Phase 2 Part A Open Label Extension Trial of Palovarotene for Treatment of Patients with Fibrodysplasia Ossificans Progressiva Continues Positive Trends

March 28, 2017

MONTREAL, CANADA, March 28, 2017 – Clementia Pharmaceuticals Inc. today announced the preliminary results of its Phase 2 Part A Open Label Extension (OLE) palovarotene trial in the treatment of fibrodysplasia ossificans progressiva (FOP). All 40 subjects who enrolled into the double-blind, placebo-controlled Phase 2 study elected to participate in the OLE Part A in which subjects received episodic palovarotene treatment in the event of any additional flare-ups. Preliminary data support the results obtained in the double-blind Phase 2 study: when the data are combined across these two studies, palovarotene resulted in approximately a 50% reduction in occurrence of new heterotopic ossification (HO) as compared to placebo; and importantly the volume of new HO was decreased by 70% for palovarotene treated subjects as compared to the placebo subjects. Palovarotene was well tolerated with no patient requiring dose-de-escalation or discontinuation from the study. Fifty subjects are now enrolled in the OLE Part B, which is evaluating a chronic palovarotene dose regimen.

“Our concern for the FOP community drives our interest in research,” 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, “We are encouraged by the progress of these studies and look forward to the upcoming Phase 3 pivotal trial.” Dr. Kaplan is the Global Principal Investigator for Clementia’s Phase 2 studies.

FOP is a rare genetic condition characterized by progressive heterotopic ossification (HO) that accumulates into segments, sheets, and ribbons of bone across the body and joints, steadily obstructing movement and leading to loss of function, disability, and risk of early death. RAR? selective agonists like palovarotene suppress HO by affecting inflammatory elements upstream, by inhibiting downstream effectors of the mutated ACVR1 gene (namely Smads 1, 5, and 8), and by redirecting prechondrogenic mesenchymal stem cells to a nonosseous soft tissue fate. The rationale for testing palovarotene in FOP was based on the 2011 Nature Medicine publication that demonstrated that RAR? agonists including palovarotene potently inhibit chondrogenesis and ultimately HO . Extensive testing in preclinical transgenic mouse models demonstrated that palovarotene blocked both injury-induced and spontaneous HO, maintained mobility, and restored skeletal growth .

The Phase 2 program was designed to translate palovarotene’s biological effects from animals in the lab to FOP affected individuals in the clinic. Clementia has thus far evaluated four different dosing regimens and measured HO in a number of different ways and under different conditions. The data collected to date add to Clementia’s pioneering experience in FOP clinical research and to accumulated insights for the design of the imminent Phase 3 pivotal trial. “We had aggressive objectives,” said Jeff Packman, Clementia’s Chief Development Officer, “and an adaptive Phase 2 design enabled us to address them by evaluating multiple dosing regimens and various assessments for purposes of informing our upcoming pivotal trial.” 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). The OLE is comprised of parts A and B, which allows dose ranging to continue: Part A evaluated the 10/5 regimen in additional flare-ups, and Part B is evaluating a chronic daily palovarotene dose of 5 mg with increased dose to 20 mg for 28 days followed by 10 mg for 56 days at the onset of a flare-up in skeletally mature subjects, with skeletally immature subjects receiving the flare-up dosing regimen only.

“We are at a watershed moment in the history of the FOP community. For the first time, a drug is entering into Phase 3 with the potential to change the trajectory of this disease. If the efficacy signals we have observed in our Phase 2 clinical trials are maintained in the Phase 3, we believe this drug could be the first approved treatment for FOP. Thanks to the collective efforts of the FOP community, we are one step closer to our mission of making palovarotene available for anyone affected by FOP” said CEO of Clementia, Clarissa Desjardins.

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

Editor’s Note: Frederick Kaplan declares no disclosures.

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 (RAR?) 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 RAR? agonist, to treat fibrodysplasia ossificans progressiva (FOP) and other diseases. For more information, please visit www.clementiapharma.com.

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