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ASX RELEASE

Completion of CimetrA™ bioanalytics Pre-clinical Trial

Key Highlights:

- MGC Pharma has completed the full pre-clinical rodents study panel for CimetrA™.
- The latest study, which was carried out at the Smart Assays laboratory in Israel, included the development of bioanalytical methods and validations for further pharmacokinetic analysis for CimetrA™.
- A study on chronic toxicity in rodents was also completed by Science in Action, in Israel, monitoring the potential development of adverse effects from using CimetrA™.
- Histopathology demonstrated the full safety profile for CimetrA™ across all study dosage groups.
- The study results are an important step ahead of the submission to the US Food and Drug Administration (FDA) for Investigational New Drug (IND) approval.
- No anomalies were observed in the biopsies, nor were any clinical or behavioural adverse events recorded.
- CimetrA™ is MGC Pharma's proprietary Investigational Medicinal Product which in previous clinical trials has demonstrated anti-inflammatory and immunomodulating properties, and is MGC's most clinically advanced product.

MGC Pharmaceuticals Ltd ('**MGC Pharma**' or '**the Company**') a European based pharmaceutical company specialising in the production and development of plant inspired medicines, has completed the pre-clinical rodent studies on **CimetrA™**, which are a key step in the clinical pathway prior to the planned FDA Investigational New Drug submission. Research using rodent and mammalian models are used to delineate the pharmacokinetic profile and general safety of a drug, as well as to identify toxicity patterns over a given period for the treatment before it advances to the next stage of trials, as required by US Food and Drug Administration (FDA) criteria.

The Study was undertaken to determine toxicological effects of **CimetrA™** over a 14-day period in rats, and was undertaken by the Smart Assays and Science in Action Laboratories in Israel, and comprised four study groups, three separate dosage groups, and one control group, with the treatment administered over a period of fourteen days, followed by a seven day review period. Blood samples for the pharmacokinetic analysis were taken on a daily basis, and histopathology tests were conducted on all organs per FDA guidelines. No anomalies were observed in the biopsies taken, nor were any clinical or behavioural adverse events recorded.

This Study is crucially important in the regulatory approval process for Investigational New Drugs (IND) approval by the FDA, and forms a key part of the metrics for the FDA's Center for Drug Evaluation and Research (CDER), the commercial and consumer watchdog, and gatekeeper to the US pharmaceutical market. There is a strict process for FDA approval: discovery, preclinical development, and clinical trial, where the boundary between preclinical development and clinical trial is sharply defined by the IND approval. Final FDA approvals will ensure that **CimetrA™** meets the criteria for further clinical study and

development in the US, and ultimately commercial sale, therefore opening up the largest healthcare market globally to MGC Pharma.

Roby Zomer, co-founder, Managing Director and CEO of MGC Pharmaceuticals, commented: "The successful completion of this study and the excellent results attained is an important milestone moment for the Company, as we continue to progress CimetrA™ along the mandated clinical pathway. The results of this study are a critical step in advancing MGC's submission to the FDA, and for the final approval of CimetrA™ as an Investigational New Drug in the US."

A summary of results from the recently completed study can be found in Annexure A below.

About CimetrA™

CimetrA™ is a nanoparticle micellar formulation based on the pharmaceutical synergetic composition consisting of Curcumin and Boswellia. In pre-clinical and clinical trials **CimetrA™** has demonstrated anti-inflammatory and immunomodulating effects, and can be designed for multiple therapeutic applications utilising Graft Polymer IP Ltd's proprietary GraftBio™ Self-nano-emulsifying Drug Delivery System.

Preclinical and clinical results to date have demonstrated **CimetrA™**'s mechanism of action as an anti-inflammatory and immunomodulatory agent which is effective in the prevention of severe inflammation by its control of increased Cytokine production resulting from an infection of the different variants of SARS-CoV-2 (the virus responsible for COVID-19); and which is the forerunner of a Cytokine Storm, which is believed to be the main reason for mortality in severe COVID-19 patients.

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About MGC Pharma

MGC Pharmaceuticals Ltd (LSE: MXC, ASX: MXC) is a European based pharmaceutical company, focused on developing and supplying accessible and ethically produced plant inspired medicines, combining in-house research with innovative technologies, with the goal of finding or producing treatments to for unmet medical conditions.

The Company's founders and executives are key figures in the global pharmaceuticals industry and the core business strategy is to develop and supply high quality plant inspired medicines for the growing demand in the medical markets in Europe, North America and Australasia.

MGC Pharma has a robust development pipeline targeting two widespread medical conditions and has further products under development.

MGC Pharma has partnered with renowned institutions and academia to optimise the development of targeted plant inspired medicines, to be produced in the Company's EU-GMP Certified manufacturing facilities.

