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Long COVID Clinical Study Results for ArtemiC™ Support

Key Highlights:

- Clinical study, sponsored by Swiss Pharmacan AG, conducted on a white-label version of MGC Pharma **ArtemiC™ Support** to assess its impact on patients suffering from Long-COVID.
- 60 COVID vaccinated patients suffering from Long-COVID were observed in clinics across Spain whist administered the study product twice a day for six weeks.
- The study assessed post-COVID symptomatology and biological markers in regular blood tests.
- Results indicate that the product may be effective in treating the symptoms of Long-COVID and other post-viral disease related symptoms.

MGC Pharmaceuticals Ltd (‘**MGC Pharma’** or ‘**the Company**’) a European based bio-pharma company specialising in the production and development of plant inspired medicines, announces the results of the open label clinical study, a white label version of **ArtemiC™ Support**.

The study was conducted across public policlinics in Madrid, Barcelona, Castellon, and Valencia, Spain, recruiting 60 COVID vaccinated patients suffering from post-acute COVID (Long-COVID). The nutraceutical, administered as a dose of 10 drops twice a day for six-weeks, was shown to alleviate symptoms of the condition unrelated to functional limitations, including pain, mental confusion, sleep disorders, and inflammation.

The product was assessed through the following parameters, incorporating primary and secondary outcomes:

- Primary outcomes: functional status according to a Post-COVID Functional Scale (PCFS) one and six weeks after the initiation of the treatment, (ANNEX IV); patients completed a Quality of Life Questionnaire (ANNEX V).
- Secondary outcomes: post-COVID symptomatology according to a 10-point Likert scale one and six weeks after the initiation of the treatment.

The results of the study show a statistically significant improvement in symptoms associated with long-COVID following the treatment, including:

- Dyspnea
- Sleep disorders
- Headache
- Depression
- Pain
- Mobility intestinal problem
- Mental confusion

The biological markers in the blood tests further proved a reduction of inflammation and enterohepatic involvement, as well as liver reactant proteins.

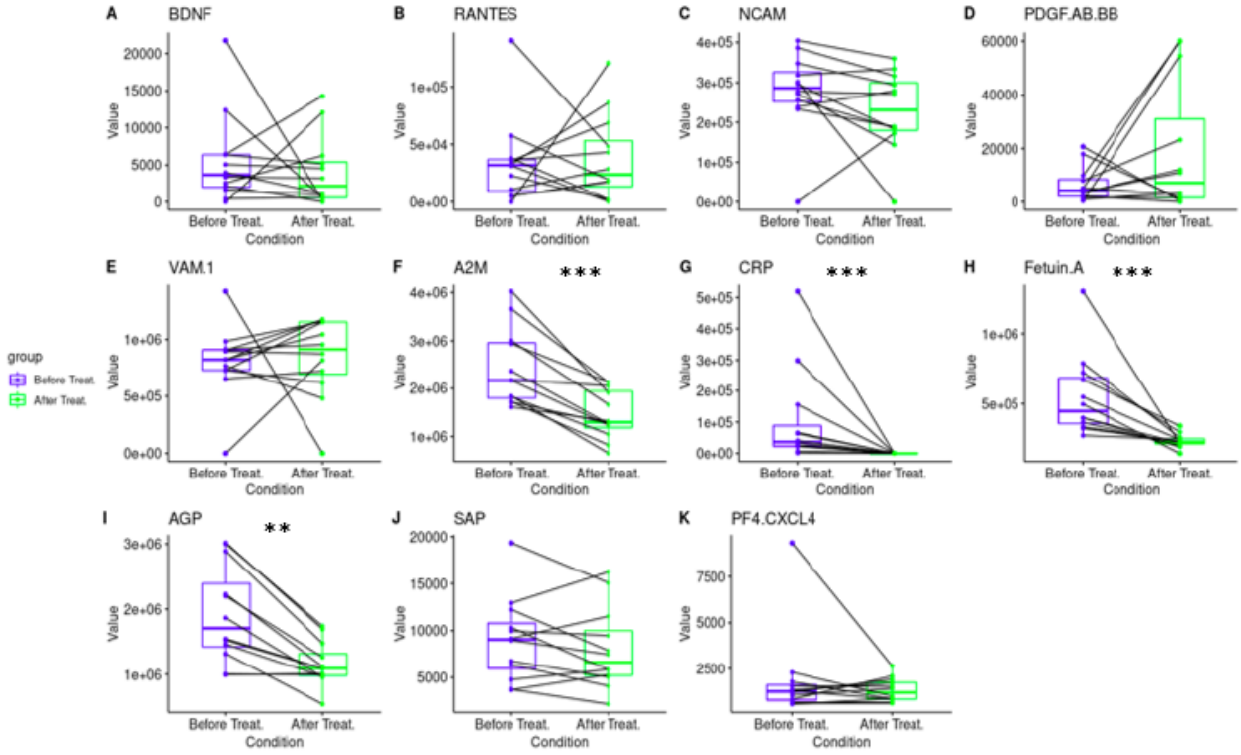
The efficacy of the nutraceutical can be measured by a quality of life, physical and cognitive symptoms improvement. As such, the following rationale is based on the biological markers measured in the blood tests:

