



PharmaDrug Receives Positive Results for DMT-Analogue Program to Treat Glaucoma

- *PharmaDrug receives encouraging potency data for candidate DMT-analogue molecules designed to treat primary open angle glaucoma*
- *Terasaki Institute advances PharmaDrug's candidate DMT-analogue molecules into next phase of potency/kinetics study*
- *Terasaki Institute initiates fabrication of novel medical device designed to deliver PharmaDrug's lead candidate to glaucoma patients*

Toronto, Ontario--(Newsfile Corp. -February 23, 2022)- PharmaDrug Inc. (CSE: PHRX) (OTC: 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 it has successfully completed a head-to-head potency comparator study of its two undisclosed DMT-analogue candidates for the treatment of primary open angle glaucoma (POAG). Following this successful outcome, the Company, in collaboration with the Terasaki Institute for Biomedical Innovation (TIBI), has initiated fabrication activities necessary to produce a novel medical device capable of delivering sustained, low (sub-psychedelic) quantities of their undisclosed tryptamine-based pharmaceutical to the front of the eye. The Company intends to use the current results in combination with several planned upcoming *in vitro* studies to elect its final development candidate. Future *in vivo* efficacy testing in an accepted model of POAG is currently being planned with the goal of providing all necessary support to file an investigative new drug (IND) application with the FDA to conduct clinical studies.

Paul Van Slyke, CSO of PharmaDrug commented, "Despite the availability of several approved medications, irreversible vision loss related to elevated intraocular pressure (IOP) remains a significant risk for patients suffering from glaucoma. We are excited to announce that our recently generated data demonstrates that the concept of using select DMT-analogues to activate protective pathways within critical cellular compartments of the eye may provide significant utility in treating elevated IOP. The next few months will be vital in further characterizing relative drug potency, selecting a single lead candidate to take forward and fabricating a novel medical device capable of delivering constant and sustained levels of drug to the anterior portion of the eye. The following research phase will focus on IND enabling efficacy studies using a well accepted animal model of POAG".

The aim of PharmaDrug's DMT-analogue research program in ocular health is to develop suitable prototype medical devices capable of sustained ocular drug-delivery while also confirming efficacy, biocompatibility and stability of its candidate molecules in models of elevated IOP. The research program scope includes full establishment and demonstration of candidate molecule loading capacity as well as release rate evaluations of conjugated



materials using appropriate models that will be used to support an IND application with the FDA in the future.

The Company has completed its initial potency evaluation of two test articles using an *in vitro* calcium mobilization assay on trabecular meshwork cells; a cell type known to be critically important in the maintenance of healthy IOP. Calcium mobilization is understood to provoke cellular contraction, and specifically in the case of trabecular meshwork cells, is thought to contribute to the maintenance of healthy IOP by channeling aqueous humor away from the front of the eye. Both test articles were found to activate calcium mobilization, to levels that were comparable or greater than the experimental positive control, ionomycin. The Company's test articles were previously examined for *in vitro* toxicity and were found to be non-toxic to trabecular meshwork cells at concentrations expected to be used in treatment for various eye diseases. Fabrication of a drug-loaded prototype medical device has been initiated and studies, including biocompatibility are underway to evaluate drug release in cell and cell-free model systems. Collectively the results of these studies will be used to select a lead development candidate that will be taken forward into *in vivo* efficacy models for eye diseases, including glaucoma.

The Need for Improved Medications to Treat Primary Open Angle Glaucoma

Glaucoma is a disorder of the optic nerve that results in irreversible vision loss and is the second leading cause of blindness in the world, according to the World Health Organization. Glaucoma impacts more than 2.7 million people aged 40 or older in the United States and current treatments are known to have poor rates of compliance of up to 80% of patients. The global market for glaucoma was estimated by Market Scope at \$4.8 billion in 2019 with the U.S. market representing \$1.9 billion. Although the exact etiology of primary open angle glaucoma remains poorly understood, and may be variable across patient subsets, it is generally accepted that the observed increase in intraocular pressure (IOP) correlates with progressive vision loss¹. Current treatments for POAG primarily consist of eyedrops that can be grouped into three main categories: prostaglandin analogues, carbonic anhydrase inhibitors, and alpha-2 agonists. While these approaches usually provide partial improvement, they often result in side effects such as redness and stinging and require multiple daily applications; all of which diminish patient compliance. Tryptamines, including DMT-analogues are thought to work in a completely distinct way to lower IOP and as such potentially embody a new class of glaucoma medications that may be used alone, or in combination with already approved medications. The Company's streamlined focus on two highly promising, undisclosed tryptamines as a potential therapeutic solution in treating glaucoma represents a potential paradigm shift.

Modulating the serotonin receptor pathway to improve glaucoma outcomes



Key regions of the eye that regulate fluid dynamics, including maintenance of healthy IOP, are known to be richly decorated with various serotonin receptor family members. Previous research has highlighted the role of serotonin receptor signaling in the regulation of IOP²⁻⁵. Tryptamines, often hallucinogenic above certain threshold concentrations, constitute a large collection of molecules that selectively act on multiple different serotonin receptors including 5-HT1A and 5-HT2A. Topical application of several different tryptamines have shown early promise in preclinical models of elevated IOP, however formulation, delivery, the potential for undesirable hallucinogenic side effects, and the controlled substances act of 1970 have all contributed to a lack of development of tryptamines to treat this serious threat to vision.

The Terasaki Institute for Biomedical Innovation is a biotechnology institute which develops medical devices and cutting-edge protocols for a variety of diagnostic, monitoring and treatment applications. Their research platforms include work in biomaterials, cellular and tissue engineering, wearable biosensors and organs-on-a-chip, with specific expertise in novel polymer development.

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 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 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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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 Company's plan to elect its final development candidate; future in vivo efficacy testing in an accepted model of POAG; the filing of an investigative new drug (IND) application with the FDA to conduct clinical studies; the ability to fabricate a novel medical device capable of delivering constant and sustained levels of drug to the anterior portion of the eye. 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 results of research efforts and work to fabricate the novel medical device referenced herein; the ability to finance the Company's planned research and development activities; 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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