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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Annexure A

Study Results

Histopathological examination

Severity of changes were scored by a 5-point scale as follows (Schafer et al., Toxicol Pathol 2018, 46:256-265):

Grade 0 – Normal (within range of normal histological variations)
Grade 1 – Minimal
Grade 2 – Mild
Grade 3 – Moderate
Grade 4 – Severe

Findings

- No pathological nor cytotoxic changes at all were found in the organs and tissue biopsies of the test subjects, i.e. All tissues of all animals were unaffected.
- The semi-quantitative results are presented below in Table A and B.
- All tissues of all animals were normal. It was concluded that the test article at the dosage administered did not induce toxicological changes.

Table A. Study design

Animal No.	Group	Number of animals	Treatment[1]
1-5	VM (Control - Male)	5	Saline
11-15	V (Control- Female)	5	Saline
61-65	HM (Test Article - Male)	5	16ul
71-75	HF (Test Article - Female)	5	16ul
	Total	20	

1. Refer annexure B “Treatment method, route, frequency, dose levels” section for treatment dosage information

Table B. A semi-quantitative analysis of the histological findings, using the scoring scale above.

Group/ treatment	Animal NO.	Lungs	Liver	Kidneys R+L	Heart	Trachea	Esophagus	Brain	Testicle/Ovary R	Comments
VM	1	0	0	0	0	0	0	0	0	
	2	0	0	0	0	0	0	0	0	
	3	0	0	0	0	0	0	0	0	
	4	0	0	0	0	0	0	0	0	
	5	0	0	0	0	0	0	0	0	
VM	**Mean**	0	0	0	0	0	0	0	0	
N=5	**SD**	0	0	0	0	0	0	0	0	
VF	11	0	0	0	0	0	0	0	0	
	12	0	0	0	0	0	0	0	0	
	13	0	0	0	0	0	0	0	0	
	14	0	0	0	0	0	0	0	0	
	15	0	0	0	0	0	0	0	0	
VF	**Mean**	0	0	0	0	0	0	0	0	
N=5	**SD**	0	0	0	0	0	0	0	0	
HM	61	0	0	0	0	0	0	0	0	
	62	0	0	0	0	0	0	0	0	
	63	0	0	0	0	0	0	0	0	
	64	0	0	0	0	0	0	0	0	
	65	0	0	0	0	NA	0	0	0	
HM	**Mean**	0	0	0	0	0	0	0	0	
N=5	**SD**	0	0	0	0	0	0	0	0	
HF	71	0	0	0	0	0	0	0	0	
	72	0	0	0	0	0	0	0	0	
	73	0	0	0	0	0	0	0	0	
	74	0	0	0	0	NA	0	0	0	
	75	0	0	0	0	0	0	0	0	

Table B. A semi-quantitative analysis of the histological findings, using the scoring scale above.

Group/ treatment	Animal NO.	Lungs	Liver	Kidneys R+L	Heart	Trachea	Esophagus	Brain	Testicle/Ovary R	Comments
HF	Mean	0	0	0	0	0	0	0	0	
N=5	SD	0	0	0	0	0	0	0	0	

Table C. A semi-quantitative analysis of the histological findings, using a scoring scale above

Group/ treatment	Animal NO.	Testicle/Ovary L	Lymph nodes	Thymus	Tongue	Stomach	Spleen	Large intestine	Small intestine	Comments
VM	1	0	0	0	0	0	0	0	0	
	2	0	0	0	0	0	0	0	0	
	3	0	0	0	0	0	0	0	0	
	4	0	0	0	0	0	0	0	0	
	5	0	0	0	0	0	0	0	0	
VM	Mean	0	0	0	0	0	0	0	0	
N=5	SD	0	0	0	0	0	0	0	0	
VF	11	0	0	NA	0	0	0	0	0	
	12	0	0	0	0	0	0	0	0	
	13	0	0	0	0	0	0	0	0	
	14	0	0	0	0	0	0	0	0	
	15	0	0	0	0	0	0	0	0	
VF	Mean	0	0	0	0	0	0	0	0	
N=5	SD	0	0	0	0	0	0	0	0	
HM	61	0	0	0	0	0	0	0	0	
	62	0	0	0	0	0	0	0	0	
	63	0	0	0	0	0	0	0	0	
	64	0	0	0	0	0	0	0	0	
	65	0	0	0	0	0	0	0	0	
HM	Mean	0	0	0	0	0	0	0	0	

Table C. A semi-quantitative analysis of the histological findings, using a scoring scale above