- Increased levels of three acute phase reactant proteins (AGP, A2M, CRP) suggest subclinical coronavirus infection in the Gastro-intestinal (GI) tract, with mucosal permeability disorder and possible dysbiosis.

- It may lead to a comprehensive disruption of the brain-hepatopulmonary axis with impact on the liver, lungs, and blood-brain barrier, where it may have mild neurocognitive consequences and behavioural consequences.
- Although increased plasma AGP, A2M, and CRP may have beneficial effects in relation to the anti-microbial response, its inflammatory basis has one or more causes that need to be investigated, especially when they coincide in the patient with alterations in GI motility.
- In fact, this hepatic response suggests persistence of viral antigens in the GI tract, as well as alterations in the perivascular bacterial dysbiosis, with alterations in the permeability of the intestinal barrier and activation of neuro-immuno-inflammatory based mechanisms such as dyspepsia and irritable colon.
- Decrease of these markers can lead to the normalisation of the GI tract function and microbiome composition. This may lead to the improvement in the cognitive condition via brain gut axis and the physical symptoms are improved via brain hepatopulmonary axis.

Biological markers were analysed by change before and after the treatment.

The following tables show the changes in the biological markers of damage to the intestinal encephalo-hepato-pulmonary axis.



Key results for the study included:

- A statistically significant improvement in pain symptoms, before and after the treatment with the nutraceutical.
- Patients reported statistically significant improvement in the symptoms of Long-COVID which were not related to the functional limitations (cognition, mood, energy, sleep).
- Patients reported statistically significant improvement in the ability to function in their daily life.
- Statistically significant improvement in the following parameters relating to Long-COVID:
  - Dyspnea: a significant difference was seen in the reported symptom intensity.
  - Sleep disorders: a significant difference was seen in the reported symptom intensity.
  - Headache: a significant difference was seen in the reported symptom intensity in each visit.
  - Depression: a significant difference was seen in the reported symptom intensity in each visit.

- Pain: a significant difference was seen in the reported symptom intensity in each visit.
- Mobility intestinal problem: a significant difference was seen in reported symptom intensity in each visit.
- Mental confusion: a significant difference was seen in the reported symptom intensity

Statistical analysis was performed according to the primary and secondary endpoints.

Analysis of data collected from the Post COVID Functional Scale

Significant differences were observed in domains 4.1 ("Do you consider that you need essential help for basic household tasks that are important for daily life? "), 6.2 ("Do you suffer from symptoms, but do not experience functional limitations? "), with a p-value of 0.039 and 0.003, respectively.

Count

		vf_ef_r62		
		0	1	Total
v0_ef_r62	0	18	17	35
	1	3	7	10
Total		21	24	45

Chi-square tests

	Value	Exact sig. (bilateral)
McNemar test		,003(a)
N of valid cases	45	

a Using the binomial distribution

Analysis of data collected from the Quality of Life Questionnaire

Significant differences between the two data collection points were observed for items 3 ("Do you have any problems performing daily activities?") and 4 ("Do you usually feel pain or discomfort?"), with p-values of 0.001 and 0.041, respectively.

