July 19, 2016

The International FOP Association is pleased to share the following news from Regeneron Pharmaceuticals.

Healthy volunteer study: an important first step in Regeneron's anti-Activin A clinical development program

- Regeneron is pleased to inform you that anti-Activin A antibody, REGN2477, is now in a clinical trial. A study in healthy volunteers initiated in Belgium in June 2016. This is an important step in the clinical development process, as it provides the first information on REGN2477's safety, tolerability and pharmacological activity in people. We plan to review this data before the end of this year and begin clinical studies in patients with FOP as soon as possible based on what we have learned.

Regeneron's work in FOP:

- Scientists in Regeneron's Skeletal Diseases Therapeutic Focus Area have been investigating FOP and related conditions for nearly 20 years. We are committed to working closely with physicians, patients and advocates in the FOP community to safely and swiftly bring our investigational treatment through the clinical and regulatory process.

- Developments in generating antibody therapeutics (an area of expertise for Regeneron), as well as breakthroughs in understanding FOP, have recently enabled us to make progress in advancing potential therapies for FOP.

- Last year, Regeneron scientists published a major discovery about the molecular mechanism of FOP by studying ACVR1, the receptor protein known to be mutated in patients with FOP. Our scientists discovered that, in cells and mice that carry the mutant receptor, a protein that usually turns *off* this receptor instead turns it *on*, and that this irregular signaling results in the formation of abnormal bone growth that is characteristic of FOP.
    - This protein is known as "Activin A." Regeneron scientists created a mouse model that carries the FOP mutation and develops abnormal growth of bone in soft tissues (heterotopic ossification) similar to what is seen in humans. They showed that Activin A could stimulate heterotopic ossification in this mouse model, and that an antibody to Activin A, "REGN2477" could prevent heterotopic ossification in the model.
    - REGN2477 was being readied for clinical trials for a different use, but now it has found an important new condition for exploration in FOP. It is important to remember that these observations were made in a mouse model and therefore need to be studied carefully in patients.
    - The *Science Translational Medicine* publication can be found here and a summary from *Science* magazine here.

Who Are We?

- Regeneron is a leading U.S. biotechnology company that has been run by physician-scientists for nearly 30 years. We are dedicated to developing life-changing medicines for patients with serious

medical conditions. We have thus far developed four approved treatments; all through original Regeneron research. Some of these medicines are for patients with relatively common conditions such as certain blindness-causing diseases. Others are for patients with less common genetic conditions, such as heterozygous familial hypercholesterolemia or Cryopyrin-Associated Periodic Syndromes (CAPS), a set of rare, yet closely related, auto-inflammatory diseases. In addition to FOP, we currently have investigational medicines in development for rheumatoid arthritis, asthma, atopic dermatitis, cancer and Ebola.

- Please stay tuned for updates on our progress and visit www.regeneron.com to learn more.