15 February 2021

ASX Code: MXC

LSE Code: MXC

ASX RELEASE

New *In-vitro* cannabinoid study on Glioblastoma treatment using proprietary nano-delivery platform to commence

Key Highlights:

- MGC Pharma's research program into the use of cannabinoids in the treatment of aggressive glioblastoma brain cancer has been expanded, in collaboration with the Slovenian National Institute of Biology and Neurosurgery Department at the University Medical Centre
- Preliminary results of MGC Pharma's proprietary cannabinoid treatment of Glioblastoma have recently completed an independent peer review and been formally published in the MDPI (Multidisciplinary Digital Publishing Institute) Medical Journal
- The new, expanded study will also explore the use of a nanoparticle delivery system to improve the effects of the glioblastoma treatment
- Delivery system is similar to the nanoparticle delivery system being used successfully in MGC Pharma's ArtemiC™ clinical trial into the treatment of COVID-19
- *In-vitro* results to date show that MGC Pharma formulated cannabigerol (CBG) can eliminate therapy-resistant glioblastoma stem cells
- Successful study results would mean a key breakthrough for MGC Pharma in the treatment of aggressive brain cancers, one of its key target clinical research treatment areas – Oncology
- The new study will shortly commence recruitment of new patients with grade IV glioblastomas to be divided into subcategories to receive a personalised treatment plan

MGC Pharmaceuticals Ltd (ASX, LSE: MXC, 'MGC Pharma' or 'the Company'), a European based bio-pharma company specialising in the production and development of phytocannabinoid-derived medicines, is pleased to announce its ongoing pre-clinical research program ('Study') into Glioblastoma Multiforme ('GBM'), has significantly progressed and has now been expanded to explore the use of nano technology in relation to the most effective treatment delivery systems. GBM is the most aggressive and, to date, therapeutically resistant primary brain tumour.

This important GBM research program is being conducted in collaboration with MGC Pharma, the National Institute of Biology ('NIB') and the Neurosurgery Department at the University Medical Centre in Ljubljana, Slovenia. It is focused on testing cannabinoid formulations on fresh glioblastoma tumour tissues, obtained from patients after surgical removal of the tumour, to determine the optimal cannabinoid preparation for the effective treatment of the remaining cancer. The program tests cannabinoids alone and in combination with chemotherapeutic temozolomide.

The objective of the pre-clinical *in-vitro* research is to develop novel formulations to define the clinical protocols for clinical trials for the treatment of high-grade brain tumours with cannabinoids.

The Study has now been expanded to include testing the effect of both cannabidiol ('CBD') and cannabigerol ('CBG') on tumour cells when delivered *via* a nanoparticle delivery system. Successful results of this testing would potentially lead to a significant breakthrough in the treatment of brain cancer through oral administration (rather than invasive treatments). Nanoparticles are believed to improve the bioavailability and the blood to brain barrier issues, which are being optimised using SNEDD (Self Nano-Emulsifying Drug Delivery).

Summary of the MGC Pharma GBM cannabinoid research to date (refer ASX releases including 17 November 2020)

- Results from an *in-vitro* study completed in November 2020 demonstrate that CBG exerts a superior effect in impairing the major hallmarks of glioblastoma progression, i.e. fast proliferation and invasion, and particularly enhancing glioblastoma cell death. Moreover, CBG can destroy therapy-resistant glioblastoma stem cells, which are the root of cancer development and extremely resistant to various treatments of this lethal cancer.
- We have demonstrated that the combination of CBG and CBD, each at sub-cytotoxic concentrations, results in additive effects on reduced cell viability and induced apoptosis, which are sufficient to replace the application of THC. Formulations containing THC are thus not needed and could be avoided due to the psychoactive activity of THC that is particularly harmful to GB patients with neurological distortions associated with tumour progression
- Results from tumour samples from 18 patients demonstrate the efficacy of MGC Pharma's proprietary CBD:CBG formulation in differing ratios
- The CBD:CBG formulation acted effectively in producing a cytotoxic effect on GBM cell viability by encouraging cell death (apoptosis) for GBM cells
- CBD is demonstrated to inhibit tumour viability and CBG is more efficient in setting off the cascade of biological processes leading to the apoptosis of glioblastoma cells
- Results also found combined cannabinoids were advantageous *vs* single treatment; recent investigations revealed the efficient formulations of CBD and CBG treatment effectively trigger a cytotoxic effect on GBM cell viability, leading to their killing effects
- The study demonstrates the additive effect between the ingredients, supporting the strategy of compounded products and the silver blanket methodology by Dr. Jonathan Grunfeld, the CMO of the company
- Most important are novel findings that CBG, the non-psycho-active cannabinoid has been poorly investigated so far as it has already shown in low doses to inhibit the invasion of GBM cells and GBM stem cells (GSC). The latter are known as the root of the disease progression and highly resistant to standard therapies
- MGC Pharma's research team reports that for the first time, increasing concentrations of CBG is efficiently setting off the cascade of biological processes leading to the apoptosis of the GSCs, opening new avenues for adjuvant therapies for this fatal type of tumour