Count

		vf_cv_3			
		1	2	3	Total
v0_cv_3	1	5	1	0	6
	2	10	17	6	33
	3	0	0	6	6
Total		15	18	12	45

Chi-square tests

	Value	gl	Asymptotic sign (bilateral)
McNemar-Bowker test	13,364		,001
N of valid cases	45		

For dyspnea, sleep disorders, headache and depression, pain, mobility, intestinal problems, and concentration problems one or more p-values have been less than 0.05, meaning that there are significant differences between the mean severity reported at each visit for each symptom. It also indicates that there are significant differences in the severity of symptoms collected between visits when compared two by two.

Count

		vf_cv_4			
		1	2	3	Total
v0_cv_4	1	3	1	0	4
	2	4	10	3	17
	3	0	11	13	24
Total		7	22	16	45

Chi-square tests

	Value	gl	Asymptotic sign (bilateral)
McNemar-Bowker test	6,371		,041
N of valid cases	45		

The study results support a similar study undertaken by MGC Pharmaceuticals and its global distribution partners, Swiss PharmaCan AG and Glow LifeTech Ltd, which indicated that **ArtemiC™** may be used as a complementary and additional treatment for the symptoms of Long-COVID[1].

Roby Zomer, co-founder and Managing Director of MGC Pharmaceuticals, commented: "The clinical study has demonstrated that MGC Pharma's ArtemiC™ Rescue formulation has markedly affected outward symptoms of Long-COVID, which is an excellent step forward in progressing the clinical proof of the benefits of ArtemiC™.

That the product could help to explain changes in the symptoms of Long-COVID patients is an extremely promising development for the Company, with significant potential commercial developments we hope to explore further through future studies."

--Ends--

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[1] Refer ASX announcement dated 14 July 2022, titled "Long COVID Study Results for ArtemiC Support"

About MGC Pharma

MGC Pharmaceuticals Ltd (LSE: MXC, ASX: MXC) is a European based bio-pharma 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 Protocol and Information

Sponsor	Swiss Pharmacan AG
Name and any unique identifier of the trial:	Research study to evaluate the clinical effectiveness of the nutritional supplement VITAMIC BIOSEN® on individuals with symptoms consistent with persistent Covid who have been vaccinated against the SARS-CoV2. (VITAMIC BIOSEN® is white label version of MGC Pharma's ArtemiC™ product)
Primary endpoint(s):	Individual self-completed surveys will be conducted by all study participants via the eCRD (Electronic Data Collection Booklet ANNEX III). These will be carried out on the day of inclusion in the study, before starting treatment, and in the sixth week at the end of treatment. Two scales will be completed: • Post-COVID Functional Scale (PCFS) (ANNEX IV) and assessing post-COVID symptomatology. • EuroQol5D Quality of Life Questionnaire (ANNEX V). After completing the surveys on the day of inclusion, they will start taking VITAMIC BIOSEN®, at a dose of 10 drops twice a day orally for 6 weeks in addition to any treatments the patient may be taking under normal clinical practice. All data will be collected in the eCRD created for the project, which will be stored encrypted and after the use of the corresponding pseudo-anonymization procedure for the protection of personal data
Secondary endpoints:	For the secondary objective, Cohort B: A subgroup of 20 participants (making up Cohort B) will have blood tests performed in routine clinical practice. A sample of venous peripheral blood (3-4 ml) will be taken from the arm, fasting and first thing in the morning. After 6 weeks, the indicated test will be repeated, and results will be compared between the baseline and final situation. The study will use the multi-analytical molecular laboratory test ENCHEPAX™, from the company PERSONA BIOMED SPAIN SL (ANNEX VI). All data will be collected in the eCRD created for the project, which will be stored encrypted and after the use of the corresponding pseudo-anonymization procedure for the protection of personal data. Symptomatology according to the 10-point Likert scale on and six weeks after treatment initiation. The following symptoms were measured:: 1. Dyspnea 2. Cough 3. Asthenia 4. Anosmia 5. Ageusia 6. Headache 7. Mental confusion
Description of Control Group:	A control group was not used in this study.
Blinding status:	N/A
Product status:	VITAMIC BIOSEN® is an approved food supplement with extensive experience of use and an excellent safety profile. As the basic type of treatment in these patients with persistent COVID remains unchanged, this study is considered to have a very low level of intervention. (Vitamic Biosen® is a white label version of MGC Pharma's ArtemiC™ product).

