

# PharmaDrug Advances Programs in Oncology with Filing of PCT Application Detailing the Use of PD-001 for Treatment of Prostate Cancer

Toronto, Ontario--(Newsfile Corp. - January 31, 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 has completed filing a PCT (Patent Cooperation Treaty) application for its lead drug, cepharanthine-2HCL (PD-001) for the treatment of prostate cancer, alone or in combination with standard of care chemotherapeutics, as well as for other indications where the drug has shown efficacy in preclinical studies. This move is expected to build significant value for the Company's investors. Filing of the PCT provides the Company with 18 months to formally elect and pursue patent protection in any of 153 member countries, including countries of strategic interest such as the United States, Canada, Japan and China.

"We are excited to take this important step in the development of PD-001 as a treatment for prostate cancer and other indications. This PCT patent filing is a significant milestone that will solidify our intellectual property portfolio and provide a clear path for commercialization," said Daniel Cohen, CEO of PharmaDrug. "This move is expected to create significant value for our investors as we bring this potentially life-saving treatment to patients around the globe suffering from these diseases."

PD-001 is a novel compound with a unique mechanism of action that has shown promising results in preclinical studies for the treatment of a wide range of diseases. These include but are not limited to prostate cancer, colorectal cancer, breast cancer and infectious disease as well as several others. The PCT patent filing will enable PharmaDrug to simultaneously seek protection for its intellectual property in multiple countries worldwide and will support claims related to the use of PD-001 alone or in combination with already approved chemotherapeutic agents. This is expected to provide a strong competitive advantage and a solid foundation for the commercialization of the drug.

## **Claims Set Forth in PCT Filing Centered Around Demonstrated Benefit of PD-001 in Pre-Clinical Prostate Cancer Study**

The Company's previously commissioned IND-enabling efficacy study 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, addition of PD-001 to cabazitaxel did not notably increase toxicity compared to cabazitaxel alone. The Company previously filed two Provisional Patent applications which support use of PD-001 plus cabazitaxel for primary, metastatic and chemotherapy-resistant prostate cancer. For further 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.

## **Third-party Validated Studies Support 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<sup>1-4</sup>.

## **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 U.S. Food and Drug Administration (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. To that end, the Company recently completed optimization and production of a large scale, cGMP lot of cepharanthine-2HCl which is earmarked for planned potential phase 1 and phase 2a clinical studies. Drug stability monitoring and production of the final, enteric coated drug product for clinical evaluation is poised to commence. The Company will provide a thorough status update on these activities in the coming weeks.

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 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, immunoregulatory, anti-cancer, anti-viral and anti-parasitic effects<sup>5,6</sup>. 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.

## **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 cancers. Sairyo is also conducting R&D in the psychedelics space for the treatment of non-neuropsychiatric conditions.

For further information, please contact:

Daniel Cohen, Chairman and CEO

[dcohen@pharmadrug.co](mailto:dcohen@pharmadrug.co)

(647) 202-1824

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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](http://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*

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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.

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