6 June 2022

ASX Code: MXC

LSE Code: MXC

ASX RELEASE

CogniCann© Phase II Clinical Trial Results

Key Highlights:

- MGC Pharma's recently completed Phase II Clinical Trial for its proprietary Dementia treatment, **CogniCann®**, demonstrates full safety and preliminary efficacy profile.
- The Clinical Trial results demonstrate the ability of **CogniCann®** to inhibit the deterioration in the behaviour of patients with Dementia.
- It is estimated that nearly 787,000 people in the UK, and 450,000 people in Australia, suffer from Alzheimer's disease, with approximately 78% of these having mild or moderate symptoms. In the top 4 European countries, this number is closer to 1 million, and is expected to grow by 15% by 2024[1].

MGC Pharmaceuticals Ltd (**ASX, LSE: MXC**, '**MGC Pharma**' or '**the Company**'), a European based bio-pharma company specialising in the production and development of phytomedicines, is pleased to provide details of the results of its Phase II Clinical Trial into the effect of its proprietary Investigational Medicinal Product, **CogniCann®**, an oral spray containing delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), on patients with Dementia.

The double-blind cross-over Clinical Trial was undertaken in conjunction with the University of Notre Dame in Western Australia and involved eligible patients commencing a six-week treatment course with **CogniCann®**, before switching (crossing over) to a six-week course of placebo, with a two-week 'washout' period between the two arms. The study's objectives were to assess the safety and efficacy of **CogniCann®**, including the assessment of the behavioural benefits of **CogniCann®** on Dementia patients measured using a number of evaluation tools including a Neuropsychiatric Inventory - Nursing homes (**NPI-NH**) Questionnaire and a Cohen-Mansfield Agitation inventory Questionnaire.

A summary of the study's protocol can be found in Annexure A of this Announcement.

The study assessed the safety profile of **CogniCann®** by monitoring adverse events and a range of observational tests undertaken by a research nurse who met with each participant to discuss their adverse event records, and measured their heart rate and blood pressure twice a week. In addition, the participant's weight and body composition measures, such as lean body mass, bone mass and fat mass were measured weekly utilising non-invasive methods. The study assessed both the safety profile and the efficacy of **CogniCann®** against a placebo, with the study results demonstrating no difference in the safety profile between the **CogniCann®** and Placebo groups i.e. indicating that **CogniCann®** was safe to use by patients with Dementia.

The efficacy of **CogniCann®** was assessed using the following three criteria:

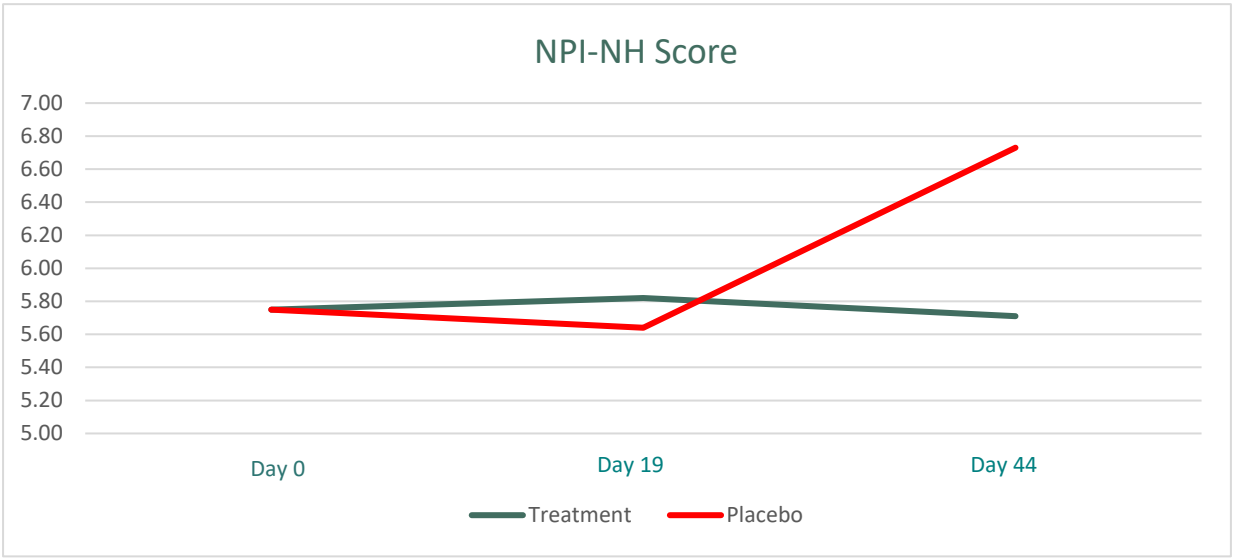
1. The participant's NPI-NH Score using the Neuropsychiatric Inventory – Nursing Home Version (**NPI-NH**) Questionnaire, which is based on responses from the participants, and from caregivers involved in their daily care.

