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ASX Code: MXC

Interim results of ArtemiC Phase II clinical trial on COVID-19 infected patients meet all Primary Objectives

ASX RELEASE

Key Highlights:

- Interim results of ArtemiC from its Phase II clinical trial meet all primary objectives and demonstrated significant improvement in patients infected with COVID-19
- Results met FDA primary endpoint of sustained clinical recovery, preventing the need of intensive care in high risk patients with genetic diversity or invasive mechanical ventilation
- No Adverse Events recorded demonstrating the safety of ArtemiC in humans based on the initial 10 patients
- The statistical results show improvement in clinical scoring parameters as laid out by the FDA
- These interim results are from first ten (10) patients undertaking the trial which has sites at Nazareth Hospital EMMS and Hillel Yaffe Hospital
- Results demonstrate the safety and preliminary efficacy of ArtemiC based on 10 patients
- Results are consistent with, and complement, the in-vivo and in-vitro results to date which show safety and reduction in excessive inflammatory response known as cytokine storm
- Importantly, in the treatment group all patients recorded no pain at all, whilst in the placebo group all patients experienced various levels of pain
- All treatment group patients were discharged with a NEWS score of 0 and this reduction across the treatment group is recognised as statistically significant ($p<0.005$)
- These results combined with the pre-clinical results support a high probability of success of the study in determining a safe and effective treatment for the symptoms of COVID-19
- MXC will now commence designing protocols and parameters of Phase IIb clinical trial and preparing production of ArtemiC to meet future demand post publication of interim results

MGC Pharmaceuticals Ltd (ASX: 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 the interim results of its Phase II double-blind, placebo-controlled clinical trial for anti-inflammatory treatment ArtemiC on persons diagnosed with COVID-19, has met all its primary end points for the safety and efficacy of the treatment on the first 10 patients.

Importantly, these interim results also met the FDA primary endpoint - sustained clinical recovery, the resolution of symptoms and prevented the need for intensive care or invasive mechanical ventilation. This is in accordance with FDA guidelines on the inclusion criteria for the treatment of high-risk, COVID-19 infected patients[1].

The statistically proven results show 2 important clinical outcomes. Firstly, a significant improvement in clinical parameters of patients in the treatment group, and secondly that **no adverse events** (AE) occurred, demonstrating the preliminary safety of the treatment based on the initial 10 patients.

[1]Source: FDA guidelines

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These findings adhere to the FDA score criteria for clinical improvement under a clinical trial and are consistent with the results from the preclinical in-vitro study which demonstrate a reduction in the excessive inflammatory response known as cytokine storm, as previously announced (refer ASX release 7th August 2020). These interim results in conjunction with the in-vitro study support expectations for desirable future results of the trial and a positive effect of the treatment.

The targeted clinical application of ArtemiC, which is the purpose of this Phase II clinical trial, is to effectively treat the symptoms of COVID-19 patients prior to them requiring hospital admission or alternatively shorten their stay as inpatients, and thus relieve the pressure on global healthcare systems caused by COVID-19. The effective treatment of symptoms of COVID-19 has been deemed important by the FDA.

Clinical improvement in Treatment Group vs Placebo Group, measured by NEWS Score

From the statistical analysis of these interim results, it is important to note the significantly higher average disease severity of those treated with the active formulation (ArtemiC) as compared to the placebo group. Four (4) of the actively treated participants entered the study with a NEWS2 score between 8 and 11, which are classified as "high". All participants in the treatment group responded well and had scores of 0 on day 15, the final day of the trial (See Charts 1 and 2). The results presented in Fig. 1 below.

Although the study group had significantly higher NEWS score in admission, all patients had NEWS score=0 at discharge (significant reduction: P=0.005), while only two (2) patients in the placebo group had NEWS score=0. One patient in the placebo group had significant deterioration of the NEWS score: from 2 in admission to 16 at discharge to another hospital. The predictive value of NEWS2 scores in the context of COVID-19 is currently being debated, however, some data suggest that scores above 7 are highly predictive of ICU admission (Gidari 2020).

