PharmaDrug Announces pre-IND Meeting Request Granted by FDA for Oral Antiviral Drug Cepharanthine for the Treatment of COVID-19 Infection

Toronto, Ontario--(Newsfile Corp. - September 28, 2021) - PharmaDrug Inc. (CSE: PHRX) (OTC Pink: LMLLF) ("**PharmaDrug**" or the "**Company**"), a specialty pharmaceutical company focused on the development and commercialization of controlled-substances and natural medicines such as psychedelics, cannabis and naturally-derived approved drugs, is pleased to announce that the Company has been granted a Pre-Investigational New Drug (pre-IND) meeting with the U.S. Food and Drug Administration (FDA) for the clinical development of its patented enteric-coated formulation of cepharanthine (PD-001), an oral antiviral pill as a potential treatment for mild-moderate COVID-19. The Company submitted a briefing package to the FDA, Office of Infectious Diseases, Center for Drug Evaluation and Research for cepharanthine and awaits further feedback on its proposed path toward human clinical development. The pre-IND meeting is a critical step in the US regulatory approval process that is meant to develop mutual understanding and agreement between the FDA and the Company regarding content required to assess manufacturing, toxicology, pre-clinical studies, clinical trials design, and rationale to support subsequent human clinical trials. PharmaDrug anticipates a written response to its pre-IND briefing package by late-November 2021.

Daniel Cohen, Chairman and CEO of PharmaDrug commented, "We are pleased to advance our patented, novel formulation of cepharanthine; a potential first-in-class oral antiviral medication for COVID-19. Forthcoming feedback from the FDA will provide us with critical information relevant to defining our parallel development paths for PharmaDrug's cepharanthine programs in both COVID-19 and rare cancers."

Cepharanthine for Covid-19

Approved for more than 70 years in Japan, cepharanthine has been used safely and effectively to treat a variety of acute and chronic diseases. To date, several third party validated library screens of approved and investigational drugs have identified cepharanthine as a forerunner candidate molecule in the treatment SARS-CoV-2, the virus that causes Covid-19[1,2,3]. In fact, cepharanthine has now been shown to be highly effective at blocking cell death following exposure to multiple different coronaviruses, including COVID-19, lab-attenuated SARS-CoV (original SARS) and the virus that causes Middle East respiratory syndrome (MERS)[1,2,3]. Despite these promising findings, translation into clinical application has thus far been hampered by the need to deliver generic cepharanthine by intravenous due to its intrinsically poor oral bioavailability. As such, it is believed that the Company's novel oral formulation of cepharanthine, PD-001 would be an ideal candidate to evaluate as a potential treatment for mild to moderate COVID-19. By leveraging its exclusive rights to U.S. Patent: 10,576,077, titled "Pharmaceutical Salt forms of Cepharanthine and Tetrandrine", PharmaDrug intends to develop and commercialize PD-001 as an oral antiviral treatment for patients with mild to moderate SARS-CoV-2 infection.

How Cepharanthine May Work to Block Coronavirus Entry

In a recent peer reviewed manuscript cepharanthine was shown to display greater antiviral potency against SARS-CoV-2 than existing clinical development candidates remdesivir, lopinavir, favipiravir, nelfinavir and chloroquine[1]. Researchers identified a putative binding site on the surface of SARS-CoV-2 spike protein known to facilitate viral docking with the human ACE2 receptor. Consistent with this mechanism of action, application of cepharanthine to cells exposed to SARS-CoV-2 fully blocked viral

internalization and subsequent production of viral particles 24 hours post infection[1].

How Cepharanthine May Work to Lessen the Effects of Coronavirus Infection

Extensive mechanism of action studies have shown cepharanthine to exhibit potent antiviral properties as well as other pharmacological traits previously found to be of benefit in treating infectious diseases including anti-oxidative, anti-inflammatory, immuno-regulatory, and anti-parasitic properties. Cell, animal, and human studies have long reported the immunomodulatory and anti-inflammatory properties of cepharanthine[4]. Agents capable of targeting host response are conceptually attractive because they minimize the potential loss of therapeutic drug effects that are sometimes noted as mRNA viruses undergo genetic mutation. Cepharanthine has previously been shown to suppress cytokine production and the expression of cyclooxygenase; both of which are crucial to viral replication and inflammatory response[5,6]. A 2019 study examined the effects of cepharanthine on human lung cells infected with the coronavirus HCoV-OC43[7]. Following pre-treatment with cepharanthine lung cells showed no virus-induced death. These findings were attributed to the ability of cepharanthine to inhibit viral RNA replication, block expression of viral proteins, and suppress production of proinflammatory molecules, thus preventing a deleterious exacerbation of cytokine response to the viral infection.

The Company would like to make it clear that is not making any express or implied claims that its product (cepharanthine) has the ability to treat, eliminate or cure COVID-19 (SARS-CoV-2) and/or other infectious diseases at this time.

Significant need for oral antiviral medications to treat Covid-19 remains

Vaccination programs aimed at controlling the impact of COVID-19 have proceeded at an unprecedented pace; the positive impact of which is clear when examining case counts in jurisdictions that have seen an efficient immunization rollout. However, with the emergence of more infectious Covid-19 variants fueling a fourth wave, even within vaccinated individuals, it is apparent that there also exists an urgent need for complimentary oral antiviral therapies to treat COVID-19 and future coronavirus outbreaks.