   The NPI-NH Questionnaire was developed to help characterise the neuropsychiatric symptoms and psychopathology of patients with Alzheimer's disease and other dementia patients residing in nursing homes or extended care facilities. The NPI-NH is also used to measure the impact of anti-dementia drugs on these patients[2].

1. Source: Alacrita Research Report: Market Projections October 2019
2. https://www.dementiaresearch.org.au/wp-content/uploads/2016/01/NPI-NH_cr.pdf

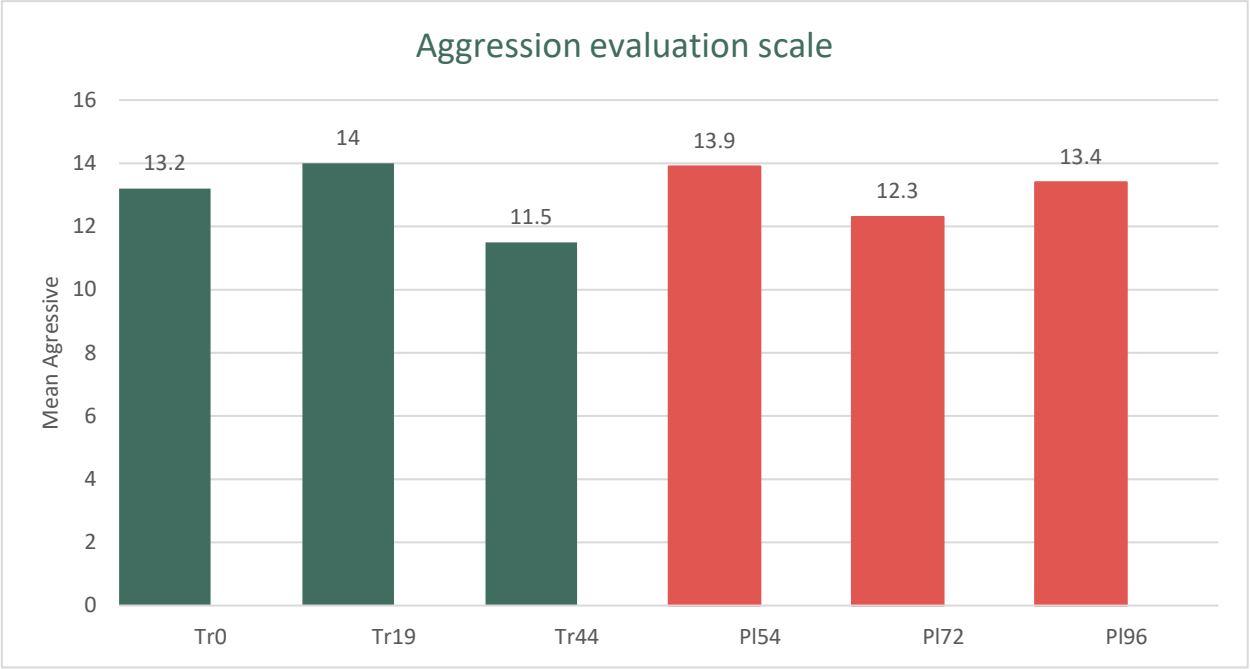
Results of the study showed that after 44 days, patients in the Placebo group experienced a deterioration in their condition, based on their NPI-NH score, compared with the stable neuropsychiatric profile of those patients treated with **CogniCann®**, indicating that the early-stage use of **CogniCann®** may be beneficial in the treatment of dementia patients.