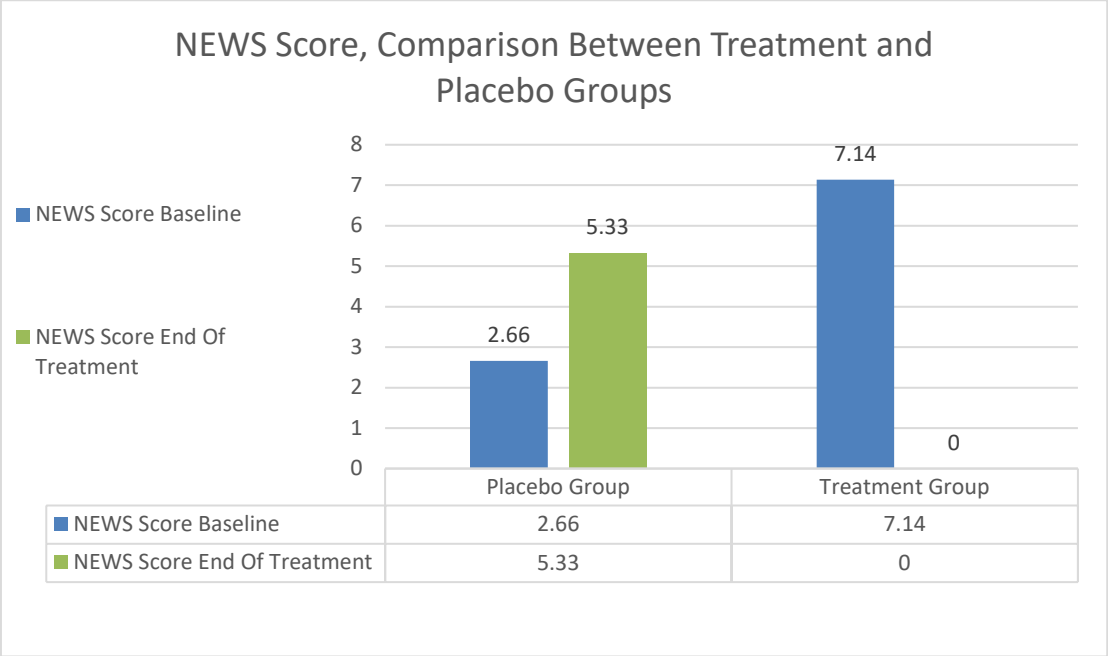

Fig. 1. Change in NEWS Score outcome, comparison between Placebo and Treatment study groups

The interim results are from the first ten (10) patients recruited to the ongoing trial with sites in Nazareth Hospital EMMS and Hillel Yaffe Hospital where the Phase II clinical trial is currently underway to evaluate the effect of ArtemiC and its ingredients (consisting of Artemisinin, Vitamin C, Curcumin, Boswellia serrata) on patients infected with COVID-19. Currently there are a further 19 patients undergoing this Phase IIa trial, with a maximum number of 50.

Beneficial Effect of ArtemiC on Pain Associated with COVID-19

The interim results data also strongly indicates a beneficial effect of ArtemiC on the related pain associated with COVID-19, with none of the actively treated participants reporting pain on the 15th day concluding the active monitoring phase, as opposed to those treated with placebo who continued to experience some level of pain, as shown in the results Annexure A Table No.4.

This is important because of the contribution of ArtemiC for the quality of life of the patients, and not only the clinical improvement.

Dr Elias Hillou, Investigator for the Clinical Trial from Hillel Yaffe Medical Centre commented on the interim trial results and its operation to date: "*At our hospital, we have had experience in treating Covid-19 patients as one of the leading treatment hospitals in Israel, and unfortunately we have had recurring disappointment with patients deteriorating, with no tools at our disposal to treat this effectively. As noted from the interim analysis for the first 10 patients, these preliminary results regarding the safety and the efficacy of ArtemiC for the treatment of COVID-19 patients is very promising. We see no deterioration in the clinical situation, for patients who had received the real medication, as expressed by the NEWS score, compared to the group of the placebo group, that had a massive deterioration with one patient near to death, and a need for an ECMO. Our aim is to treat 50 patients according to the well-designed clinical research protocol to hopefully demonstrate ArtemiC is safe and efficient for COVID-19 pandemic battle and helping with effective treatment of infected patients."*

Dr Nadya Lisovoder, Chief Research Officer of the Phase IIa trial and CEO of Galilee Clinical Bio Research, commented: *"We are very happy to be a part of this important project that has demonstrated it has the potential to help with treatment of Covid-19 infected patients and have positive implications for health management in the current global pandemic we are dealing with today."*

Roby Zomer, Co-founder and Managing Director of MGC Pharma, commented: "*We are very pleased with the Phase II interim results of ArtemiC which have so far met all primary endpoints while also demonstrating safety of the treatment on the initial 10 patients. These results combined with our recent preclinical results are important for designing the protocols and markers for our next Phase IIb clinical trial. We look forward to updating the market as we continue to receive results of this trial."*

Importance of Pre-Clinical Study Results Data and Phase II Clinical Trial Interim Results

The ArtemiC clinical study on COVID-19 patients is managed under GCP requirements and local Helsinki Committee approval. The independent management of the study was performed by Dr Nadya Lisovoder, CEO of Galilee Clinical Bio Research, an external Clinical Research Organization (CRO), ensuring all required regulatory conditions were followed answering FDA requirements. Galilee-CBR is an independent Clinical Research Organisation located in Israel provides a full spectrum of clinical development phases I to IV in pharma and medical devices. Galilee-CBR is working with an Israeli Government for the bio medical research promotion in the hospital in Northern Israel. Certified Electronic Data Capture system was used for the data collection and 100% of the study data was monitored in order to ensure the data quality.

