PharmaDrug Announces Initiation of Manufacturing of Cepharanthine (PD-001) For Clinical Programs in Rare Cancers And COVID-19

Establishing cGMP supply for IND-enabling and up to Phase 2 clinical studies for PD-001 oral formulation for esophageal cancer and mild to moderate COVID-19

Toronto, Ontario--(Newsfile Corp. - January 26, 2022) - PharmaDrug Inc. (CSE: PHRX) (OTCQB: LMLLF) ("**PharmaDrug**" or the "**Company**"), 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, is pleased to announce that the Company has initiated the manufacturing of PD-001, a patented enteric-coated oral formulation of cepharanthine, for non-clinical and clinical studies in cancer and infectious diseases. This follows the Company's recent announcements of the successful completion of its pre-IND meeting with the U.S. Food and Drug Administration (the "**FDA**") regarding the proposed development of PD-001 for the treatment of mild to moderate COVID-19 and positive preclinical study results with PD-001 for esophageal cancer and other undisclosed cancers. The current scale of manufacturing activities should fully support development of PD-001 through IND-enabling studies and potential future FDA Phase 1 and 2a clinical studies.

Consistent with FDA requirements, a core battery of drug development activities need to be completed prior to initiation of human testing regardless of the disease indication under development. As such, parallel development of PD-001 for oncology and infectious disease indications will provide valuable time and cost efficiencies to the Company by way of eliminating the need to duplicate multiple standard activities. One such place relates to drug manufacturing control and the need to reproducibly generate a sufficient quantity and quality of drug material to support all non-clinical and clinical testing. To that end, PharmaDrug has purchased a significant quantity of bulk cepharanthine material and has engaged Southwest Research Institute (SwRI) to initiate cGMP manufacturing activities in Q1, 2022. SwRI has a previous track record for producing the Company's drug substance and drug product according to required specifications. Following receipt of feedback from the FDA in November 2021 on its pre-IND application to treat COVID-19, the Company is confident of its ability to simultaneously execute on both its PD-001 programs (COVID-19 and esophageal cancer) and that the drug product manufactured using existing methodology will yield material that complies with the rigorous standards set forth by the regulator.

Daniel Cohen, CEO and Chairman of PharmaDrug commented, "We are extremely excited to be moving forward with the manufacturing of a cGMP lot of PD-001. We believe cepharanthine has tremendous potential to treat several indications. Following the completion of a successful pre-IND meeting with the FDA and ongoing studies in both rare cancers and COVID-19, we are confident we have a clear path to the clinic on a number of fronts."

About PD-001 (Enteric-coated Oral Cepharanthine)

Cepharanthine is a natural product and an approved drug used for more than 70 years in Japan to successfully treat a variety of acute and chronic diseases. In clinical research, Cepharanthine has been shown to exhibit multiple pharmacological properties including anti-oxidative, anti-inflammatory, immuno-regulatory, anti-cancer, anti-viral and anti-parasitic effects[1,2]. However, historically cepharanthine's low oral bioavailability has represented a major obstacle to realizing its full clinical potential.

The Company is focused on advancing the clinical development of an improved and patented enteric-coated oral formulation of cepharanthine (PD-001) to treat rare cancers and COVID-19. Compared to generic cepharanthine, PD-001 has been shown in rodent and non-rodent models to possess markedly superior bioavailability (more easily absorbed). These findings support the development of an orally administered formulation, and in so doing, removes the undesirable requirement for frequent intravenous dosing.

PD-001 for Cancer

PharmaDrug's cancer program is based on cepharanthine's known anti-cancer activities. Cepharanthine has been shown in multiple preclinical efficacy models to inhibit cancer cell proliferation, induce cancer cell apoptosis (death) and restore cancer cell sensitivity to multiple unrelated classes of chemotherapy. Multidrug resistance continues to represent a considerable clinical challenge. As such, preclinical cancer studies aimed at elucidating the mechanisms that underly chemoresistance; including the critical role drug efflux pumps play in this phenomenon by reducing the intracellular concentration of chemotherapeutic drugs, are of particular interest to PharmaDrug. Cepharanthine has been shown in preclinical studies to potently reverse chemoresistance by downregulating expression of ABCB1, the transcript of which codes for multidrug resistance protein 1, (MDR1, aka P- glycoprotein). Importantly, several prior in vitro and in vivo studies have shown that cepharanthine-mediated reductions in ABCB1 expression restores cancer cell sensitivity to a range of chemotherapeutics including taxanes, vinca alkaloids and platinum-based drugs[3-6]. Collectively the two studies already completed by the Company, and those currently underway aim to identify and provide focus to novel opportunities in oncology by revealing optimal cancer cell types as a monotherapy and/or drug combinations and situations where PD-001 can prevent, lessen, or reverse chemoresistance, and provide additive or synergistic benefit to existing standard of care treatments (for reference please see previous press releases Nov 18, Oct 15 and July 28, 2021). The Company's ongoing animal efficacy studies are designed to experimentally examine the role of cepharanthine in restoring chemosensitivity. Based on compelling preclinical data in esophageal cancer and a streamlined path to approval which comes by way of a recently granted FDA Orphan Drug Designation, the Company continues its plans to pursue cepharanthine for this indication.

