PharmaTher Holdings Submits Fast Track Application to FDA for KETARX™ (Ketamine) for the Treatment of Parkinson's Disease

TORONTO, May 2, 2023 -- PharmaTher Holdings Ltd. (the "Company" or "PharmaTher") (OTCQB: PHRRF) (CSE: PHRM), a specialty pharmaceutical company, today announced the submission of a Fast Track Application to the U.S. Food and Drug Administration ("FDA") for KETARX™ (ketamine) for the treatment for levodopa-induced dyskinesia in Parkinson's disease ("LID-PD").

Fast Track designation aims to expedite the development and review of new drugs that are intended to treat serious or life-threatening conditions and demonstrate the potential to fill unmet medical needs. The purpose is to get important new drugs to patients faster. Filling an unmet medical need is defined as providing a therapy where none exists or providing a therapy which may be potentially better than available therapy. Drugs that are granted this designation are given the opportunity for more frequent meetings with FDA to discuss the drug's development plan and ensure collection of appropriate data needed to support drug approval; more frequent written communication with FDA about such things as the design of the proposed clinical trials and use of biomarker; Eligibility for Accelerated Approval and Priority Review, if relevant criteria are met; and, Rolling Review, which means that a drug company can submit completed sections of its New Drug Application (NDA) for review by FDA, rather than waiting until every section of the NDA is completed before the entire application can be reviewed. NDA review usually does not begin until the drug company has submitted the entire application to the FDA.

Following its recently announced Type C meeting with the FDA for advancing KETARX™ towards Phase 3 clinical development, the Company is evaluating a Phase 3 clinical trial design to align with the FDA's recommendations that would allow for a potential FDA approval. 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.**

For more information about PharmaTher, please contact:

Fabio Chianelli
Chief Executive Officer
PharmaTher Holdings Ltd.
Tel: 1-888-846-3171

Email: info@pharmather.com
Website: www.pharmather.com

Neither the Canadian Securities Exchange nor its Regulation Services Provider have reviewed or accept responsibility for the adequacy or accuracy of this release.

Cautionary Statement

This press release contains 'forward-looking information' within the meaning of applicable Canadian securities legislation. These statements relate to future events or future performance. The use of any of the words "could", "would", "intend", "expect", "believe", "will", "projected", "estimated", "potential", "aim", "may", "plan", "proposed", "lead", "toward", and similar expressions and statements relating to matters that are not historical facts are intended to identify forward-looking information and are based on PharmaTher Holdings Ltd. (the "Company") current belief or assumptions as to the outcome and timing of such future events. Forward-looking information is based on reasonable assumptions that have been made by the Company at the date of the information and is subject to known and unknown risks, uncertainties, and other factors that may cause actual results or events to differ materially from those anticipated in the forward-looking information. Given these risks, uncertainties and assumptions, you should not unduly rely on these forward-looking statements. The forward-looking information contained in this press release is made as of the date hereof, and Company is not obligated to update or revise any forward-looking information, whether as a result of new information, future events or otherwise, except as required by applicable securities laws. The foregoing statements expressly qualify any forward-looking information contained herein. Factors that could cause actual results to differ materially from those anticipated in these forward-looking statements are described under the caption "Risk Factors" in Company's management's discussion and analysis for the three and nine months ended February 28, 2023 ("MD&A"), dated April 28, 2023, which is available on the Company's profile at ***www.sedar.com****.*

This news release does not constitute an offer to sell or the solicitation of an offer to buy, and shall not constitute an offer, solicitation or sale in any state, province, territory or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state, province, territory or jurisdiction.