MDPI Medical Journal Publication of Glioblastoma Study Results

The results to date for MGC Pharma's Glioblastoma CBD/CBG study have completed an independent peer review and have been recently published in the MDPI (Multidisciplinary Digital Publishing Institute) Medical Journal, providing strong credibility and validation to the research being undertaken.

The published article titled ***"Cannabigerol Is a Potential Therapeutic Agent in a Novel Combined Therapy for Glioblastoma"*** can be found on https://www.mdpi.com/2073-4409/10/2/340 and its publication follows an independent peer review.

Next Steps

MGC Pharma and NIB will now commence testing of its CBD and CBG in nano emulsifying formulations on human tissue *in-vitro.* The general aim of the Research project is to reveal the effect of purified natural substances – cannabinoids CBD and CBG in nano-emulsion and their combinations for the treatment of high-grade brain tumours (glioblastoma) *in-vitro* with the goal of *in-vivo* translation to clinics.

The *in-vitro* preclinical study will specifically be focused on defining the most efficient cannabinoid nano-emulsion preparations of CBD and CBG that are likely to benefit to each individual patient that differ in (a) glioblastoma sub-types and (b) most relevant cannabinoid receptors.

Additional patients with grade IV glioblastomas will be recruited to the study and further divided into subgroups based on their tumour genotype and characteristics. These will be carefully analysed to enable a personalised therapeutic approach.

Roby Zomer, Co-founder and Managing Director of MGC Pharma, commented: "The publication of our research in such a prestigious medical journal such as MDPI is a great achievement and validates our findings of using cannabinoids on GBM. Prior to its publication, all research is required to undergo a peer review process where other medical researchers scrutinise the research procedures and subsequent findings. Importantly, we are now moving forward with our next stage research which will now incorporate a new and innovative drug delivery systems. This is a very significant step for our research program and IP, as we look to transform and advance the way brain tumours are treated."

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About MGC Pharma

MGC Pharmaceuticals Ltd (LSE: MXC, ASX: MXC) is a European based bio-pharma company developing and supplying affordable standardised phytocannabinoid derived medicines to patients globally. The Company's founders were key figures in the global medical cannabis industry and the core business strategy is to develop and supply high quality phytocannabinoid derived medicines for the growing demand in the medical markets in Europe, North America and Australasia. MGC Pharma has a robust product offering targeting two widespread medical conditions – epilepsy and dementia – and has further products in the development pipeline.

Employing its 'Nature to Medicine' strategy, MGC Pharma has partnered with renowned institutions and academia to optimise cultivation and the development of targeted phytocannabinoid derived medicines products prior to production in the Company's EU-GMP Certified manufacturing facility.

MGC Pharma has a number of research collaborations with world renowned academic institutions, and including recent research highlighting the positive impact of using specific phytocannabinoid formulations developed by MGC Pharma in the treatment of glioblastoma, the most aggressive and so far therapeutically resistant primary brain tumour.

MGC Pharma has a growing patient base in Australia, the UK, Brazil and Ireland and has a global distribution footprint via an extensive network of commercial partners meaning that it is poised to supply the global market.

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About Glioblastoma

Glioblastoma, also known as glioblastoma multiforme (GBM), remains one of the most malignant cancer types despite the modern modalities of chemotherapy and irradiation treatment, the cancer usually recurs. The typical duration of survival following diagnosis is 12 to 15 months, with fewer than 3 to 7% of people surviving longer than five years. Several phytochemicals exhibit important properties against this form of cancer, including the cannabinoids delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) from Cannabis sativa. These bind to specific transmembrane proteins which are highly expressed on the tumour cell surface and facilitate entrance into the glioblastoma cells. Once inside, the cannabinoids interfere with specific biochemical pathways, promote tumour cells' growth arrest, inhibit their invasion and cause cell death. In over 20 animal studies, CBD/THC was found to drastically decrease the size of and even eliminate glioblastoma. Furthermore, in a few clinical trials and published reports, the variable anti-glioblastoma effects of these two cannabinoids, in combination with other therapeutic modalities, have been demonstrated. However, wider clinical application of these preparations is hindered due to the psychotropic effects of THC. This often limits the clinical usage of THC and CBD mixtures in glioblastoma patients as many will already present with adverse neuropsychiatric symptoms, including impaired cognition.