Treatment method, route, frequency, dose levels:	Following the initial assessment, a decision was made for inclusion of the candidate, given all inclusion criteria work and no exclusion criteria harm. Following this, two bottles of VITAMIC BIOSEN® was provided to the patient and a demonstration was done to show how the portioning by drops should be done. Cohort A: Study entry data were collected through interviews conducted by healthcare personnel. In this interview, data were collected on the state of health (symptoms present, using a 10 point Likert scale), any doubts they might have about the treatment or the study were resolved, and the functional impairment and quality of life scales were performed. After six weeks (at the end of the study), this process was repeated by means of an interview conducted by health personnel, in such a way that the symptoms present were recorded as well as the evaluation of the Functional Affectation Scale and the Quality of Life Scale. Cohort B: Input data were collected for the 20 participants by the Principal Investigator, through personal interview where in addition to collecting the clinical data necessary to perform the biomarker test, questions or doubts related to the study or treatment were addressed. Similarly, the functional assessment and quality of life scales were carried out, both at the beginning and at the end of the 6-week follow-up of the study. Day one (1) was the day of first intake. On the day of inclusion and first assessment, the investigator carefully explained the aim and the design of the study and delivered a relevant information sheet. Following this, the patient signed the consent form. Case Report Form (CRF): A database tool was designed specifically for this study. The data was registered at the moment of the interview, either on paper, or electronically. Concomitant medication was documented. Investigators were encouraged to just observe and document what they saw and heard in a highly objective way. Key tools that were used were the Post Covid Functional Scale (PCFS), EuroQol5D Quality of Life Questionnaire and 10-point Likert Scales regarding Dyspnea, Cough, Asthenia, Anosmia, Ageusia, Headache and Mental Confusion. Data was collected by healthcare professionals, either nurses or medics.
Number of trial subjects:	Total of 60 patients in Spain who suffer from post-acute COVID Syndrome (Long COVID Syndrome). • 87.5% women with an average age of 47.76 years • 12.5% male with an average age of 43.16 years 100% vaccinated at first interview. The 60 patients included in the study and were assigned to the two cohorts as follows: - Cohort A (does not include biomarker analysis): made up of 40 patients who met all the criteria and who, for various reasons (place of residence, self-will, reduced mobility,...), did not wish to undergo blood collection

	twice (as indicated in the protocol), to determine biomarker values. - Cohort B (includes biomarker analysis), formed by 20 patients, who communicated their willingness and disposition to undergo both extractions in the clinics authorized for this purpose and on the dates indicated in order to comply with the deadlines established in the protocol. Likewise, in order to create a homogeneous cohort, the persons with the most similar clinical, anthropometric and hygienic and dietary profile were selected. The individuals were selected from all the Spanish territory and the follow-up was carried out by means of personal interviews with the research team of the study. Likewise, an e-mail address was set up on the web site created for the study to attend to any doubts or questions that the participants might have during the 6 weeks of follow-up of the study. In this regard, 19 queries were registered through this system, which were answered by the principal investigator. For the extraction of the blood samples necessary for the biomarker test, 4 clinics with clinical analysis services were selected, located in the cities of: Madrid, Barcelona, Castellon and Valencia. Each patient underwent two extractions in the same center 6 weeks apart and after treatment with VITAMIC BIOSEN. The samples obtained were processed according to the procedures defined by the manufacturer of the ENCHEPAX™ test, and were duly coded to ensure compliance with the data protection law. The analytical procedure was performed at the facilities of PERSONA BIOMED SPAIN, as the manufacturer of the ENCHEPAX test, and all samples were processed by them on the same analytical plate to avoid any possible distortion factor.
Subject selection criteria:	Screening of patients was based on subjects attending consultations in medical practices and on associations caring for patients suffering from Long-COVID. Subjects who met the overall inclusion criteria were invited to participate in the study. <u>Inclusion Criteria</u> • Persisting post-acute COVID syndrome (PACS) symptomatology of more than one month, with Post Covid Functional Score (PCFS) between one and four. • Individuals between 18 and 80 years of age presenting some of the following symptoms: cough, dyspnoea, asthenia, anosmia, ageusia, headache and mental confusion. • The patient must have received at least one dose of any vaccine offered by the Spanish health system. • The patient must be able to complete the follow-up assessments. • The patient agrees to take the VITAMIC BIOSEN® food supplement, assigned during the 6 weeks. <u>Exclusion Criteria</u> • Known hypersensitivity to VITAMIC BIOSEN® • Active malignancy • Current or recent chemotherapy treatment (<6 months)

