



PharmaTher Announces Publication of Research Data for KETABET™

Second published study to demonstrate the potential therapeutic utility and mechanism of action of KETABET™ (patented combination of ketamine and betaine) in models of depression

Repeated use of KETABET™ exhibits potential protective and reversing effects on ketamine-elicited psychotomimetic behaviors and cognitive impairments

Supports clinical initiatives as a potential next generation ketamine treatment for mental health and pain disorders with patent protection into 2036

TORONTO, Jan. 04, 2022 (GLOBE NEWSWIRE) -- PharmaTher Holdings Ltd. (the "Company" or "PharmaTher") (OTCQB: PHRRF) (CSE: PHRM), a life sciences company focused on the development and commercialization of specialty ketamine prescription-based products, today announced the publication of a scientific article demonstrating the potential of KETABET™, a patented combination formulation of FDA-approved ketamine and betaine anhydrous, to prevent the potential adverse psychiatric effects of repeated ketamine treatment for depression and other indications including suicidal ideation, substance abuse, post-traumatic stress disorder, and chronic pain. The article titled, "Betaine prevents and reverses the behavioral deficits and synaptic dysfunction induced by repeated ketamine exposure in mice", is published in *Biomedicine & Pharmacotherapy* and can be found [here](#).

The newly published study further validates the potential of KETABET™ and support the Company's ongoing investigator-led observational studies evaluating the impact of betaine on the unwanted ketamine side effects seen post ketamine treatment for subjects with either depression or pain. Based on the outcome from the ongoing observational studies, the Company will advance the KETABET™ program with its microneedle patch technology in Phase 2 clinical studies in H2-2022.

Modulation of glutamatergic NMDA receptor by betaine might be the underlying mechanisms accounting for cognitive dysfunction, behavioral deficits, and synaptic neurotransmission induced by chronic ketamine use. The present published study aimed to assess whether repeated co-treatment with betaine and ketamine improved behavioral impairments and hippocampal synaptic plasticity. The experimental results showed that both co-treatment and post-treatment with betaine could exhibit the protective and reversing effects on subchronic ketamine-elicited psychotomimetic behaviors, cognitive impairments, and decreases in synaptic function, LTP, and PSD-95 protein expression. Therefore, betaine may enhance the therapeutic effect when combined or post-treated with ketamine for treatment-resistant depression or other mood disorders, and benefit substance abuse disorders.¹ A previously published study revealed that betaine could promote the antidepressant-like effects, yet abolish the psychotomimetic action as well as motor- and cognitive-impairing effects of acute ketamine treatment in mice,² indicating that betaine might potentially enhance the antidepressant efficacy of ketamine and reduce the acute psychotic symptoms in patients when receive ketamine to treat depression. However, it remained unknown if repeated co-treatment with betaine could minimize the adverse psychiatric effects observed after repeated ketamine use, either medically or recreationally. The present published study supported the repeated use of betaine with ketamine.¹

Fabio Chianelli, Chief Executive Officer of PharmaTher, said, "The published data demonstrates the potential of KETABET™'s ability to eliminate the unwanted psychomimetic effects and limitations of ketamine, and aims to be a safe and effective at-home treatment option for mental health, neurological and pain disorders. As such, we remain focused on expanding our clinical programs with KETABET™ for FDA approval."

PharmaTher has an exclusive license agreement with the National Health Research Institutes to develop and commercialize of the intellectual portfolio protecting KETABET™, the patent titled "Method and Composition for Decreasing the Psychotomimetic Side Effect and Addictive Disorder of Ketamine". Granted patents are issued in Japan (Patent no. 6967532) and Taiwan (Patent no. I648049). In addition, the Company expects to convert the current patent applications in the U.S., Europe, Canada, Israel and China into granted patents. Patent protection is expected to expire in 2036.

About PharmaTher Holdings Ltd.

PharmaTher Holdings Ltd. (OTCQB: PHRRF) (CSE: PHRM) is focused on the development and commercialization of specialty ketamine prescription-based products such as KETAPATCH™, a ketamine microneedle patch for mental health and pain disorders, and KETARX™, a ketamine hydrochloride injection USP product for anesthesia, procedural sedation and neurological disorders including Parkinson's disease and Amyotrophic Lateral Sclerosis. Learn more at [PharmaTher.com](#), [Twitter](#) and [LinkedIn](#).

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References:

1. Chen, Shao-Tsu et al. "Betaine prevents and reverses the behavioral deficits and synaptic dysfunction induced by repeated ketamine exposure in mice." *Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie* vol. 144 (2021): 112369. doi:10.1016/j.bio
2. J.-C. Lin, M.-Y. Lee, M.-H. Chan, Y.-C. Chen, H.-H. Chen, Betaine enhances antidepressant-like, but blocks psychotomimetic effects of ketamine in mice, *Psychopharmacology (Berl)*. 233 (2016) 3223–32