The graph below shows the NPI-NH score of patients administered **CogniCann®** versus the Placebo, with the higher NPI-NH score indicating a deterioration in the patient's condition.



2. Aggressive behaviour

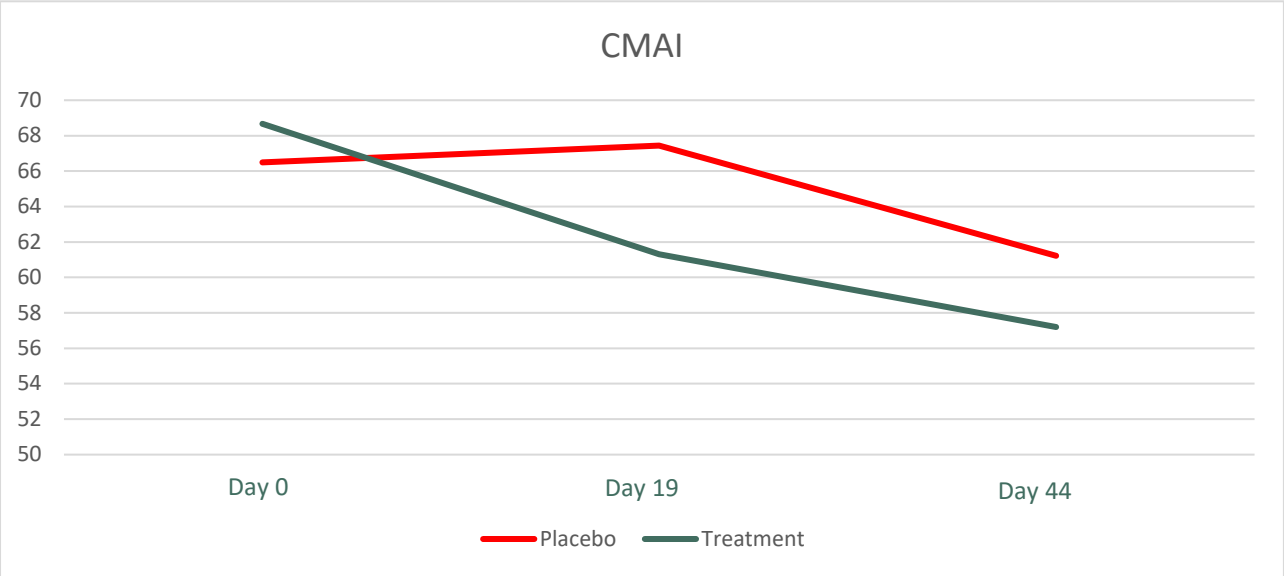
Aggressive behaviour is one of the most serious of the disturbances experienced by dementia patients, and is a common cause for psychiatric referral, admission to hospital and drug treatment. During the 44-day study period the treatment group's Cohen-Mansfield Agitation Inventory Aggressive subscale improved by 13%, compared with the Placebo group which improved by 4%. This important finding indicates not only improvement in the health status of the patients, but also the improved quality of life of the families and caregivers that are taking care of dementia patients. The graph below demonstrates the change in the aggressive behaviour between the Treatment and Placebo groups. Both groups started from similar Aggression evaluation scale values, with the Treatment group (green columns) showing increased improvement compared to the Placebo, or Control group (red columns). These results can be considered as a vector and will be studied in future clinical trials using a larger sample size.



