PharmaTher Announces Submission of IND Application with the FDA for Phase 2 Clinical Trial Evaluating Ketamine in the Treatment of Parkinson's Disease

TORONTO, April 20, 2021 -- PharmaTher Holdings Ltd. (the "Company" or "PharmaTher") (CSE: PHRM) (OTCQB: PHRRF), a specialty psychedelic pharmaceutical company, today announced it submitted an Investigational New Drug ("IND") application with the U.S. Food and Drug Administration ("FDA") for the initiation of a Phase 2 clinical trial to evaluate the safety, efficacy and pharmacokinetics of low-dose ketamine in the treatment of levodopa-induced dyskinesia in patients with Parkinson's disease ("LID-PD").

"The submission of our IND application with the FDA is an important milestone as it provides us with a solid foundation to advance our ambition in commercializing ketamine and unlocking its therapeutic potential through novel uses, formulations and delivery methods in the treatment of neurodegenerative diseases (ie. Parkinson's disease and Lou Gehrig's disease), mental illness (ie. Depression and PTSD) and chronic pain," said Fabio Chianelli, CEO of PharmaTher.

Ketamine is an FDA-approved N-methyl-D-aspartate ("NMDA") receptor-modulating drug that is widely used as an anesthetic agent either alone or in combination with other anesthetic agents [Smith et al, 1987; Pacheco et al, 2014]. The possible therapeutic effect of low-dose ketamine on LID was noted in a retrospective analysis of PD patients who received ketamine for pain relief. During this analysis, it was observed that the patients experienced an improvement in LID lasting several weeks beyond treatment [Sherman et al, 2016]. These results were corroborated in a test of low-dose ketamine in a rodent LID model, and this possible effect has also been examined in a controlled study [Bartlett et al, 2016]. Ketamine may also have additional benefits in the treatment of pain [Niesters et al, 2014] and depression [Diamond et al, 2014; Murrough et al, 2013], which are frequent comorbidities of Parkinson's disease.

The clinical trial is titled "A Multi-Center, Phase IIA, Randomized, Double-Blind, Prospective, Active Placebo-Controlled Trial of Sub-Anesthetic Ketamine to Treat Levodopa-Induced Dyskinesia in Subjects with Parkinson's Disease." It is anticipated that up to eight clinical sites in the U.S. will randomize a total of up to 36 subjects to the investigational product (ketamine) or active control (midazolam). The primary end-point of the study is the change in the Unified Dyskinesia Rating Scale ("UDysRS") total score from Baseline to Week 8. Secondary endpoints of the study include the change in Total Objective Scores of the UDysRS, total daily OFF times as assessed by subject-completed 24-hour diaries and change in the UPDRS total and sum scores

of motor and dyskinesia from Baseline to Week 8. Because LID can markedly affect a Parkinson patient's everyday activities, a reduction in LID could improve the patient's quality of life.

Assuming the Phase 2 clinical trial is positive, the Company will request a meeting with the FDA to discuss its plan and obtain an agreement to move to a pivotal Phase 3 clinical study under the 505(b)(2) regulatory pathway. However, there can be no assurance that the FDA will support any potential request for an expedited path to approval or further development.

About Parkinson's Disease

Parkinson's disease is a debilitating disorder that affects over 1 million people in the U.S. and more than 7 million people worldwide. There is currently no cure for Parkinson's disease. Although the etiology of PD is not fully understood, it is thought to result from loss of pigmented dopaminergic neurons in the Substantia nigra and their striatal projections, leading to dopamine deficiency in the striatum [Schapira and Jenner, 2011]. This ultimately affects the cortico-striatal system that controls movement.

As a progressive neurogenerative disorder of the central nervous system that primarily affects the motor nerve system, symptoms of Parkinson's disease may emerge slowly and include tremors, rigidity, bradykinesia, and postural instability [Paulson and Stern, 2004]. Also, patients may experience non-motor symptoms such as autonomic dysfunction (orthostatic hypotension, constipation, bladder dysfunction), psychiatric (depression), cognitive and sensory symptoms (pain) [Olanow, et al, 2009]. These non-motor symptoms become more common as the disease progresses.

Treatments, including levodopa and dopamine agonists, which restore the dopamine deficits in the brain, have been employed for almost 50 years. However, with continued treatment using levodopa, dose-limiting motor side-effects often emerge. This includes the emergence of abnormal involuntary movements termed Levodopa Induced Dyskinesias, which can be identified in about 50% of patients within five years after initiation of levodopa treatment and in almost all patients within ten years post-treatment initiation. These side effects often limit further dose increases in dopaminergic therapy.

About PharmaTher Holdings Ltd.

PharmaTher Holdings Ltd. (CSE: PHRM) (OTCQB: PHRRF) is a specialty psychedelic pharmaceutical company focused on the research, development and commercialization of

ketamine and novel microneedle patches for delivering psychedelics to treat neuropsychiatric, neurodegenerative and pain disorders.

Learn more at: **PharmaTher.com** and follow us on **Twitter** and **LinkedIn**.

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