



## PharmaTher Announces Notice of Allowance for U.S. Patent Covering Ketamine for the Potential Treatment of Parkinson's Disease and Motor Disorders

TORONTO, July 13, 2022 -- PharmaTher Holdings Ltd. (the "Company" or "PharmaTher") (OTCQB: PHRRF) (CSE: PHRM), a leader in specialty ketamine pharmaceuticals, announced today that the United States Patent and Trademark Office ("USPTO") has provided a Notice of Allowance for patent application No. 15/574,346, 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 (the "Patent").

A Notice of Allowance is issued after the USPTO makes the determination that a patent should be granted from an application. A patent from the recently allowed application is expected to be issued in the coming months.

In August 2020, the Company entered into an exclusive license agreement with the University of Arizona to develop and commercialize the Patent. PharmaTher is advancing the development of ketamine for the potential treatment of Parkinson's disease. The positive topline data from the dose-finding and tolerability clinical study (the "Study") of ketamine for the treatment of levodopa-induced dyskinesia ("LID") in patients with Parkinson's disease has been submitted for presentation to a medical congress and expects to have the results made available in in late-Q3 2022.

The Study evaluated the safety, tolerability and efficacy of low-dose ketamine infusion for the treatment of LID in patients with Parkinson's disease. Efficacy data from the Study demonstrated that 100% of patients treated with ketamine demonstrated a reduction in dyskinesias as measured by the Unified Dyskinesia Rating Scale during the Study period compared to the pre-treatment baseline. Safety data from the Study demonstrated that ketamine was well tolerated with no serious adverse events reported. All adverse events were mild or moderate and reflected the expected side-effects of ketamine administration. This Study further supports the previous findings in the observational study publication, titled "Case Reports Showing a Long-Term Effect of Subanesthetic Ketamine Infusion in Reducing L-DOPA-Induced Dyskinesias," regarding the positive impact of ketamine in reducing LID. In addition, the Study results are adequate to give an effect size in powering a Phase 3 clinical study.

Fabio Chianelli, CEO of PharmaTher, commented: "The US Notice of Allowance of the Patent Application not only adds to our intellectual property portfolio covering novel uses, delivery forms and formulations of ketamine, but it also strengthens our commercial opportunities with ketamine as a potential treatment for Parkinson's disease and movement disorders. We are focused on advancing a potential Phase 3 clinical study for ketamine in the treatment of levodopa-induced dyskinesia in patients with Parkinson's disease."

Based on the Study results, the Company is preparing to engage the FDA to establish the next steps for a planned Phase 3 clinical study to allow for ketamine's approval for Parkinson's disease under the 505(b)(2) regulatory pathway. The Company plans to use its proprietary ketamine intravenous product, KETARX™, for the planned Phase 3 clinical study.

### *Ketamine's Potential In 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. 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] and it is estimated that the potential market opportunity for LID Parkinson's disease to be over USD \$3 billion in the U.S. alone.

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 neurodegenerative 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 focused on the development and commercialization of specialty ketamine pharmaceuticals for mental health, neurological, and pain disorders. Learn more at [PharmaTher.com](https://www.pharmather.com).

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