PharmaTher Holdings Submits FDA Meeting Package to Discuss Phase 3 Program and Fast Track Designation for KETARX™ (Ketamine) in Parkinson's Disease

TORONTO, February 1, 2023 -- PharmaTher Holdings Ltd. (the "Company" or "PharmaTher") (OTCQB: PHRRF) (CSE: PHRM), a leader in advancing specialty ketamine pharmaceuticals, today submitted its meeting package with the U.S. Food and Drug Administration ("FDA") to discuss advancing KETARX™ (racemic ketamine) into Phase 3 development as a treatment for levodopa-induced dyskinesia in Parkinson's disease ("LID-PD"). This Type C meeting allows the Company to discuss with the FDA its plans for a Phase 3 clinical study to support the submission of a new drug application under the 505(b)(2) regulatory pathway for KETARX™ in treating LID-PD. In addition, the Company has requested guidance from the FDA to obtain Fast Track Designation for KETARX™. The Type C meeting is via written responses. The goal date for the FDA in providing its written responses is March 20, 2023.

The Company believes the safety and efficacy results from its previously announced presentation of the completed clinical study may support the investigation of KETARX™ in a proposed Phase 3 clinical study as a potential new treatment for LID-PD.

Summary results of the study:

- Enrolled subjects with moderate to advanced Parkinson's disease with a target infusion rate being 0.30 mg/kg/hr. Data highlight that ketamine was safe, well-tolerated, and demonstrated that 100% of subjects treated with ketamine had a reduction in dyskinesias as measured by UDysRS.

- UDysRS showed a 51% reduction from baseline during Infusion 2 (p=0.003), 49% at 3 weeks (p=0.006) and 41% at 3 months (p=0.011) post-ketamine.

- The maximum tolerated infusion rate ranged from 0.20-0.30 mg/kg/hr, which was dependent on either discomfort due to dissociation or hypertension. There were no adverse events post-infusion.

PharmaTher retains rights to US Patent No: 11,426,366 (expires May 2036), titled "Compositions and Methods for Treating Motor Disorders," which includes claims intended to cover ketamine in

the potential treatment of Parkinson's Disease and motor disorders that cause involuntary or uncontrollable movement or actions of the body.

Fast Track is a process designed to facilitate the development and expedite the review of investigational drugs to treat serious conditions and fill an unmet medical need. Drugs that receive Fast Track Designation may be eligible for more frequent communications and meetings with the FDA to discuss the drug's development plan, including the design of the proposed clinical trials, and ensure the collection of appropriate data needed to support approval. Clinical programs conducted under Fast Track Designation may be eligible for Accelerated Approval and Priority Review of new drug applications if relevant criteria are met.

Ketamine's Potential In Parkinson's Disease

Parkinson's disease is a debilitating disorder that affects an estimated 1 million people in the U.S. and 10 million people worldwide. The global Parkinson's disease market is expected to grow from USD $5 billion in 2019 to USD $7.5 billion by the end of 2025 [360iResearch 2020].

Ketamine is an FDA-approved N-methyl-D-aspartate receptor-modulating (NDMA) 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 levodopa-induced dyskinesia was noted in a retrospective analysis of Parkinson's disease 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.

About Parkinson's Disease

There is currently no cure for Parkinson's disease, although some drug combinations are used to treat the disease symptoms. Although the etiology of Parkinson's disease 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.

There can be no assurance that the FDA will support any potential request for an expedited path to approval or further development for ketamine in the treatment of Parkinson's disease.

About PharmaTher Holdings Ltd.

PharmaTher Holdings Ltd. (OTCQB: PHRRF) (CSE: PHRM) is a specialty pharmaceutical company focused on developing and commercializing KETARX™ (racemic ketamine) via unique delivery methods for mental health, neurological and pain disorders. Learn more at **PharmaTher.com.**

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