Statistical analysis of the results from first 10 patients was performed by an external and independent biostatistician, Dr Nira Morag, a senior lecture in Tel Aviv University, Department of Biostatistics. Dr Morag has more than 30 years of experience in biostatistics in pharma industry. The scope of the statistical analysis is included in Annexure A.

According to the general FDA requirements for the pharma industry and guidelines published especially for COVID-19 studies, MGC Pharma is currently managing preclinical studies in parallel to this Phase II clinical trial.

The focus of the preclinical program was to demonstrate the safety, toxicity and mechanism of action of ArtemiC as a drug for COVID-19 infection. All information obtained from the interim data from this current Phase II trial will serve the Company to design Phase IIb and Phase III clinical trials, with the trial protocols, procedures and endpoints to be defined based on the preclinical studies and these Phase II results. In addition, the toxicity study results recently published support the definition of maximum tolerated dose and dose finding process, which will be required as a part of the R&D process by the regulatory authorities.

Based on the current patient recruitment status at the clinical trial sites in Israel and India, the Company expects to complete the current Phase IIa clinical trial late September/early October 2020 to provide the final Phase IIa trial results in October or November 2020, with the follow on Phase IIb trial expected to commence in December 2020, the planning for which is underway.

Current clinical evidence in COVID-19 patients indicate that the cytokine storm is an uncontrolled over-production of soluble markers of inflammation which, in turn, sustain a systemic inflammatory response, and is a major factor responsible for the occurrence of Acute Respiratory Distress Syndrome – the main mortality reason in COVID-19 patients. ArtemiC is currently being tested in a clinical trial where some of the participants may be affected by a cytokine storm, with interim patient statistical analysis of this Phase II clinical trial analysing the patient's response to these conditions.

Details on the trial required for compliance with the ASX Code of Best Practice for Reporting by Life Science Companies are included in Annexure A.

Chart 1: The NEWS scoring system

Physiological parameter	Score 3	2	1	0	1	2	3
Respiration rate (per minute)	≤8		9–11	12–20		21–24	≥25
SpO_2 Scale 1 (%)	≤91	92–93	94–95	≥96			
SpO_2 Scale 2 (%)	≤83	84–85	86–87	88–92 ≥93 on air	93–94 on oxygen	95–96 on oxygen	≥97 on oxygen
Air or oxygen?		Oxygen		Air			
Systolic blood pressure (mmHg)	≤90	91–100	101–110	111–219			≥220
Pulse (per minute)	≤40		41–50	51–90	91–110	111–130	≥131
Consciousness				Alert			CVPU
Temperature (°C)	≤35.0		35.1–36.0	36.1–38.0	38.1–39.0	≥39.1	

Chart 2: NEWS thresholds and triggers

NEW score	Clinical risk	Response
Aggregate score 0–4	Low	Ward-based response
Red score Score of 3 in any individual parameter	Low–medium	Urgent ward-based response*
Aggregate score 5–6	Medium	Key threshold for urgent response*
Aggregate score 7 or more	High	Urgent or emergency response**

* Response by a clinician or team with competence in the assessment and treatment of acutely ill patients and in recognising when the escalation of care to a critical care team is appropriate.

**The response team must also include staff with critical care skills, including airway management.

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About MGC Pharma

MGC Pharmaceuticals Ltd (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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Bibliography:

Gidari, A., G. V. De Socio, S. Sabbatini and D. Francisci (2020). "Predictive value of National Early Warning Score 2 (NEWS2) for intensive care unit admission in patients with SARS-CoV-2 infection." Infectious Diseases: 1-7.

Royal College of Physicians. National Early Warning Score (NEWS) 2: Standardising the assessment of acute-illness severity in the NHS. Updated report of a working party. London: RCP, 2017.

