

Frequently Asked Questions: LPA and Pharmaceutical Company Engagement

Why is LPA interested in what pharma is doing?

Prior to any interaction with LPA, pharmaceutical companies (“pharma”) began developing biochemical therapies to treat symptoms of achondroplasia. To varying degrees, each pharma company is attempting to signal the FGFR3 gene, which acts as a growth receptor and when it mutates, it causes achondroplasia. These treatments are in various stages of clinical trials, measuring height velocity and ancillary descriptors of achondroplasia including spinal stenosis, compression of the brainstem and sleep apnea. The outcomes of these therapies have a very real chance to change the height, physical appearance and perhaps the health of people with Achondroplasia, which in turn affects the organization as a whole.

The four companies (and the drug name and status of the clinical trials) are:

- BioMarin (Vosoritide – Phase II trial underway)
- Ascendis (TransCon CNP – Phase II trial underway)
- Theracon (TA-46 – recruitment underway for clinical observation)
- QED Therapeutics (Infigratinib –initiating clinical observations).

What are clinical trials?

Clinical trials are made up of three different phases with the following goals:

- Phase I – Drug/chemical treatment tests on healthy volunteers for safety; involves testing multiple doses (dose-ranging)
- Phase II – Drug/chemical treatment on patients to assess efficacy and side effects
- Phase III – Drug/chemical treatment on patients to assess efficacy, effectiveness, and safety

How long has LPA been in contact with these organizations?

In 2012, members of LPA, including some board members, were invited to meet with BioMarin staff. People had individual reasons for attending, but the LPA National board representatives joined to learn BioMarin’s objectives for this new drug. After the meeting, the LPA National board decided to disengage communications with BioMarin, due to skepticism in believing that BioMarin understood the needs of our community. In the meantime, BioMarin successfully recruited the families needed for studies and initiated the FDA approval process, focusing on height velocity. Other firms also began their clinical trials. In hindsight, we believe LPA lost an opportunity to have a real-time conversation with BioMarin while they were in therapy development and lost the chance to influence the company’s priorities to better match the quality of life issues LPA is

concerned with.

In 2017, after much discussion, LPA decided to re-engage with BioMarin and we began formal conversations with the 3 other companies researching the same FGFR3 growth inhibitor, while they are in the early stages of their drug development.

What are LPA's position and priorities on pharma treatments?

LPA's 2012 Position Statement continues to guide the National Board's decisions and can be referenced here: <https://www.lpaonline.org/genetic-biotechnology-research-position-statement>. We have long celebrated dwarfism as a valuable contribution to human diversity. LPA also values diversity within our own community and respects the choices of its members regarding medical intervention. While LPA has never actively promoted medical research aimed at treating or curing dwarfism, LPA is not opposed to medical research if it holds the potential to improve quality of life by treating symptoms that can range from uncomfortable to lethal. LPA will continue providing access to accurate information to its members.

Recently, in testimony to the FDA and in conversations with pharma companies, LPA has shared the message of dwarf pride and urged a clinical focus on the quality of life issues, such as spinal stenosis, compression of the brainstem and sleep apnea; not height velocity. Further, we repeatedly and strongly encourage pharma companies to fund and provide long-term psychological support for individuals and families participating in the trials, especially in the event the child is in the placebo group, or if the clinical trials fail to achieve the stated goals.

How has the Medical Advisory Board (MAB) been involved in this process?

LPA and the MAB have different perspectives and priorities when it comes to our engagement with pharma companies. The MAB has been a critical partner in keeping the LPA informed and encouraging LPA to engage early with pharma companies to keep them focused on the medical and psychological quality of life issues.

Some MAB doctors and their clinics are directly engaged with a few of the pharma companies and are running clinical trials with patients. Some of the skeletal dysplasia clinics are also responsible for the development of and recruiting for, natural history studies documenting the psychological and psychosocial issues and experiences of people with achondroplasia as per the request and financial backing of the pharma companies.