

Positive Effects of Palovarotene on Spontaneous Heterotopic Ossification, Mobility, and Skeletal Growth in Mouse Models of FOP Reported in *Journal of Bone and Mineral Research*

MONTREAL, CANADA, April 14, 2016 – Clementia Pharmaceuticals Inc. today reports that the *Journal of Bone and Mineral Research* has published online a non-Clementia sponsored study describing palovarotene’s novel, beneficial effects on spontaneous heterotopic ossification, mobility, and skeletal growth in mouse models of fibrodysplasia ossificans progressiva (FOP). FOP is a rare, severely disabling myopathy characterized by extra-skeletal bone formation (heterotopic ossification [HO]) in muscle and soft tissues. Clementia is currently investigating palovarotene as a potential treatment for FOP in Phase 2 clinical trials.

FOP is caused by gain of function mutations in the ACVR1 gene encoding for the ALK2 receptor in the bone morphogenetic protein (BMP) pathway, which is critical in controlling the formation of the skeleton and ensuring normal bone growth. The mutated receptor drives heterotopic ossification by means of increased BMP signaling. Previous animal studies have shown that palovarotene potently inhibits injury-induced heterotopic ossification primarily by inhibiting excessive BMP signaling; however, the impact of palovarotene on spontaneous heterotopic ossification, mobility, and skeletal growth was unknown. This is the first study to investigate these questions in a mouse model that specifically expresses the most common mutation (R206H) that occurs in most people with FOP.

The study demonstrated that palovarotene treatment prevents spontaneous heterotopic ossification in FOP mice and suggested that it may do so by acting to counterbalance the excessive BMP signaling characteristic of FOP, thereby restoring it to more physiologic levels. Heterotopic ossification progressively imprisons individuals with FOP – limiting and interfering with multiple body functions such as walking, bending, breathing, chewing, and swallowing. Most affected persons are confined to a wheelchair by the third decade of their life.

According to the study, the increase in BMP signaling results in the progressive heterotopic ossification that causes severely limited mobility and functioning in FOP mice. In contrast to untreated FOP mice, those treated with palovarotene maintained joint, limb and body motion. “The correlation between progressive heterotopic ossification and decreasing function is currently being evaluated in our Phase 2 trials investigating palovarotene in individuals with FOP as well as in our Natural History Study,” said Donna Grogan, M.D., Chief Medical Officer of Clementia. “The Natural History Study is a non-interventional study examining FOP disease progression over time. The results of this study will be vital to any subsequent clinical trial design.”

In addition to studying palovarotene's impact on spontaneous heterotopic ossification and mobility, the study also demonstrated the drug's positive impact on skeletal growth. In untreated FOP mice, long bone growth as well as growth plate structure and function were impaired as a presumed result of excessive BMP signaling and accumulation of heterotopic bone. In contrast, FOP mice treated with palovarotene exhibited both a restoration of growth plate morphology and a significant improvement in long bone growth.

"The growth plate recovery seen in FOP mice treated with palovarotene introduces the possibility that palovarotene might not only prevent heterotopic ossification but may also have additional benefits," said Clarissa Desjardins, Ph.D., CEO and Founder of Clementia. "Although we do not know if palovarotene will have the same effects in humans, we are encouraged by all of these findings and are currently assessing palovarotene's effects on new bone formation, mobility, and skeletal growth in both adults and children with FOP as part of our Phase 2 trials."

For more information about Clementia clinical trials, visit <http://clementiapharma.com/clinical-trials/>

Chakkalakal, S. A., Uchibe, K., Convente, M. R., Zhang, D., Economides, A. N., Kaplan, F. S., Pacifici, M., Iwamoto, M. and Shore, E. M. (2016), Palovarotene Inhibits Heterotopic Ossification and Maintains Limb Mobility and Growth in Mice With the Human ACVR1R206H Fibrodysplasia Ossificans Progressiva (FOP) Mutation. J Bone Miner Res. doi: 10.1002/jbmr.2820

About Fibrodysplasia Ossificans Progressiva (FOP)

FOP is a rare, severely disabling myopathy characterized by heterotopic ossification (HO) of muscle and soft tissues. Heterotopic bone formation progressively restricts movement by locking joints and leads to cumulative loss of function, disability, and increased risk of early death. Virtually all newborns with FOP have a hallmark toe malformation in which both big toes are shortened and bent inwards. FOP is caused by a mutation in the ACVR1 gene resulting in increased activity of the activin receptor type I (ALK2) involved in the bone morphogenetic protein (BMP) pathway, a key pathway controlling bone growth and development. There are currently no approved treatments for FOP.

About Palovarotene

Palovarotene is a retinoic acid receptor gamma agonist being investigated as a treatment for FOP. Preclinical studies demonstrated that palovarotene blocked both injury-induced and spontaneous heterotopic ossification, maintained mobility, and restored skeletal growth in mouse models of FOP. Clementia licensed palovarotene from Roche Pharmaceuticals, which previously evaluated the compound in more than 800 subjects. Palovarotene received Fast Track designation from the U.S. Food and Drug Administration (FDA) and orphan designations for the treatment of FOP from both the FDA and the European Medicines Agency (EMA).

About Clementia Pharmaceuticals Inc.

Clementia is a clinical stage biopharmaceutical company committed to delivering treatments to people who have none. The company is developing its lead candidate palovarotene, a novel retinoic acid receptor gamma agonist, to treat fibrodysplasia ossificans progressiva (FOP) and other diseases. For more information, please visit www.clementiapharma.com.

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