ANNEXURE A – DETAIL ON INITIAL ANALYSIS FROM PHASE IIA ARTEMIC TRIAL

Name and any unique identifier of the trial:	A Phase II, double blind placebo controlled clinical trial designed to evaluate the effect of ArtemiC in patients diagnosed with COVID-19 (ID: MOH_2020-04-16_008859; ClinicalTrials.gov Identifier NCT04382040)
Blinding status:	Double Blinded
Treatment method, route, frequency, dose levels:	**Agent name and composition:** ArtemiC, medical spray composed of a combination of 6 mg/ml of Artemisinin and 20 mg/ml of Curcumin. **Dose:** Maximum dose during a day by medicated spray, divided over 2 times day. **Study Procedures:** The study will last 2 weeks and additional time required for follow up till hospital discharge in order to check side effects and study drug efficacy. **Methodology:** Safety will be assessed through collection and analysis of adverse events, blood and urine laboratory assessments and vital signs. After Screening visit, the study drug will be administrated during 2 days twice a day. All patients will be monitored till the hospital discharge.
Number of trial subjects:	Full trial to be on 50 patients, currently results have been received for 10 patients across both Hillel Yaffe Hospital and Nazareth Hospital EMMS in Israel
Dropout rate:	1 patient in Placebo Group dropped out on Day 13 (out of 15) due to SAE, ICU admission, ventilation and transfer to other hospital. The patient was included in the statistical analysis.
Subject demographics:	7 patients were randomized to the Treatment Group. Demographical characteristics – - 3 males and 4 females - Mean age – 60.3±16.2 (36-79) - 6 Caucasians, 1 Black - 4 non smokers, 3 smokers. - Mean weight - 75.3 ±11.5 - Mean height - 170± 7.2 - Mean BMI - 26.0± 2.6 All 7 patients have complicated medical history. From the point of view of risk factors for COVID-19, 5 out of 7 patients has chronic respiratory system diseases, obesity, renal failure. According to the NEWS Score (health status score), placebo group had a higher score at admission (mean – 7.14).
Control Group:	3 patients were randomized to the Treatment Group. Demographical characteristics – - 1 males and 2 females - Mean age – 58.6± 14.6 (36-79) - 3 Caucasians, 0 Black - 2 non smokers, 1 smokers. - Average weight - 72.4± 11.6 - Average height - 168 ±7.9 - Average BMI - 25.5 ±2.4 2 out of 3 patients have complicated medical history. From the point of view of risk factors for COVID-19, only one patient has kidney disease. According to the NEWS Score (health status score), placebo group had a lower score at admission (mean – 2.66). The difference with the treatment group was statistically significant (p<0.03).
Primary endpoint(s):	• Time to clinical improvement, defined as a national Early Warning Score 2 (NEWS2) of </= 2 Maintained for 24 Hours in comparison to routine treatment Although the study group had significantly higher NEWS score in admission, all patients had NEWS score=0 at discharge, while only 2 patients in the placebo group had NEWS score=0. One patient had significant deterioration of the NEWS score: from 2 in admission to 16 at discharge to another hospital. • Percentage of participants with definite or probable drug related adverse events

	The safety was assessed by descriptive statistics of AEs and laboratory tests. The incidence of reported AEs and the values of laboratory tests from all subjects will be presented with and without regard to causality based on the Investigator's judgment. In the Treatment group no drug related AEs were reported. In the Placebo group 1 AE was reported (Acute respiratory distress syndrome), that was defined as unlikely related to study drug.
Secondary endpoints:	• Time until negative PCR Placebo group: 1 missing data (due to drop out of the ventilated patient), 2 Negatives on day 15. Study group: 1 missing, 1 Negative from day 4, 5 Negatives on day 15. • Proportion of participants with normalization of fever and oxygen saturation through day 14 since onset of symptoms 96.9% in the treatment group vs 96.0 in the placebo group • COVID-19 related survival Only 1 patient is in life threatening condition (Placebo group). No death cases were reported during a study. • Incidence and duration of mechanical ventilation Only one patient (Placebo group) was on mechanical ventilation. The patient dropped out from the study on day 13 of the trial. • Incidence of Intensive Care Init (ICU) stay Patient randomized to Placebo group was transferred to ICU on Day 13. • Duration of ICU stay The status of the ICU stay for the patient prom Placebo group is ongoing • Duration of time on supplemental oxygen The patient from Placebo group is still on the supplemental oxygen
Safety and tolerability:	No AEs related to the study drug were reported during a study. One unlikely related AE was reported in the patient from the Placebo group.

Statistical Analysis Details

All measured variables and derived parameters will be listed individually and, where appropriate, tabulated by descriptive statistics. For descriptive statistics summary tables are provided giving sample size, absolute and relative frequency by study group and sample size, arithmetic mean, standard deviation, coefficient of variation (if appropriate), median, minimum and maximum, percentiles, p values, and 95% CI (Confidence Interval) by study group for means of continuous variables.