	• Medical history of Human Immunodeficiency Virus (HIV) infection, or any serious • immunocompromised state • Use of montelukast or zafirlukast ≤ 30 days prior inclusion • Having participated in another clinical trial in the previous month • Women that are pregnant or breastfeeding
Trial locations:	Madrid, Barcelona, Castellon and Valencia.
Report Author:	Dr. Francisco Mera Cordero
Statistical Analysis	The statistical analysis will be descriptive. The change in the three scales will be described, comparing the scales on the day of inclusion with those at week six. A description will also be given for each of the seven 10-point Likert scales, comparing the item values on the day of inclusion with those at week six. Convenience sampling, which is a non-probability, non-random sampling technique, will be carried out in which the persons included in the research project are purposively determined based on the inclusion and exclusion criteria mentioned above. Subsequently, the type of variables collected in the study will be determined as a preliminary step to choose the most appropriate and valid methods of analysis of the dependent variables, independent variables, factors related to the patient, the disease, and the treatment, which will be studied to determine whether there is an association with the dependent variable. Measures of central tendency (mean, median and mode) and dispersion will be used for quantitative variables, and, in the case of qualitative variables, data will be collected in frequency tables, expressed in terms of proportion, and noted in brackets. To carry out association studies, a univariate analysis will be carried out for each of the independent variables mentioned above. To compare groups of categorical variables, the chi-square (X2) and Fisher's exact probability tests will be used as hypothesis tests; the student's t-test or the Mann-Whitney U-test will be applied for quantitative data. To compare continuous quantitative variables in related samples, the t-test shall be used if the distribution is normal or the Wilcoxon signed-rank test if the distribution is non-normal. The significance level will be considered at < 0.05 (two-tailed). Hierarchical cluster analysis will be used to group patients according to their pattern of similarity by plasma levels of the biomarkers studied. The analysis will use mathematical algorithms to quantify the similarities between subjects within each subgroup and define subgroups where similarities are strongest between patients in the same subgroup and weakest in relation to patients in other subgroups. Hierarchical cluster analysis will also identify patterns of association between molecular and genetic biomarkers, which will help to interpret mechanistic relationships in the processes in which they are involved.

Trial standard:	The study will be governed by the basic ethical principles contained in the Declaration of Helsinki (WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI. Ethical Principles For Medical Research Involving Human Subjects. Adopted by the 18th WMA General Assembly Helsinki, Finland, June 1964 and amended by the 29th WMA General Assembly, Tokyo, Japan, October 1975; 35th WMA General Assembly, Venice, Italy, October 1983; 41st WMA General Assembly, Hong Kong, September 1989; 48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996 and the 52nd WMA General Assembly, Edinburgh, Scotland, October 2000 and note of clarification on paragraph 29 added by the WMA General Assembly, Washington 2002) and in the Spanish regulations in force for the performance of observational studies (SAS/3470/2009, of 16 December) and will be subject to prior approval by the Ethics Committee of any of the hospitals involved.