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MGC Pharma signs Manufacturing and Distribution Agreement with European bio-tech company targeting anti-viral treatments

ASX RELEASE

MGC Pharmaceuticals Ltd (ASX: MXC, 'MGC' or 'the Company'), a European based 'Seed to Medicine' bio-pharma company specialising in the production and development of phytocannabinoid-derived medicines, advises on 4 April 2020 it executed a binding Contract Manufacturing and Distribution Agreement (**'Agreement'**) with Micelle Technology AG ('**Micelle**'), the parent company of Swiss PharmaCan AG (together the **'Parties'**) for necessary research support, commercial manufacturing and distribution of a natural anti-infective based formulation with the aim to treat human patients with serious viral infections with inflammatory complications (**'Product'**). The Product is based on the Parties' patented MyCell Enhanced™ delivery system technology ('**MyCell™**'). This Agreement supersedes and replaces a binding term sheet executed between the Company and the Parties on 21 March 2020.

Binding Agreement and Product Highlights

- MGC has signed a binding Contract Manufacturing and Distribution Agreement with Micelle for the necessary research support, production and wholesale distribution of the Product
- The Product has been designed with the scientific aim to target viral infections with inflammatory complications
- Micelle completed a study of the Product for Malaria on 127 patients with successful results of eliminating all parasites within 7 days, conducted under WHO guidelines
- Micelle holds the exclusive right to the award-winning[1] and patented MyCell™ delivery system technology that is used in the formulation of the product
- MyCell™ technology is a unique platform to deliver natural ingredients more effectively in higher concentrations to the cells, improving bioavailability of natural ingredients
- Under the Agreement, MGC will be the pharmaceutical partner and have responsibility for all future clinical trials, EU GMP production and wholesale distribution of the Product

MGC has signed the Agreement with Micelle, a European bio-tech company that holds the exclusive right to a unique award-winning and patented drug carrier platform[2] that is being used to deliver uniquely formulated natural anti-infective, antioxidant and anti-inflammatory products. Micelle, through its subsidiary Swiss PharmaCan AG, has developed formulations which are utilising the proprietary delivery system MyCell™, designed to improve the pharmacokinetics of natural active ingredients, lending them consistent high bioavailability to the sites of action in the diseased organism.

MGC advises that there is presently no reasonable basis established for the Product to treat or cure COVID-19 symptoms or that the Product kills the COVID-19 virus. This would require clinical testing to be conducted to establish such clinical basis. Therefore, MGC retracts the reference to COVID-19 in its recent Trading Halt and Suspension Notices, and investors should not rely on those references.

Micelle Product, Key Active Ingredient and Proprietary Delivery System

One of Micelle's lead products is a natural supplement formula based on Artemisinin, a well-known natural active ingredient with anti-infective properties (see Annexure A), combined with its proprietary delivery system MyCell™ (the Product). The MyCell™ technology has delivered successful test results to date for Micelle on patients with infectious diseases and acute illnesses, including Malaria.

[1] 2018 Award - Excellence in Pharma: Formulation by MiVital AG (part of the Micelle group of companies)
[2] Patent number: EP2066310A1 granted on 18 April 2012

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Specifically, Micelle has previously completed a study which involved non-controlled open label testing of the Product in Africa conducted under World Health Organisation guidelines on 127 patients infected with Malaria as a potential treatment. Testing was deemed successful with all patients having no malaria parasites in their system within 7 days after having received a single dose of the Product. Patients were followed until day 60 and no relapse was reported. Additional information on the study is provided in Annexure B.

The Product is currently designated as a food supplement and MGC will be responsible for the manufacture and packaging for commercial orders from its EU GMP facility in Slovenia under the Agreement. This opportunity will not impact MGC's current operations or the production and delivery of its leading phytocannabinoid based medicines – (including CannEpil® and CogniCann®).

Key Terms of the Agreement

- The Agreement is for the necessary research, production and wholesale distribution of the Product
- Micelle will continue developing and testing the Product to generate a final marketable product, MGC will render Micelle with necessary research support
- Under the Agreement Micelle will supply MGC with the Product in bulk form, and MGC will manufacture and pack the finished Product
- MGC will lead the design and management of future clinical studies on the Product
- MGC will commit the necessary resources to set-up the production of the Product, based on future commercial wholesale supply agreements
- MGC will serve as a manufacturer and wholesaler of the finished Product in all countries worldwide
- Sales, marketing and retail distribution of the Product will be managed by an independent third party and established regional distributors of medical or pharmaceutical products in key territories
- There are no minimum order quantities under the Agreement, the financial impact of the Agreement would be determined following the Company entering into any commercial purchase orders
- The Agreement is for an initial term of five years and thereafter automatically renews for an additional one year. Either Party may terminate the Agreement at the end of the initial term or any renewal term by written notice six months before the end of the initial term or renewal term
- Either Party may terminate the Agreement if the other party breaches any material term and, if capable of remedying, fails to remedy within thirty days after receiving a notice to such effect from the other party.

