PharmaTher Provides Update on Product Pipeline and Expected Milestones for 2022

Focused on becoming a leader in the development and commercialization of specialty ketamine prescription-based products

*Expected milestones for 2022 include initiating Phase 3 clinical study for ketamine to treat Parkinson's disease **(KETLID)**; completing Phase 2 clinical study for ketamine to treat ALS **(KETALS)**; completing observational study with ketamine and betaine for depression and pain **(KETABET)**; initiating Phase 2 clinical study for ketamine microneedle patch **(KETAPATCH)**; and seeking FDA approval for Ketamine Hydrochloride Injection USP product **(KETARX)***

TORONTO, Dec. 21, 2021 (GLOBE NEWSWIRE) -- PharmaTher Holdings Ltd. (the "Company" or "PharmaTher") (OTCQB: PHRRF) (CSE: PHRM), a company focused on the development and commercialization of specialty ketamine prescription-based products, is pleased to provide a product pipeline update and expected milestones for 2022.

Fabio Chianelli, Chief Executive Officer of PharmaTher, said, "2021 proved to be a foundational year for PharmaTher as we achieved a number of milestones which have paved the way for an exciting 2022 in unlocking ketamine's therapeutic potential for treating Parkinson's disease and ALS, the development of our ketamine hydrochloride injection USP product and our ketamine microneedle patch as a potential next-generation therapeutic solution for mental health, neurological and pain disorders. We are now in a position both operationally and financially to seek FDA approval for KETARX, our ketamine prescription product, and to enter clinical studies for KETAPATCH, our ketamine patch product, in 2022."

Project KETLID: Ketamine for **L**evodopa-**I**nduced **D**yskinesia in Parkinson's Disease

The Company's Phase 2 clinical trial (ClinicalTrials.gov Identifier: NCT04912115) to evaluate the safety, efficacy and pharmacokinetics of ketamine in the treatment of levodopa-induced dyskinesia ("LID") in patients with Parkinson's disease is currently ongoing and the Company now expects topline results in Q1-2022. Positive Phase 2 clinical results will allow the Company to request a meeting with the FDA to discuss its plan and obtain an agreement to move to a Phase 3 clinical study under the 505(b)2 regulatory pathway by Q3-2022.

PharmaTher has an exclusive license agreement with the University of Arizona for the intellectual property protecting the potential use of ketamine to treat movement disorders. The possible therapeutic effect of low-dose ketamine on LID 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].

Project KETALS: Ketamine for **A**myotrophic **L**ateral **S**clerosis (ALS or Lou Gehrig's Disease)

An Investigator-initiated IND application has been submitted and it is expected the FDA will accept the IND to proceed to a clinical study for ketamine to treat ALS patients within the next 30 days. Patient enrollment is targeted for Q1-2022. On August 3rd, 2021, the Company was granted orphan drug designation by the FDA for ketamine to treat ALS.

PharmaTher has an exclusive license agreement with the University of Kansas for the intellectual property protecting the potential use of ketamine to treat ALS. Ketamine has the potential to effectively increase the life expectancy of those with ALS at any stage and slow the progressive loss of muscle associated with poor outcomes of the disease. The University of Kansas Medical Center researchers and inventors of the potential use of ketamine to treat ALS, Dr. Richard J. Barohn, M.D., John A. Stanford, Ph.D., and Dr. Matthew Macaluso, D.O., have made the promising discovery that ketamine can be administered as an effective treatment for ALS. In addition, unpublished and patent-pending preclinical research has shown that the administration of ketamine preserves muscle function in advancing ALS and increases life expectancy when given in the early stages of muscle decline.

Project KETABET: Ketamine and **Bet**aine Combination Formulation

The Company is supporting an Investigator-lead observational study to evaluate the impact of betaine anhydrous on the unwanted ketamine side effects seen post ketamine treatment for subjects with depression. The Company now expects results to be reported in early Q1-2022. Based on the results, the Company will advance the KETABET program with its microneedle patch for clinical studies in the H2-2022.

PharmaTher has an exclusive license agreement with the National Health Research Institutes for the development and commercialization of a patented combination formulation of FDA-approved ketamine and betaine. KETABET has been shown in research to enhance the antidepressant effect while having the potential to reduce the known negative side effects of ketamine significantly. The combination of ketamine and betaine anhydrous produced more robust antidepressant-like responses than their individual effects and that the combination blocked the psychotomimetic effects of ketamine [Lin, Jen-Cheng et al., 2016].

Project KETAPATCH: Ketamine Microneedle **Patch**

In collaboration with The Queen's University of Belfast ("QUB"), led by Professor Ryan Donnelly, the Company has successfully completed the evaluation of a patented hydrogel-forming microneedle patch to deliver Ketamine and KETABET as a potential next-generation treatment for neuropsychiatric, neurodegenerative and pain disorders. This de-risking milestone supports the Company's expansion in finalizing IND-enabling studies and the clinical manufacturing scale up with LTS Lohmann, a leader in transdermal delivery systems, to support FDA and international regulatory submissions. Validation and tech transfer activities to support clinical studies are in progress and the Company expects to conduct clinical studies in H2-2022.

PharmaTher has an exclusive license agreement with QUB for the development and commercialization of a patented hydrogel-forming microneedle delivery technology developed by Professor Ryan Donnelly to support PharmaTher's product and clinical development initiatives with ketamine and psychedelics. Professor Donnelly's lab successfully completed research and published a paper titled "Hydrogel-forming microneedle arrays as a therapeutic option for transdermal esketamine delivery" validating the delivery of esketamine, the *S*(+) enantiomer of ketamine, in a novel microneedle patch which may overcome the drawbacks associated with ketamine administration in an intravenous or nasal spray format [Courtenay, Aaron J et al., 2020].

Project KETARX: Ketamine Prescription **(Rx)** Product

The Company is developing its own Ketamine Hydrochloride Injection USP product as part of its plans to support the Company's future Phase 3 clinical studies and its commercialization plans in the U.S. via a supplemental Abbreviated New Drug Application ("sANDA") with the FDA for use in anesthesia and procedural sedation. The Company expects to file for its sANDA in Q4-2022 for commercialization in the U.S. and international markets thereafter.

PharmaTher has entered into an agreement with Alcami Corporation, a global pharmaceutical contract development and manufacturing organization with extensive experience in cGMP sterile fill-finish products and handling of controlled substances, for the clinical and commercial manufacturing for the Company's KETARX project. The Company expects to form partnerships with research labs, ketamine clinics and pharmaceutical companies that are: seeking a secure supply of cGMP ketamine and ketamine products for current portfolios; exploring alternative dose forms for multiple existing indications; and requiring support to develop and eventually commercialize specific ketamine products for new indications. In addition, the Company will enter the market with KETARX targeting ketamine's FDA approved label for anesthesia and procedural sedation.

About PharmaTher Holdings Ltd.

PharmaTher Holdings Ltd. (OTCQB: PHRRF) (CSE: PHRM) is focused on the research, development and commercialization of specialty ketamine prescription-based products including KETAPATCH, a ketamine microneedle patch for mental health, neurological and pain disorders, and KETARX, a ketamine hydrochloride injection USP product for anesthesia and procedural sedation. Learn more at **PharmaTher.com**, **Twitter** and **LinkedIn**.

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