PD-001 for COVID-19

The global significance of coronavirus infection has been rising following the emergence and identification of the virus that causes severe acute respiratory syndrome (SARS) was first documented in Guandong, China in 2002. Since then, a related virus causing middle east respiratory syndrome (MERS) in 2012 and currently SARS-CoV-2, first identified in 2019, have revealed obvious vulnerabilities related to containing and treating novel coronavirus outbreaks. 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[7-9]. 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)[7-9]. In November 2021 an independent research group examined the potential of cepharanthine to limit the cytopathic effects of the South African COVID-19 variant, B.1.3514. It was found that cepharanthine was at least 6-times more active against the South African variant strain than original SARS-CoV-2, and that cepharanthine was the most effective of all the drugs used in the in vitro screen that was perfomed[10]. Although the recent Omicron variant discovered in South African nations shares several features in common with the previous South African variant, B.1.351, it remains to be determined how well cepharanthine will perform at treating this ongoing threat. Despite the promising findings for cepharanthine noted above, translation into clinical application has thus far been hampered by the need for the generic formulation of the drug to be delivered 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 and variants thereof.

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[7]. 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[7].

Ongoing Need for a Deep Arsenal of Oral Antiviral Medications

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. With increasing population density, shifts in agricultural practice, international trade and expanded travel all contributing to elevated health and financial burden related to infectious disease, continued focus on development of oral antivirals to treat existing and emerging viral strains is expected to remain a worldwide priority for the foreseeable future.

The Company is not making any express or implied claims that its product has the ability to eliminate, cure or contain the Covid-19 (or SARS-2 Coronavirus) at this time.

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. PharmaDrug owns 100% of Pharmadrug Production GmbH ("Pharmadrug Production"), 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 European Union. PharmaDrug owns 100% Sairiyo Therapeutics ("Sairiyo"), a biotech company that specializes in researching and reformulating established natural medicines with a goal of bringing them through clinical trials and the associated regulatory approval process in the US and Europe. Sairiyo is currently developing its patented reformulation of cepharanthine, a drug that has shown substantial third party validated potential for the treatment of COVID-19 and rare cancers. Sairiyo is also conducting R&D in the psychedelics space for the treatment of non-neuropsychiatric conditions. The Company also owns 100% of Super Smart, a company building a vertically integrated retail business with the goal to elevate the use of functional mushrooms, and psilocybin mushrooms where federally legal, as natural based medicines.

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This press release contains "forward-looking information" within the meaning of applicable securities legislation. All statements, other than statements of historical fact, included herein are forward-looking information. Generally, forward-looking information may be identified by the use of forward-looking terminology such as "plans", "expects" or "does not expect", "proposed", "is expected", "budgets",

"scheduled", "estimates", "forecasts", "intends", "anticipates" or "does not anticipate", or "believes", or variations of such words and phrases, or by the use of words or phrases which state that certain actions, events or results may, could, would, or might occur or be achieved. In particular, this press release contains forward-looking information in relation to: the development and commercialization of cepharanthine, the results of the Company's research and development in the psychedelics space and the development of the Supersmart business . This forward-looking information reflects the Company's current beliefs and is based on information currently available to the Company and on assumptions the Company believes are reasonable. These assumptions include, but are not limited to the ability of the Company to successfully execute on its plans for the Company and its affiliated entities; the ability to obtain required regulatory approvals and the Company's continued response and ability to navigate the COVID-19 pandemic being consistent with, or better than, its ability and response to date.

Forward-looking information is subject to known and unknown risks, uncertainties and other factors that may cause the actual results, level of activity, performance or achievements of the Company to be materially different from those expressed or implied by such forward-looking information. Such risks and other factors may include, but are not limited to: general business, economic, competitive, political and social uncertainties; general capital market conditions and market prices for securities; the actual results of the Company's future operations; competition; changes in legislation affecting the Company; the ability to obtain and maintain required permits and approvals, the timing and availability of external financing on acceptable terms; lack of qualified, skilled labour or loss of key individuals; risks related to the COVID-19 pandemic including various recommendations, orders and measures of governmental authorities to try to limit the pandemic, including travel restrictions, border closures, non-essential business closures, service disruptions, quarantines, self-isolations, shelters-in-place and social distancing, disruptions to markets, economic activity, financing, supply chains and sales channels, and a deterioration of general economic conditions; and a deterioration of financial markets that could limit the Company's ability to obtain external financing.

A description of additional risk factors that may cause actual results to differ materially from forward-looking information can be found in the Company's disclosure documents on the SEDAR website at www.sedar.com. Although the Company has attempted to identify important factors that could cause actual results to differ materially from those contained in forward-looking information, there may be other factors that cause results not to be as anticipated, estimated or intended. Accordingly, readers should not place undue reliance on forward-looking information. Readers are cautioned that the foregoing list of factors is not exhaustive. Readers are further cautioned not to place undue reliance on forward-looking information as there can be no assurance that the plans, intentions or expectations upon which they are placed will occur. Such information, although considered reasonable by management at the time of preparation, may prove to be incorrect and actual results may differ materially from those anticipated.

The Company's securities have not been registered under the U.S. Securities Act of 1933, as amended (the "U.S. Securities Act"), or applicable state securities laws, and may not be offered or sold to, or for the account or benefit of, persons in the United States or "U.S. Persons", as such term is defined in Regulations under the U.S. Securities Act, absent registration or an applicable exemption from such registration requirements. This press release shall not constitute an offer to sell or the solicitation of an offer to buy nor shall there be any sale of the securities in the United States or any jurisdiction in which such offer, solicitation or sale would be unlawful.

Forward-looking information contained in this press release is expressly qualified by this cautionary statement. The forward-looking information contained in this press release represents the expectations of the Company as of the date of this press release and, accordingly, are subject to change after such date. However, the Company expressly disclaims any intention or obligation to update or revise any forward-looking information, whether as a result of newinformation, future events

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