PharmaDrug Successfully Completes Key Milestone to Support cGMP Production of Clinical Lead Candidate PD-001, Its Patented, Orally Available Version of Cepharanthine for Oncology and Infectious Disease

- *Completes qualification of all necessary analytical methodologies to support production of Cepharanthine-2HCL drug substance*
- *Clinical trial-scale production of cGMP Cepharanthine-2HCL drug substance scheduled for delivery in second half of September 2022*
- *Genvion Corporation formally engaged to conduct ICH-compliant stability, forced degradation and drug product manufacturing in support of IND filing and clinical requirements*

Toronto, Ontario--(Newsfile Corp. - August 19, 2022) - 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 has now completed the significant groundwork, including sourcing and characterization of bulk materials, preparation of reference standards and qualification of all necessary analytical methodologies to support multi-kilogram, cGMP production of cepharanthine-2HCL drug substance for use in the final drug product production of PD-001, its patented, orally bioavailable version of cepharanthine. Completion of this lot, slated for September 2022, significantly advances the Company's efforts to support pre-clinical and clinical development, including to the commencement of potential Phase 2 clinical studies, for parallel indications in oncology and infectious disease. Consistent with these advancements, the Company has formally engaged Genvion Corporation to complete necessary ICH-compliant stability testing and forced degradation studies in support of future IND filings to the U.S. Food and Drug Administration (FDA). On behalf of the Company, Genvion Corporation will take receipt of the cGMP drug substance and complete all manufacturing efforts necessary to produce the orally bioavailable clinical drug product, PD-001.

Daniel Cohen, CEO and Chairman of PharmaDrug commented, "The sourcing and subsequent characterization of bulk materials, including generic cepharanthine, followed by the preparation of cGMP calibre analytical methodologies as required by the FDA represents the majority of the effort in this initial cGMP production initiative. With these activities now complete, we are positioned to initiate the cGMP manufacturing run of our lead candidate PD-001. Achieving this milestone represents an important inflection point in our preclinical and clinical development programs in oncology and infectious disease."

Parallel Development Paths for Oncology and Infectious Disease Create Efficiency

Following submission of its Type B pre-IND meeting request and briefing package to the FDA, the Company received a written response regarding its clinical development plan for PD-001, as a potential oral antiviral pill for COVID-19 and variants of concern. PharmaDrug has executed on feedback, specifically as it related to necessary chemistry and manufacturing controls set forth by the regulator, to meaningfully advance its preclinical development programs for PD-001 as a potential treatment for infectious disease and oncology indications including prostate and esophageal cancers.

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 is endeavouring 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[3-6].

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

A previous IND-enabling efficacy study commissioned by the Company demonstrated that a once-per-day oral regimen of PD-001, in combination with standard of care chemotherapy (SoC), cabazitaxel provided statistically significant benefit from day 10 through to the end of dosing (day 21). The degree of tumor growth inhibition improved for those groups receiving the combination of PD-001 and cabazitaxel versus cabazitaxel-alone, suggesting that PD-001 add-on therapy might provide clinically relevant adjunctive care options as an oral medication. Significantly, PD-001 delivered at doses of 3, 9, or 27 mg/kg/day combined with cabazitaxel (3mg/kg/Q3D) provided up to a 64% tumor growth inhibition compared to 37% noted for treatment with cabazitaxel alone. Addition of PD-001 to the SoC, cabazitaxel was found to improve tumor growth inhibition by 73% compared to cabazitaxel-alone. Study results were deemed to be highly statistically significant, with a p-value less than 0.001 (day 21). Importantly, the addition of PD-001 to cabazitaxel did not notably increase toxicity compared to cabazitaxel alone. Based on the data generated thus far, the Company has filed two recent provisional patent applications which support use of PD-001 plus cabazitaxel for primary, metastatic and chemotherapy-resistant prostate cancer. For reference to PharmaDrug's ongoing efforts in the prostate cancer space please see previous press releases from April 19, March 9, Feb 1, 2022 and Nov 18, Oct 15, July 28, 2021.

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

In addition to its ongoing investigations of PD-001 for prostate cancer, the Company plans to fully leverage the streamlined path to approval which comes by way of its granted FDA Orphan Drug Designation PD-001 for the treatment of esophageal cancer. 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 Nov 18, Oct 15, July 28, 2021.

PD-001 For Infectious Disease, Including Covid-19

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.1.351. 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[8]. 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. Intriguingly, the same authors also noted that cepharanthine displayed significant potency with a favorable selectivity index for other RNA viruses including Zika and Ebola[10]. 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[7]. Researchers identified a putative binding site on the surface of the 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].

The Company is not making any express or implied claims that its product has the ability to eliminate or cure COVID-19 (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 and previously

approved drugs. 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 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. 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 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 timing of the clinical trial-scale production of cGMP Cepharanthine-2HCL 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.

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