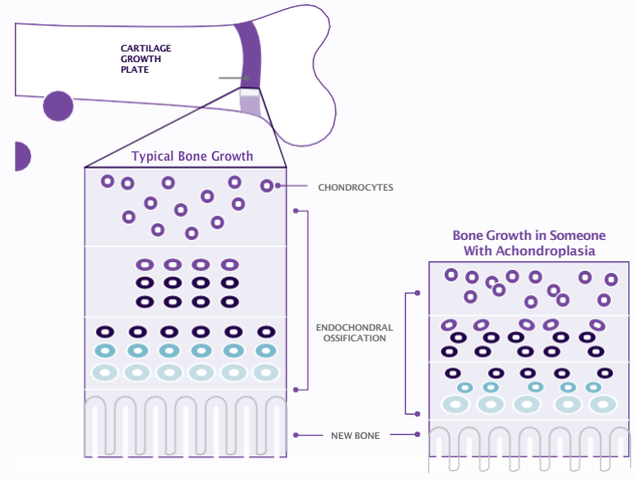
This study is the second in a series of planned studies for the investigational drug in people with achondroplasia. Each enrolled participant has the potential to make a significant contribution to our scientific understanding of the study drug and preparation for future long-term studies.

The participant and parent/guardian-related travel expenses will be covered by the Sponsor; however this may vary based on local requirements. For further details on what expenses are covered and additional information about the study please contact the study doctor.

For more details about the trial please refer to:

https://clinicaltrials.gov/study/nct06067425

The agent mentioned here is investigational and has not been approved by the US Food and Drug Administration (FDA) of any other regulatory agency worldwide for the uses under investigation. No conclusions regarding safety and efficacy should be drawn for such agents.



upreACH-2 Key Enrollment Criteria

At this early stage in development of SAR442501, Sanofi is recruiting a narrowly defined range of patients. We anticipate expanding eligibility requirements in future studies.

Inclusion criteria:

- Confirmed mutation in the FGFR3 gene.
- Participants from birth up to age 12.

Exclusion criteria:

- Have hypochondroplasia (or short stature condition other than achondroplasia).
- Have received any dose of medications or investigational product, including human growth hormone, intended to affect participants' stature or body proportions within 6 months of enrollment.
- Have a history of growth plate closure.

Additional inclusion/exclusion criteria apply