Product Collaboration and Development Partnership

Micelle has been working with MGC for nearly one year on exploring potential research and product collaborations. Micelle operates with a disruptive view of the biopharma industry, they are dedicated to researching and developing natural nano-drug carriers to improve the bioavailability of natural ingredients (i.e. vitamins and minerals) as an effective, complementary, alternative to conventional medicines.

The vision of Micelle is to reach the maximum efficiency of a substance by formulating it with their patented MyCell™ technology. Through the ongoing research and development with those food supplements, it showed up that the anti-parasitic, anti-bacterial, anti-viral, antioxidant and anti-inflammatory effects of some well-known ingredients can be leveraged through the MyCell™ technology. The effectiveness of the technology has been proven in several trials to date under clinical conditions.

MGC with its experience in using natural active ingredients (including phytocannabinoids, of which there are synergies with the active ingredients being used by Micelle in its research and development), its production facilities, and emerging global distribution network, will play an active role in supporting and assisting Micelle in the research and development process and in taking the Product to market as a pharmaceutical grade product. The research and development work will include development of the optimal delivery system to the patient.

Roby Zomer, Co-founder and Managing Director of MGC Pharma, commented: "We believe that Phytomedicine will effectively treat previously unmet medical needs and improve the lives of patients in this critical time. We are working hard with Micelle to provide support during its research, development, and testing of its Product and we look forward to updating the market in due course."

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About MGC Pharma

MGC Pharmaceuticals Ltd (ASX: MXC, OTCQB: MGCLF) 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 'Seed 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 recent research conducted in collaboration with the National Institute of Biology and University Medical Centre Ljubljana, highlighted the positive impact of using specific phytocannabinoid formulations 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. In order to meet the demands of becoming a key global supplier the company is constructing a large scale GMP state of the art facility in Malta.

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About Micelle Technology AG/Swiss PharmaCan AG

Micelle Technology AG is a dynamic company dedicated to R&D using natural active ingredients (i.e. vitamins and minerals) as an effective alternative to traditional medicines to treat common viral diseases. As one of the leading manufacturers of plant micelle solubilisates, Micelle Technology AG offers a unique encapsulation technology, which enables the company to harness the full potential of herbal active ingredients, thereby using them in a more efficient and targeted manner.

Micelle Technology AG holds the exclusive right to a unique award-winning and patented drug carrier platform, patented MyCell Enhanced™ technology, which mimics the creation of micelles in a laboratory. Micelles are a cluster of water-soluble molecules, acting as a carrier, responsible for the transportation of substances into the human cell. The MyCell Enhanced™ technology mimics this natural process. This makes it possible to put a 'skin' over substances, which makes them water-soluble. The benefit of this is that oily substances, which is the basic form of natural ingredient, always have to pass the liver first, before they can start working. However, the liver filters up to 90% of the active ingredient and only 10% of the active ingredient reaches the human cell (this varies from ingredient to ingredient). Through the water-solubility from the MyCell Enhanced ™ technology, up to 100% of the active ingredients reach the human cell.

ANNEXURE A

Artemisinin

Artemisinin and its derivatives (collectively referred to as ARTs) rapidly reduce the parasite burden in Plasmodium falciparum infections, and antimalarial control is highly dependent on ART combination therapies (ACTs). Decreased sensitivity to ARTs is emerging, making it critically important to understand the mechanism of action of ARTs. Preclinical and clinical studies demonstrate that dihydroartemisinin (DHA), the clinically relevant ART, kills parasites via a two-pronged mechanism, causing protein damage, and compromising parasite proteasome function. The consequent accumulation of proteasome substrates, i.e., unfolded/damaged and polyubiquitinated proteins, activates the ER stress response and underpins DHA-mediated killing. Specific inhibitors of the proteasome cause a similar build-up of polyubiquitinated proteins, leading to parasite killing. Blocking protein synthesis with a translation inhibitor or inhibiting the ubiquitin-activating enzyme, E1, reduces the level of damaged, polyubiquitinated proteins, alleviates the stress response, and dramatically antagonizes DHA activity (Jessica L. Bridgford, Nature, 2018).

Antimalarial activity of Artemisinin

In malaria, the classical mechanism is thought to involve reaction of the endoperoxide bridge with free heme-iron liberated during degradation of hemoglobin inside the parasite food vacuole (O'Neill PM, J Med Chem, 2004).