The safety objective of the study was assessed by descriptive statistics of AEs and laboratory tests. The incidence of reported AEs and the values of laboratory tests from all subjects will be presented with and without regard to causality based on the Investigator's judgment. Paired T-Test or Signed Rank test (as appropriate) was applied for testing the statistical significance of the changes from baseline in laboratory results within each study group.

The ANOVA model was applied for testing the statistical significance of the difference in NEWS score and the secondary endpoint parameters between the study groups. The only material statistical significance observed in the analysis was the decreasing in NEWS score in the treatment group ($p<0.005$).

Table 1. Medical history

Patient	Group	Medical history
P 1	P	Thyroid, surgery, gastritis, anxiety, obesity, anemia, sensitivity to augmentin & paroxetine.
P 2	T	Anemia, xerosis, bronchiectasis, chronic cough
P 3	P	HBP, hyperlipidemia, DM, neuropathy, fatty liver, anemia, hyperkalemia, kidney disease
P 4	T	MI, PCI, HBP, hyperlipidemia, COPD, DM, polyps-benign, catheterization, renal failure, anemia
P 5	T	Anemia, hypomagnesemia, myelodysplastic, spelenome, hypokalemia
P 6	P	Sleep apnea
P 7	T	Gastriis, h.pylori, internal hemorrhoids, sen to augmentin
P 8	T	HBP, hyperlipidemia, cough
P 9	T	Gastro. Reflux, occipital neuralgia, mounth benigh tumor
P 10	T	MI, PVD, hyperlipidemia, DM, diarrhoea, liver cyst, cyst and pseudocyst at pancreas, osteopenia, lymphnode enlargement, ptosis,

Table 2. List of SAEs reported during the study

Patient	Group	SAE	Severity	Relation to study drug
P 2	T	Worsening of pannus	Mild	Not related
P 3	P	ARDS	Severe	Unlikely
P 4	T	Worsening of anemia	Moderate	Not related
P 6	P	FALL	Mils	Not related
P 8	T	Worsening of cough	Moderate	Not related
P 9	T	Pneumonia	Moderate	Not related
P 10	T	Chest pain	Mild	Not related

Table 3. NEWS score differences between groups

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
NEWS0	Placebo	3	2.6667	.57735	.33333
	Study	7	7.1429	4.37526	1.65369

P=0.035

Table 4. NEWS Score

	Patient	*Grp*	*NEWS Baseline*	*NEWS EOT*	*Saturation Baseline*	*Saturation EOT*	*Breath Baseline*	*Breath EOT*	*Pain Base line*	*Pain EOT*
1	*1.00*	*P*	*3.00*	*.00*	*99.00*	*98.00*	*13.00*	*12.00*	*3.00*	*1.00*
2	*2.00*	*T*	*12.00*	*.00*	*98.00*	*99.00*	*12.00*	*13.00*	*.00*	*0*
3	*3.00*	*P*	*2.00*	*16.00*	*97.00*	*95.00*	*12.00*	*23.00*	*5.00*	*3.00*
4	*4.00*	*T*	*3.00*	*.00*	*97.00*	*95.00*	*12.00*	*12.00*	*.00*	*0*
5	*5.00*	*T*	*3.00*	*.00*	*100.00*	*96.00*	*12.00*	*12.00*	*1.00*	*0*
6	*6.00*	*P*	*3.00*	*.00*	*96.00*	*95.00*	*16.00*	*12.00*	*1.00*	*2.00*
7	*7.00*	*T*	*2.00*	*.00*	*100.00*	*100.00*	*12.00*	*12.00*	*2.00*	*0*
8	*8.00*	*T*	*11.00*	*.00*	*100.00*	*95.00*	*12.00*	*12.00*	*.00*	*0*
9	*9.00*	*T*	*8.00*	*.00*	*94.00*	*97.00*	*12.00*	*14.00*	*3.00*	*0*
10	*10.00*	*T*	*11.00*	*.00*	*94.00*	*96.00*	*11.00*	*12.00*	*.00*	*0*
Total	*10*	*10*	*10*	*10*	*10*	*10*	*10*	*10*	*10*	*10*
a. Limited to first 100 cases.										

These interim analysis results will be submitted to the Ethics Committee at Hillel Yaffe and Nazareth EMMS Hospitals. The Company confirms these results are interim results from ten (10) patients treated in the trial, nineteen (19) additional patients are recruited and with twenty one (21) patients still to be treated to complete the trial.