PharmaDrug Advances Product and Clinical Development of Cepharanthine to Treat Infectious Diseases Including COVID-19

Toronto, Ontario--(Newsfile Corp. - June 22, 2021) - PharmaDrug Inc. (CSE: BUZZ) (OTC Pink: 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 preparation of a Pre-Investigational New Drug Application (pre-IND) for its patented enteric-coated formulation of cepharanthine (PD-001), an oral antiviral pill to treat mild-moderate COVID-19.

Vaccination programs aimed at controlling the impact of COVID-19 have proceeded at an unprecedented pace; the positive impact of which is clear when examining case counts in jurisdictions that have seen an efficient immunization rollout. However, there remains an urgent need for additional antiviral therapies for COVID-19 and future coronavirus outbreaks.

On June 17, 2021 the U.S. government announced a 'Whole-of-Government Effort' to spend more than $3 billion on developing next generation COVID-19 treatments in preparation to respond to future virus threats. A major focus for the spend is earmarked to develop oral antiviral drugs for home use, following onset of disease symptoms and to treat people who are vulnerable to the virus such as those who are immunosuppressed or unvaccinated.

According to Dr. David Kessler, Chief Science Officer for the Biden Administration's COVID-19 Response, "An easily administered oral antiviral drug would be an important part of our therapeutic arsenal that would complement the great success of our vaccine efforts."

Approved for more than 70 years in Japan, cepharanthine has been used to successfully treat a variety of acute and chronic diseases. Extensive mechanism of action studies have shown cepharanthine to exhibit potent antiviral properties as well as other pharmacological traits that are of benefit in treating infectious diseases including anti-oxidative, anti-inflammatory, immuno-regulatory, and anti-parasitic properties. To date, several third party validated library screens of approved and investigational drugs have identified cepharanthine as a forerunner candidate based on the superior antiviral properties it displays against 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[1,2,3]. As such, it is believed that the Company's novel formulation of cepharanthine, PD-001 would be an ideal candidate to evaluate as a potential treatment for mild to moderate COVID-19. The U.S. FDA commitment in supporting novel therapies for mild to moderate COVID-19 is apparent with the issuance of Emergency Use Authorization ("EUA") for bamlanivimab (manufacturer Eli Lilly) and the combination of casirivimab and imdevimab (manufacturer Regeneron) for the treatment of mild to moderate COVID-19.

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. On June 9th, 2021, the U.S. Government announced that it has committed to purchase $1.2 billion worth of 5-day treatment courses of molnupiravir only if FDA grants EUA or approval. Molnupiravir aims to reduce the replication of the SAR-CoV-2 virus and is being evaluated in an ongoing Phase 3 trial for its potential to reduce the risk of hospitalization or death in non-hospitalized patients who have symptoms for five days or less and are at high risk for severe illness.

Cepharanthine was found to block viral cell entry of lab-attenuated SARS-CoV (original SARS), the virus

that causes Middle East respiratory syndrome (MERS)[2]. However, optimism thus far for translating these findings into an improved treatment for COVID-19 has been limited based on the need to deliver generic cepharanthine by intravenous due to its intrinsically poor oral bioavailability. 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.

The Company will capitalize on the known potential of cepharanthine by evaluating the benefit of their novel oral formulation of PD-001 as a potential oral antiviral therapeutic agent to treat mild-moderate COVID-19. The Company has already initiated a fair amount of preparation and expects to be in a position to proceed with filing a Pre-IND with the FDA before the end of July to determine the appropriate next steps to advance to human clinical studies that would position PD-001 as a potential first-in-class therapeutic against coronaviruses and future pandemics.

Daniel Cohen, Chairman and CEO of PharmaDrug commented, "We are committed to advance the development of our patented and novel formulated version of cepharanthine, designated as PD-001, for infectious diseases, with a particular focus on developing it as a potential first-in-class oral antiviral pill to complement vaccines in the treatment of COVID-19 and future coronaviruses globally"

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.

