PharmaDrug Announces Plans for First-In-Human Clinical Study with PD-001 (Enteric-Coated Cepharanthine -2HCL) in Esophageal Cancer

Toronto, Ontario--(Newsfile Corp. - February 13, 2023) - PharmaDrug Inc. (CSE: PHRX) (OTCQB: LMLLF) ("**PharmaDrug**" or the "**Company**"), a specialty pharmaceutical company focused on the research, development and commercialization of psychedelics and other naturally-derived approved drugs, is pleased to announce that the Company intends to pursue a first-in-human study of its lead development candidate, PD-001, enteric coated cepharanthine-2HCL (for oral administration), in Australia during the second half of 2023.

"We are committed to advancing the development of new treatments for patients with esophageal cancer, and we believe that PD-001 has the potential to be a breakthrough therapy," said Daniel Cohen, CEO of PharmaDrug. "We intend to leverage the benefits of our orphan drug designation and the data generated from the first-in-human clinical study to support planned Food and Drug Administration (FDA) clinical trials in the U.S. We believe that this cost-efficient strategy will greatly enhance the value of our company for our investors."

The proposed first-in-human study aims to be a prospective multi-site open label randomized controlled clinical investigation of the safety, tolerability, and pharmacokinetics of PD-001 in esophageal cancer subjects. The Company's decision to pursue clinical development of PD-001 for esophageal cancer initially in Australia derives from a streamlined regulatory framework established by Australia's Therapeutic Goods Administration (TGA) that permits a sponsor to bypass the lengthy and costly process of filing an IND application that would be required by the FDA, while also allowing a sponsor to evaluate its investigational drug prior to committing to larger clinical studies in the U.S. and Europe. In addition to the world-class facilities and deep clinical trial expertise located in Australia, the Company intends to take advantage of Australia's Research and Development (R&D) tax incentive program which will provide the Company with up to a 43.5% refund on all R&D expenditures. Strict adherence to guidelines set forth by TGA ensures that the Company's clinical trial data will be acceptable to other regulatory bodies including the FDA. For the Company, human clinical data generated from Australia would de-risk PD-001's clinical development plan and support further investigation of PD-001 in subsequent Phase 2 and confirmatory studies in the U.S. under an IND with the FDA. PharmaDrug's investigational drug, PD-001, has been granted orphan drug designation by the FDA for the treatment of esophageal cancer.

Efforts to support clinical evaluation of PD-001 for esophageal cancer are currently underway. A large-scale cGMP lot of cepharanthine-2HCL has been completed and specific test methods required by the FDA for the quantification of drug attributes have been developed during Q4 of 2022 to support the issuance of the certificate of analysis and master batch record. Final release testing is ongoing and the Company plans to transfer this material to its contract manufacturer, Genvion Corporation. Material transfer is planned for March, 2023 and once complete, Genvion will execute all necessary ICH-compliant stability testing and forced degradation studies in support of future filings to the TGA and FDA. Downstream manufacturing efforts required to produce the orally bioavailable clinical drug product, PD-001 will also be completed by Genvion Corporation.

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 responsive cancers and COVID-19. Compared to generic cepharanthine, PD-001 has been shown in rodent and non-rodent models to possess markedly improved oral 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 to maintain therapeutic levels of drug in circulation. The Company endeavours to develop an efficacious oral therapeutic to potentially improve outcomes for infectious disease and oncology applications.

Third-party Validated Studies Reveal Potential for Cepharanthine in Treating Cancer

PharmaDrug's oncology program is based on cepharanthine's known anti-cancer activities. Cepharanthine has been shown in over 160 peer-reviewed publications 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[1-4].

PD-001 Demonstrates Benefit in IND-Enabling Esophageal Cancer Study

The Company previously announced (June 16, 2022) that a once-per-day oral regimen of PD-001, in combination with a SoC chemotherapeutic drug, paclitaxel significantly reduced tumor volume and improved tumor inhibition at the scheduled end of dosing (day 28 post implantation) in its recently completed esophageal cancer efficacy study. Following 28 days of paclitaxel administration tumor volume was reduced by 53% compared to the untreated control group. Paclitaxel provided robust tumor growth inhibition in the early portion of the study, but during the second half, the rate of tumor growth tended to accelerate. This observation mirrors that which is often noted in the clinical treatment of esophageal cancer patients; with the development of chemoresistance often noted after a period of treatment. PD-001 delivered at a dose of 27 mg/kg/day combined with paclitaxel provided an improvement of 41% in tumor volume reduction beyond that of paclitaxel alone (day 28 post tumor implantation). This result was found to be statistically significant versus paclitaxel alone ($p=0.0049$). PD-001 (27 mg/kg/day) tended to provide tumor growth inhibition as early as day 17 post implantation (40% greater than paclitaxel alone), that peaked at day 20 (84% greater than paclitaxel alone). The Company has issued previous press releases related to the use of PD-001 for the treatment of esophageal cancer on November 18, 2021, October 15, 2021 and July 28, 2021.

Potential of PD-001 to treat Esophageal Cancer

Despite standard, targeted and immunotherapy options, survival from esophageal cancer is dismal. The 5-year survival rate of people with cancer located only in the esophagus is 47%. The 5-year survival rate for those with disease that has spread to surrounding tissues or organs and/or the regional lymph nodes is 25%. If it has spread to distant parts of the body, the survival rate is 5%[5,6]. Cepharanthine is a natural alkaloid extracted from S. cepharantha Hayata that has been used in Japan to treat several acute and chronic diseases with only rare reports of safety issues and side effects. The Company recently filed a PCT application to protect findings which showed the efficacious use of cepharanthine-2HCL when combined with cabazitaxel, a second generation taxane, for the treatment of prostate cancer. Treatment

of esophageal cancer is highly varied based on clinical presentation and the physician's own preference/experience. Treatment with taxane family member, paclitaxel remains a common approach for esophageal cancer, however chemoresistance to paclitaxel represents a significant clinical challenge[7]. The observation that cepharanthine can decrease or overcome development of chemoresistance, in particular to taxanes points to the potential of PD-001 to be a novel targeted therapy for use as a neoadjuvant and/or adjuvant treatment which could provide increased survival benefit.

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 and previously approved drugs. PharmaDrug owns 100% of 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 infectious disease (including Covid-19) and rare cancers. Sairiyo is also conducting R&D in the psychedelics space for the treatment of non-neuropsychiatric conditions.

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THE CANADIAN SECURITIES EXCHANGE HAS NOT REVIEWED NOR DOES IT ACCEPT RESPONSIBILITY FOR THE ADEQUACY OR ACCURACY OF THIS RELEASE.

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 timing of study of the proposed first-in-human study of its lead development candidate, PD-001, enteric coated cepharanthine-2HCL (for oral administration); the potential for PD-001; the completion of planned FDA clinical trials in the U.S; the ability to take advantage of Australia's tax incentive program for R&D expenses; statements regarding the issuance of a certificate of analysis and master batch record; the timing of the transfer of the large-scale cGMP lot of cepharanthine-2HCL; the development and commercialization of cepharanthine, the timing of the clinical trial-scale production of cGMP Cepharanthine-2HCL; and the results of the Company's research and development in the psychedelics space. 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 new information, future events or otherwise, except as expressly required by applicable securities law.

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