Artemisinin derivatives are tolerated well by patients. Mild and reversible hematological and electrocardiographic abnormalities, such as neutropenia and first-degree heart block, have been observed infrequently. Neurotoxic effects have been repeatedly reported in experiments with mice, rats, and dogs, as reviewed elsewhere. Affected areas in the brain stem are the reticular system with regard to autonomic control, the vestibular system, the auditory system (trapezoid nucleus), and the red nucleus, which is important for coordination. A longer exposure time to a lower peak blood concentration of an artemisinin derivative is more neurotoxic than a shorter duration of exposure and a higher peak blood concentration (Thomas Efferth, Clinical Infectious Diseases, 2008).

A clinical safety review by Ribeiro IR (BMC Infectious Diseases, 2008), of 108 clinical studies that enrolled 9241 malaria patients provided ample evidence that artemisinins are safe and without serious adverse effects or significant severe toxicity, including neurotoxicity. Ataxia, slurred speech, and hearing loss have been reported in few patients treated with artemisinin. Although the artemisinin derivative artesunate seems to be without toxicity, van Hensbroek et al. observed delayed coma recovery times in Gambian children with malaria who were treated with intramuscular artemether versus intravenous quinine. Because of these conflicting results, Stepniewska et al. performed a meta-analysis of 7 studies involving 1919 patients with malaria. Applying a uniform coma recovery time definition, no significant difference in coma recovery time was found between patients treated with artemether and quinine. Additionally, no statistically significant difference was observed with regard to neurological sequelae. In a recent study by Dondorp et al. [56], patients with malaria who were treated with artesunate were compared with patients who were treated with quinine. The authors did not find significant differences in terms of neurotoxic symptoms (i.e., times to speak, eat, and sit) between treatment groups. Neurological sequelae did not occur after treatment. Interestingly, patients with malaria who developed late onset hypoglycemia had a higher incidence of death than did patients treated with artesunate who did not have hypoglycemia. This may be an issue that deserves additional investigation.

ANNEXURE B

Results of the Study on Malaria patients

Name and any unique identifier of the trial	Open label on oral administration of water-soluble Artemisinin formula for the treatment of Malaria in Children
Blinding status	Open Label
Treatment method, route, frequency and dose levels	Oral administration, 1ml Single use once a week
Number of trial subjects	127 children
Dropout rate	Zero dropout
Subject demographics	The subject range 3-15 years old
Control group	There was no control group
Conductor and regulator	The study was conducted through the Swiss Tropical and Public Health Institute under the regulation of the World Health Organisation
Safety and tolerability	There is sufficient literature for the use and the safety of the active ingredient there was no need for safety trial. Safety and tolerability were therefore not a primary endpoint. Safety data were collected, no study drug adverse events were observed
Data on the outcome **Primary endpoint results** Data on the outcome of all the primary endpoints set out in the trial protocol	The patients received a single dose of the formula, Polymerase Chain Reaction (PCR) results showed a total absence of parasite in blood within 7 days after drug administration. Patients were followed until day 60 and no relapse was recorded (by PCR). The trial was concluded. Additional Phase IIB and Phase III would be needed for market authorisation
The results of the primary analysis as prescribed in a statistical analysis plan devised before the lifting of the blind should be reported;	N/A in this study, as it was open label and not a blinded study
For a safety endpoint, a statement such as "the drug was safe and generally well tolerated" may be insufficient;	N/A. There was no safety endpoint in this study as it was open label, the objective was an efficacy study. During the study, safety data were collected, according to the GCP requirements. No study drug adverse events were recorded
For each pharmacodynamic primary endpoint, where relevant, the numerical and statistical results obtained for each dose group including placebo should be reported.	After a single dose, 100% of patients were PCR-negative on day 7 of follow up. Additional PCR tests were performed on days 30 and 60 and the results were negative for all participants in the study
Any post-hoc analysis of the trial data relevant to the endpoints, such as post-hoc analysis based on subgroups of the trial subjects (e.g. "those more severely affected by the disease benefited most") or post-hoc analysis based on measurements relevant to the primary endpoint but not part of the statistical analysis plan, may be reported but should be reported after the above analyses and clearly identified as post-hoc;	N/A. There was no further analysis
In the case of a blinded trial, the only other reports on the trial progress before the results report should relate to progress of recruitment and expected date of availability of results.	N/A. It was not a blinded trial
Secondary endpoint(s) results Data on the outcome of secondary endpoints set out in the trial protocol may be provided. If so, all requirements of reporting on the primary end points should also be adhered to in respect of the secondary endpoints.	There is no secondary endpoint data
If provided, the results of the secondary endpoint(s) should be reported after the primary endpoint(s)	N/A as no secondary endpoint data