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]. The authors 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 hypothesis, application of cepharanthine to cells simultaneously exposed to SARS-CoV-2 fully blocked viral internalization and subsequent production of viral particles 24 hours post infection[1]. Cepharanthine-mediated inhibition of SARS-CoV-2 viral entry is further supported by the work of Chen CZ, et al[2]. Using a panel of 2678 approved drugs, the authors identified 6 promising SARS-CoV-2 viral entry inhibitors. Among the six, cepharanthine was favorably non-toxic and displayed the greatest capacity to reduce viral entry and block virus-induced cell death. Of additional note, cepharanthine was also found to block viral cell entry of lab-attenuated SARS-CoV (original SARS) as well as to the virus that causes Middle East respiratory syndrome (MERS), suggesting that cepharanthine might have considerable utility as an 'off the shelf' pan-coronavirus antiviral[2]. Finally, using a two libraries of 2406 clinically approved drugs, a third research group used a SARS-CoV-2-related corona virus isolated from pangolin to identify potential repurposing candidates. Like SARS-CoV-2, the related virus (called 2019-nCoV-related) was found to use ACE2 as the cell docking receptor. The pangolin coronavirus model was used to identify drugs capable of inhibiting virus-induced cell death[3]. The spike protein of coronavirus 2019-nCoV shares 92.2% amino acid identity with that of SARS-CoV-2. Of all compounds screened, cepharanthine provided the most potent inhibition of 2019-nCoV-related infection.

How Cepharanthine May Work to Lessen the Effects of Coronavirus Infection

Cell, animal, and human studies have long reported the immunomodulatory and anti-inflammatory properties of cepharanthine[4]. Agents capable of targeting host response are conceptually attractive because they minimize the potential loss of therapeutic drug effects that are sometimes noted as mRNA viruses undergo genetic mutation. Cepharanthine has previously been shown to suppress cytokine production and the expression of cyclooxygenase; both of which are crucial to viral replication and inflammatory response[5,6]. A 2019 study examined the effects of cepharanthine on human lung cells infected with the coronavirus HCoV-OC43[7]. Following pre-treatment with cepharanthine lung cells

showed no virus-induced death. These findings were attributed to the ability of cepharanthine to inhibit viral RNA replication, block expression of viral proteins, and suppress production of proinflammatory molecules, thus preventing a deleterious exacerbation of cytokine response to the viral infection.

Cepharanthine for Cancer

The Company is focused on advancing the clinical development of its improved highly bioavailable, patented enteric-coated formulation of cepharanthine, 'PD-001' to treat rare, serious, high unmet medical needs including cancer and infectious disease. PharmaDrug remains fully committed to its cancer strategy and sees it as a parallel path for the development of PD-001. As a reminder, The Company was granted Orphan Drug Designation (ODD) by the FDA for Cepharanthine in the treatment of esophageal cancer in January of 2021 and subsequently added some world class experts to its scientific advisory team. Before requesting an IND meeting with the FDA, management made the decision to conduct some pre-clinical work to more fully evaluate the mechanism of action for cepharanthine given that the drug displays potential as a direct anti-cancer agent as well a prospect for reducing resistance to common chemotherapies. Furthermore, there is ample literature that speaks to cepharanthine's potential with other cancers and PharmaDrug believes it makes sense to explore other potential avenues as well.

As previously announced in a press release dated May 06, 2021, PharmaDrug has signed a service agreement with a contract research organization to evaluate Cepharanthine in a broad panel of human cancers. The first phase of the study will compare Cepharanthine to the current standard of care in 60 human cancers. The company has already seen preliminary results from approximately 25% of the planned cell lines and several cancers were shown to be impacted by cepharanthine. The company expects final results from all 60 cell lines by mid to late July and will inform the market of all its findings. The following phase of the program will compare cepharanthine in conjunction with 3 types of chemo to assess the drug's potential in reducing chemo resistance in cancer cells. The company will then move to initiate an animal study in the fall for Esophageal Cancer as well as any other cancer type that shows comparable potential.

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. The Company owns 80% of Pharmadrug Production GmbH, 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 EU. The Company also owns 100% of Super Smart, a Dutch company building a modern adult use psychedelic retail business with an elevated and educational focus. PharmaDrug recently acquired Sairiyo Therapeutics, a biotech company that specializes in researching and reformulating established natural medicines with a goal of bringing them through regulatory and research driven clinical trials.

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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 the proposed non-clinical and clinical manufacturing of Cepharanthine for the Company's rare cancer and infectious diseases programs; the ability to expedite development timelines by leveraging SwRI's existing Cepharanthine preclinical data sets and manufacturing know-how; the ability to advance clinical development of an improved oral formulation of Cepharanthine to treat rare cancers and infectious diseases; the ability to obtain applicable approval for the use of Cepharanthine to treat esophageal cancer; the timing and potential results of the Company's plan to initiate high throughput studies to screen a large panel of additional cancers; the Company's plans to evaluate the benefit of its novel oral formulation of Cepharanthine in an animal model of SARS-CoV-2 infection and its proposed discussions with regulators regarding same. 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 Sairiyo; the ability to complete the studies referenced herein nd the results thereto; 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

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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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