PharmaTher Holdings Announces Update of Type C Meeting with the FDA for KETARX™ (Ketamine) in Parkinson's Disease

TORONTO, March 29, 2023 -- PharmaTher Holdings Ltd. (the "Company" or "PharmaTher") (OTCQB: PHRRF) (CSE: PHRM), a specialty pharmaceutical company, today announced an update on the Type C meeting with the U.S. Food and Drug Administration ("FDA") for advancing KETARX™ (ketamine) towards Phase 3 clinical development as a treatment for levodopa-induced dyskinesia in Parkinson's disease ("LID-PD").

The FDA supported the Company's overall approach for the LID-PD program and offered the following feedback:

- Agreed that with the appropriate data, a new drug submission would be considered under the 505(b)(2) regulatory pathway;
- Confirmed that a single confirmatory trial can be the basis for marketing approval under specific circumstances, including treatment duration and final study results;
- Guided on treatment duration, use of evaluation scales and selection of endpoints to ensure treatment approach aligns with expectations for a chronic condition;
- Provided information to enhance the safety monitoring to ensure potential physical and cognitive performance issues can be minimized, adverse events do not go unnoticed, and strategies to minimize patient risk;
- Identified the need for certain short-term non-clinical studies to support increased treatment duration; and
- Advised the Company to make a formal submission to be considered for Fast Track designation.

The Company plans to adapt its proposed clinical development program to align with the FDA's recommendations and the Company's resources towards study evaluations leading into a Phase 3 clinical study and a potential FDA approval via the 505(b)(2) regulatory pathway. The Company will provide updates to its clinical development initiatives as they arise.

"We are satisfied with the feedback we received from the Type C meeting with the FDA, which lays out the pathway to include certain study evaluations to support our proposed Phase 3 clinical study for KETARX™ (ketamine) as a potential treatment for levodopa-induced dyskinesia in Parkinson's disease," said Fabio Chianelli, CEO of PharmaTher. "We are evaluating our clinical

development plan to conform to the FDA's guidance that could potentially lead to a marketing approval via the 505(b)(2) regulatory pathway."

The safety and efficacy results from its previously announced presentation of the Phase I/II clinical study evaluating ketamine as a potential new treatment for LID-PD will be used to support the investigation of KETARX™ in a proposed Phase 3 clinical study.

Summary results of the Phase I/II clinical 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.

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 Phase I/II clinical study [presentation], and 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 Company will proceed with the clinical development towards a Phase 3 clinical study and that the FDA will support any potential request for an expedited path to approval, such as Fast Track designation, or further development for ketamine in the treatment of Parkinson's disease.

About PharmaTher Holdings Ltd.

PharmaTher Holdings Ltd. (OTCQB: PHRRF) (CSE: PHRM) develops and commercializes specialty pharmaceuticals exhibiting growing adoption and permitting novel delivery methods to enhance patient outcomes and prescriber workflow. The Company's lead product is KETARX™ (ketamine) to fill the unmet medical needs for anesthesia, sedation, pain, mental health, and neurological indications. Learn more at **PharmaTher.com.**

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November 30, 2022 ("MD&A"), dated January 23, 2023, which is available on the Company's profile at ***www.sedar.com****.*

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