3. Cohen-Mansfield Agitation Inventory (**CMAI**)[3]

The CMAI is a 29-item scale widely used to assess the frequency of manifestations of agitated behaviours in elderly persons, which is completed by a proxy (i.e. family carer or nursing home staff members). The study demonstrated that the Treatment group's CMAI score improved by ~17%, from 69 to 57, compared with the Placebo group's improvement of ~8% over the 44-day period. Agitation is a behavioural syndrome characterised by increased, often undirected, motor activity, restlessness, aggressiveness, and emotional distress. According to several observations, agitation prevalence ranges from 30 to 50% in dementia patients.[3]

The Clinical Trial, which commenced in March 2020, initially planned to enrol 50 patients from a number of Aged Care Facilities across Perth, Western Australia, however, as a result of the COVID-19 pandemic, and the resulting restrictions place on accessing Aged Care Facilities by Australian government agencies, the time taken to complete the trial was longer than anticipated, resulting in the number of patients enrolled in the trial being reduced from the initial target of 50 to 22.



Results from the study will be used in the design of the next phase of clinical trials for **Cognicann®,** including defining the appropriate End Points and patient sample size.

About CogniCann®

CogniCann® is a phytocannabinoid derived Investigational Medicinal Product and designed to treat patients with Dementia and Alzheimer's disease. The specific ratio of THC to CBD in the blend is designed to improve behaviour and cognition in dementia patients.

MGC Pharma recently signed a supply and distribution agreement with Sciensus Rare for the distribution of **CogniCann®** in key European countries, details of which can be found in MGC Pharma's ASX Announcement on 5 April 2022 titled "MGC Pharmaceuticals enters partnership with Sciensus Rare for the distribution of **CannEpil®** and **CogniCann®** in the EU and UK".

In October 2019 MGC Pharma commissioned a Market Projections Study for **CogniCann®** by Alacrita Research, to determine the estimated market size for **CogniCann®**. This study estimated that in Europe and the UK alone, there were approximately 1.5 million mild to moderate sufferers of Alzheimer's disease, the most common form of Dementia.[4] (refer following table)

3. C. Carrarini et al, Agitation and Dementia: Prevention and Treatment Strategies in Acute and Chronic Conditions, Front Neurol, 2021
4. https://www.dementiaresearch.org.au/wp-content/uploads/2016/06/CMAI_Manual.pdf

Territory	AD population	% diagnosed mild	% mild receiving drug treatment	% diagnosed moderate	% moderate receiving drug treatment	Total mild-AD	Total mild and moderate-AD
UK	776,950	44%	67%	40%	81%	229,045	480,777
France	386,546	43%	77%	39%	85%	127,986	256,126
Spain	275,553	35%	90%	46%	94%	86,800	205,950
Germany	537,512	37%	76%	40%	82%	151,149	327,453
Italy	317,043	37%	82%	40%	87%	96,191	206,522
Average		*39%*	*78%*	*41%*	*86%*		
Total	2,293,604					**691,171**	**1,476,828**

Data taken from Datamonitor who surveyed 223 physicians in 2015 and extrapolated values countrywide – Accessed May 2019

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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 phytomedicines 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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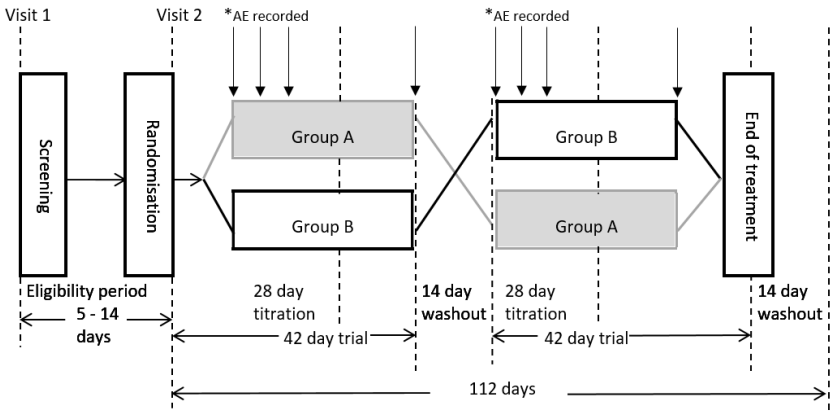
Annexure A

