Clementia Announces Top-line Results from Phase 2 Trial of Palovarotene for Treatment of Patients with Fibrodysplasia Ossificans Progressiva

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MONTREAL, CANADA, October, 14, 2016 – Clementia Pharmaceuticals Inc. today announced top-line results from its Phase 2 clinical trial investigating palovarotene for the treatment of fibrodysplasia ossificans progressiva (FOP). FOP is an extremely rare, serious disease in which an accumulation of heterotopic ossification (HO, extraskeletal bone) in muscle and soft tissue progressively restricts movement by locking joints leading to loss of function, physical disability, and risk of early death. Several positive trends were detected in this 40-subject placebo-controlled trial, including palovarotene-related reductions in the proportion of subjects who developed new HO, reductions in volume of new HO, reductions in patient-reported pain associated with flare-ups, and reductions in the time to resolution of FOP-related flare-ups though none reached statistical significance. Palovarotene was well-tolerated, with all subjects completing the 12-week trial and enrolling into the open-label extension trial.

“The results of this landmark clinical trial are encouraging and closely mirror what was observed in previously reported animal studies with palovarotene,” said principal investigator, Frederick Kaplan, MD, the Isaac & Rose Nassau Professor of Orthopaedic Molecular Medicine and Chief of the Division of Molecular Orthopaedic Medicine in the Perelman School of Medicine at the University of Pennsylvania. “This study has considerably enhanced our knowledge of FOP and is a significant step forward for the entire FOP community.”

The 12-week Phase 2 trial randomized subjects to three dose groups: 10 mg palovarotene for 2 weeks followed by 5 mg for 4 weeks (10/5), 5 mg for 2 weeks followed by 2.5 mg for 4 weeks (5/2.5), or placebo. Treatment was initiated within 7 days of the onset of a flare-up with evaluations made at baseline, at the end of treatment (6 weeks), and after a 6-week observation period (12 weeks). Subjects on placebo were at 2.6 times greater risk of forming HO than those on palovarotene 10/5 mg treatment, while those on either palovarotene regimen with new HO formed less HO than those on placebo. Subjects on the 10/5 regimen reported a greater improvement in pain associated with flare-ups and a reduction in the duration of overall flare-up symptoms. Though a dose-related increase in the incidence of mucocutaneous adverse events was observed, no subject required a reduction in dose due to tolerability issues nor was discontinued from the trial.

Full results of the Phase 2 trial are expected to be published next year. Clementia continues to gather important additional data in the Phase 2 extension trial and in the ongoing observational Natural History Study. Data from these studies will inform the design of a Phase 3 registration trial, which is expected to start in 2017. “That patients were able to tolerate palovarotene with no discontinuations for safety reasons at a 10-mg dose encouraged us to implement a higher dose in the Phase 2 open-label extension and to extend the number of days dosed,” said Donna Grogan, MD, CMO of Clementia. The extension trial has also introduced a chronic daily dose based on new research conducted by scientists at Penn and The Children’s Hospital of Philadelphia (CHOP) and findings from the completed Phase 2 trial.

Many years of laboratory research paved the way for this clinical trial. A leading investigator, Maurizio

Pacifici, PhD, director of Orthopedic Research at CHOP, and his collaborators first showed that palovarotene produces powerful biological effects in transgenic mouse models of human FOP and inhibits HO markedly. "Those results have provided the basis and rationale for testing palovarotene to prevent HO in FOP patients in this trial," said Pacifici.

"We would like to thank the patients, their families, the investigators, and their research teams," said CEO of Clementia, Clarissa Desjardins. "Developing a potential treatment for FOP is our passion and our goal, and we will continue to press forward as rapidly and rigorously as possible to deliver a much needed potential therapy for all FOP patients."

Additional information about palovarotene and Clementia's clinical program can be found at clementiapharma.com.

Editor's Note: Kaplan declares no disclosures and is the Global Principal Investigator for Clementia's Phase 2 Study.

About Fibrodysplasia Ossificans Progressiva (FOP)
FOP is a rare, severely disabling congenital myopathy characterized by heterotopic ossification (HO) of muscle and soft tissues. Heterotopic ossification is bone that forms outside the normal skeleton and, in FOP, progressively restricts movement by locking joints leading to a cumulative loss of function, disability, and 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 BMP Type I receptor or ALK2 receptor involved in the bone morphogenetic (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 (RARγ) being investigated as a treatment for FOP. Preclinical studies in mouse models of FOP demonstrated that palovarotene blocked both injury-induced and spontaneous heterotopic ossification, maintained mobility, and restored skeletal growth. 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 RARγ agonist, to treat fibrodysplasia ossificans progressiva (FOP) and other diseases. For more information, please visit www.clementiapharma.com.