Group/ treatment	Animal NO.	Testicle/Ovary L	Lymph nodes	Thymus	Tongue	Stomach	Spleen	Large intestine	Small intestine	Comments
N=5	SD	0	0	0	0	0	0	0	0	
HF	71	0	0	0	0	0	0	0	0	
	72	0	0	0	0	0	0	0	0	
	73	0	0	0	0	0	0	0	0	
	74	0	0	0	0	0	0	0	0	
	75	0	0	0	0	0	0	0	0	
HF	Mean	0	0	0	0	0	0	0	0	
N=5	SD	0	0	0	0	0	0	0	0	

ANNEXURE B
Study Protocols

Sponsor	MGC Pharmaceuticals Limited
Name and any unique identifier of the trial:	NON-GLP 14 Day TOX/TK Study daily Oral spray dose of CimetrA™ oromucosal in SD rats. Study number: S-22-612
Test Article	CimetrA™ oromucosal oral spray of varying dosages
Objective	The objective of the study is to determine toxicological effect of CimetrA™ oromucosal oral spray over 14 days in rats, conducting histopathological examinations as part of a safety-toxicological evaluation of the Test Article in rats, using histological tools.
Design	Evaluation of histopathological changes in various tissue samples of rats following high dose of tested item (ointment + particles), after an oral spray administration, in a frame of toxicological study.
Description of Control Group:	The control group consisted of 10 test subjects (5 Male and 5 Female) which was administered a phosphate-buffer saline solution with no Test Article. Inclusion of each test subject in a test group was. randomised
Blinding status:	N/A
Treatment method, route, frequency, dose levels:	The Test Article was administered as an oral spray. (The oral spray route is an intended route of administration in humans) The tox study included 80 animals. Animals were allocated randomly into the study groups. Group — Dosage (ul/rat) — Main Study 14d (Males/Females) — Recovery 7d (Males/Females) — TK Control — 0ul — 5/5 — 5/5 — 3/3 Low Dose — 4ul — 5/5 — 5/5 — 6/6 Mid Dose — 8ul — 5/5 — 5/5 — 6/6 High Dose — 16ul — 5/5 — 5/5 — 6/6 TK: Toxicology

	Dosage: 0ul = PBS/50ul 4ul = 0.028mg/0.060mg/50ul 8ul = 0.056mg/0.120mg/50ul 16ul = 0.112mg/0.240mg/50ul PBS: Phosphate-buffer saline Animals were randomised into 4 groups according to a group designation table and treated according to the group dosage table above. Treatment was given to all animals in all groups once a day by oral spray for 14 days. The TK/PK groups also received treatment like the rest of the main and the recovery experiment groups. On days 1 immediately after giving the first treatment, and on day 14 after the 14th treatment, blood was taken for plasma from the TK/PK groups at 1 hr., 4 hr., 6 hr., 8 hr., 12 hr. and 24 hr, (3/3 rat for each time point), and from the Vehicle Control group at 1 hr., 6 hr., 12 hr. To test the concentration of the tested substance in the blood.
Analysis	Tissues/organs collected for histopathological examination Samples of 4% formaldehyde-fixed Lung, Liver, Kidneys (L+R), Heart, Trachea , Esophagus, Brain, Testicle R+L, Ovary R+L, Cervical Glands, Thymus, Tongue, Stomach, Spleen, Colon , Duodenum, Jejunum with Peyer's Patch and Ileum were received at Patho-Logica, where they were further fixed for 48 hours. Then, the tissues were trimmed, put in embedding cassettes and processed routinely for paraffin embedding. Twelve cassettes were prepared per animal as follows (see embedding list). Paraffin-embedded tissues were sectioned at 4 µ thickness, put on histological glass slides, stained with Hematoxylin and Eosin, and examined by light microscopy. Embedding list per rat: ▪ Slide #1: Lung (inflated with fixative) ▪ Slide #2: Liver (three lobes) ▪ Slide #3: Kidneys (L+R) ▪ Slide #4: Heart, trachea + esophagus ▪ Slide #5: Brain (three cross sections) ▪ Slide #6: Testicle R / Ovary R ▪ Slide #7: Testicle L / Ovary L ▪ Slide #8: Lymph nodes ▪ Slide #9: Thymus, tongue ▪ Slide #10: Stomach + Spleen ▪ Slide #11: Colon + cecum. ▪ Slide #12: Duodenum, Jejunum + Peyer's Patch, Ileum
Number of trial subjects:	The tox study included 10 male and 10 female rats per Main and Recovery group. (5 animals of each sex is the minimal number of animals per group required for toxicity testing).
Trial locations:	Science in Action, Israel Smart Assays, Israel
Trial standard:	Non-GLP. This study was performed under the approval of the national ethics committee in compliance with "The Israel Animal Welfare Act".