On June 17, 2021 the U.S. government announced a 'Whole-of-Government Effort' to spend more than $3 billion on developing next generation COVID-19 treatments in preparation to respond to future virus threats. A major focus for the spend is earmarked to develop oral antiviral drugs for home use, following onset of disease symptoms and to treat people who are vulnerable to the virus such as those who are immunosuppressed or unvaccinated.

According to Dr. David Kessler, Chief Science Officer for the Biden Administration's COVID-19 Response, "An easily administered oral antiviral drug would be an important part of our therapeutic arsenal that would complement the great success of our vaccine efforts."

The magnitude of the current pandemic has brought into sharp focus how susceptible the world remains to known and novel coronaviruses and has underlined the extreme and urgent need for additional research aimed at pre-emptively developing broad classes of oral antiviral agents that can be stockpiled for rapid distribution. Exemplifying the urgent need for oral antivirals, the U.S. Government recently announced that it has committed to purchase $1.2 billion worth of 5-day treatment courses of molnupiravir only if FDA grants EUA or approval. Molnupiravir aims to reduce the replication of the SAR-CoV-2 virus and is being evaluated in an ongoing Phase 3 trial for its potential to reduce the risk of hospitalization or death in non-hospitalized patients who have symptoms for five days or less and are at high risk for severe illness.

About PharmaDrug Inc.

PharmaDrug is a specialty pharmaceutical company focused on the research, development and commercialization of controlled-substances and natural medicines such as psychedelics, cannabis and

naturally-derived approved drugs. The Company owns 100% of Pharmadrug Production GmbH, a German medical cannabis distributor, with a Schedule I European Union narcotics license and German EuGMP certification allowing for the importation and distribution of medical cannabis to pharmacies in Germany and throughout the EU. The Company also owns 100% of Super Smart, a Dutch company building a modern adult use psychedelic retail business with an elevated and educational focus. PharmaDrug recently acquired Sairiyo Therapeutics, a biotech company that specializes in researching and reformulating established natural medicines with a goal of bringing them through regulatory and research driven clinical trials.

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References:

1) Ohashi H, Watashi K, Saso W, Shionoya K, Iwanami S, Hirokawa T, Shirai T, Kanaya S, Ito Y, Kim KS, Nomura T, Suzuki T, Nishioka K, Ando S, Ejima K, Koizumi Y, Tanaka T, Aoki S, Kuramochi K, Suzuki T, Hashiguchi T, Maenaka K, Matano T, Muramatsu M, Saijo M, Aihara K, Iwami S, Takeda M, McKeating JA, Wakita T. Potential anti-COVID-19 agents, cepharanthine and nelfinavir, and their usage for combination treatment. iScience. 2021 Apr 23;24(4):102367. doi: 10.1016/j.isci.2021.102367. Epub 2021 Mar 26. PMID: 33817567; PMCID: PMC7997640.

2) Chen CZ, Xu M, Pradhan M, Gorshkov K, Petersen JD, Straus MR, Zhu W, Shinn P, Guo H, Shen M, Klumpp-Thomas C, Michael SG, Zimmerberg J, Zheng W, Whittaker GR. Identifying SARS-CoV-2 Entry Inhibitors through Drug Repurposing Screens of SARS-S and MERS-S Pseudotyped Particles. ACS Pharmacol Transl Sci. 2020 Oct 19;3(6):1165-1175. doi: 10.1021/acsptsci.0c00112. PMID: 33330839; PMCID: PMC7586456.

3) Fan HH, Wang LQ, Liu WL, An XP, Liu ZD, He XQ, Song LH, Tong YG. Repurposing of clinically approved drugs for treatment of coronavirus disease 2019 in a 2019-novel coronavirus-related coronavirus model. Chin Med J (Engl). 2020 May 5;133(9):1051-1056. doi: 10.1097/CM9.0000000000000797. PMID: 32149769; PMCID: PMC7147283.

4) Rogosnitzky M, Okediji P, Koman I. Cepharanthine: a reviewof the antiviral potential of a Japanese-approved alopecia drug in COVID-19. Pharmacol Rep. 2020 Dec;72(6):1509-1516. doi: 10.1007/s43440-020-00132-z. Epub 2020 Jul 22. PMID: 32700247; PMCID: PMC7375448.

5) Ershun Z, Yunhe F, Zhengkai W, Yongguo C, Naisheng Z, Zhengtao Y. Cepharanthine attenuates lipopolysaccharide-induced mice mastitis by suppressing the NF-κB signaling pathway. Inflammation. 2014 Apr;37(2):331-7. doi: 10.1007/s10753-013-9744-6. PMID: 24062060.

6) Paudel KR, Karki R, Kim DW. Cepharanthine inhibits in vitro VSMC proliferation and migration and vascular inflammatory responses mediated by RAW264.7. Toxicol In Vitro. 2016 Aug;34:16-25. doi: 10.1016/j.tiv.2016.03.010. Epub 2016 Mar 25. PMID: 27021874.

7) Kim DE, Min JS, Jang MS, Lee JY, Shin YS, Song JH, Kim HR, Kim S, Jin YH, Kwon S. Natural Bis-Benzylisoquinoline Alkaloids-Tetrandrine, Fangchinoline, and Cepharanthine, Inhibit Human Coronavirus OC43 Infection of MRC-5 Human Lung Cells. Biomolecules. 2019 Nov 4;9(11):696. doi: 10.3390/biom9110696. PMID: 31690059; PMCID: PMC6921063.

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