Pharmadrug Announces Successful Completion of Pre-IND Meeting with FDA Regarding Proposed Development of Its Cepharanthine for Treatment of Mild to Moderate COVID-19 Infection

- *Established alignment with FDA on the path forward for the development of PD-001, a patented enteric-coated formulation of cepharanthine, towards clinical studies for mild-moderate COVID-19 infection*
- *Meeting response validates CMC package for PD-001 as an oral anti-viral to treat COVID-19 infection*
- *PharmaDrug intends to pursue FDA Expedited Programs, such as Breakthrough Designation pending future clinical study data for PD-001*
- *PharmaDrug plans to initiate clinical studies in the second half of 2022*
- *Focusing on building a pipeline in a pill strategy with PD-001 targeting rare diseases and life-threatening conditions*

Toronto, Ontario--(Newsfile Corp. - November 30, 2021) - 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 the successful completion of its Type B pre-IND meeting with the U.S. Food and Drug Administration (FDA), for which a pre-IND briefing package and meeting request letter was submitted in September 2021. The FDA has provided written responses to the Company regarding its clinical development plan for PD-001, a patented enteric-coated formulation of cepharanthine, as a potential oral antiviral pill for COVID-19. PharmaDrug believes the written response provides a path to agreements on IND-enabling studies, the design of a Phase 1/2 clinical study, and the overall clinical development plan to move PD-001 forward as an oral treatment for COVID-19. By extension, the FDA guidance also provides important insights on advancing PD-001 as a potential treatment for oncology indications as part of the Company's ongoing strategy of targeting rare and life-threatening conditions. The Company continues to focus on completing the remaining IND-enabling studies to support future clinical studies in 2022.

As the pandemic has evolved rapidly, so too have the FDA's views and requirements on what pre-clinical and non-clinical data sets will be necessary to support initiation of a first in human clinical trial for COVID-19. In written responses to the questions provided by the Company, the FDA addressed PharmaDrug's questions related to manufacturing, safety/toxicology, pre-clinical efficacy studies, clinical trial design, and rationale necessary to support subsequent human clinical trials. The feedback provides the Company with greater clarity on the current requirements needed to file an IND to initiate a Phase 1/2 clinical trial of PD-001 in patients with COVID-19. Based upon the historical clinical data for generic cepharanthine and the Company's preclinical testing performed on PD-001 thus far, PharmaDrug anticipates filing an IND in the second half of 2022. In addition, PharmaDrug intends to pursue FDA Expedited Programs, such as Breakthrough Designation pending the development of preliminary clinical evidence to support such designation.

PharmaDrug intends to advance its IND-enabling activities for PD-001 as follows based on the written response it recently received from the FDA:

- The proposed PD-001 formulation and drug substance specifications are reasonable.
- The Chemistry and Manufacturing Control (CMC) module received generally positive feedback for the current stage of development.

- Alignment on planned IND-enabling toxicology and primary virology programs established.

Following FDA feedback, the Company plans to continue the development of PD-001 for COVID-19. The Company will be conducting several nonclinical safety, toxicology, virology assessments, as well as scale-up of drug product manufacturing. The currently described work is necessary to bring PD-001 to the clinic for COVID-19 and is highly complementary to the safety/tox/manufacturing efforts already underway for its cepharanthine program in oncology.

"The FDA's response to our recent pre-IND submission will allow us to be efficient and systematic about completing the remaining activities necessary to safely transition our cepharanthine program from pre-clinical into full clinical evaluation as a novel, oral antiviral to treat COVID-19. The continued emergence of COVID-19 variants, including the recent Omicron variant, some of which may eventually evolve to evade the protection afforded by existing vaccines, underscores an urgent need to develop an effective and diverse arsenal of orally active antiviral medications," said Dr Van Slyke, Chief Scientific Officer of PharmaDrug.

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.

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]. 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.1.351[4]. 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[4]. 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 emerging 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.

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].

About PD-001 (Enteric-coated 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[5,6]. 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 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.

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 recently acquired 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 or otherwise, except as expressly required by applicable securities law.

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