Study Title	Medicinal cannabis and dementia: Effects on behavioral symptoms among older residential care recipients.
Study Drug	The medical cannabis oil, "CogniCann", was provided in a sealed 10ml glass spray bottle which contained a mix of THC and CBD in a 3:2 ratio (25 mg/ml THC, 17 mg/ml CBD) in a Medium-Chained Triglyceride (MCT) oil base.
Participant Details	N=22 (Male: 5, Female: 17). Average Age: 85 years
Protocol	A Phase II, randomised, double blind cross-over, placebo-controlled clinical study designed to evaluate the clinical efficacy of the Study Drug and determine the therapeutic individual dose response
Study Arms	The Study Drug will be administrated as the following: For those participants who meet the eligibility period, CogniCann will be administered to the residential aged care facilities by the pharmacist following the steps below: • The bottles will be delivered every Monday to the residential aged care facilities. • The bottles will be collected after 7 days of use (even if they are half full) and returned to the pharmacy where they can determine how much was used (or left) and then dispose of the bottles to meet Therapeutic Goods Administration (TGA) requirements. • At the start of the titration phase, 1 bottle will be administered for each participant (as the lower dose of 2.5mg allows for each bottle to hold 2-3 weeks of the medication). • As participants being to reach a higher dose (titration phase, see Table 1 below), 2-3 bottles will be provided on a weekly basis, so each participant will have sufficient medication to last for 7 days. An upper limit of 50 mg/day of THC was permitted in those who did not experience any adverse events from the medication.
Study Purpose	To evaluate the clinical efficacy and the potential behavioral benefits that CogniCann® may have on patients with Dementia and Alzheimer's disease.
Methodology and study procedures	Study participants will include participants who are living within a residential aged care facility. Inclusion criteria: aged 65+ years who have a diagnosis of dementia but still have the capacity to provide informed consent, able to speak and understand English. Study participants will be recruited from residential aged care facilities who have three residential aged care facilities across Western Australia. The residential aged care's affiliated pharmacist will store, label, manage and distribute the medication to these facilities. A locum medical practitioner will prescribe participants with 'Congicann' and will be asked not to change any other prescribed medications for the duration of the study (14 weeks).
Study Duration	This randomised, double-blind cross-over study will run for 18 weeks consisting of a two week 'Eligibility period' for screening and clinical assessment, and a 16 week 'Experimental period' of two six-week arms of treatment and placebo separated by a two week 'washout' period between the treatment arms, and a two-week washout period following the completion of the second arm (see Figure below).



*Adverse events (AE) will be recorded with each dose increase during the titration phase and on the last dose during the intervention phase

Eligibility Period

People expressing interest in participating in the study will initially be screened based on the criteria listed below, and if suitable, then they will undergo clinical investigation to ensure they are able to provide informed consent.

- Live within a residential aged care facility, and
- Aged 65 year or older, and
- Have a diagnosis of dementia, and
- Able to speak English, and
- Known compliance to taking medication, and
- Not bed ridden, and

To minimize the likelihood of an adverse event, people with certain health conditions or on some medications will be excluded from the study. These include:

- Diagnosis of one or more of the following conditions:
- Frontotemporal or Lewy body dementia,
- Other diseases such as Epilepsy, Anorexia nervosa, comorbid psychiatric conditions,
- Parkinson's disease,
- Congestive heart failure,
- History of myocardial infarction or anginal pain,
- History of stroke,
- Liver disease,
- Renal disease.
- Taking medications that may interact with cannabis metabolism such as Primidone, Phenobarbital, Carbamazepine, Rifampicin, Rifabutin, Troglitazone, Hypericum perforatum, and valproic acid (to be finalized through consultation with a pharmacist).

Following the initial screening process, potential participants will then undergo a thorough clinical investigation to ensure they have the cognitive capacity to provide informed consent that will also include the use of a standard bank of tests such as the Mini-Mental State Examination (MMSE).

Study Endpoints

The primary outcomes:

Efficacy endpoint:

- Change in Neuropsychiatric Inventory Questionnaire - Nursing homes (NPI-NH)in treatment group compared with Placebo
- Change in Aggressive Behavior in treatment group compared with Placebo
- Change in Cohen-Mansfield Agitation Inventory (CMAI) in treatment group compared with Placebo