**Bonus BioGroup Ltd.**

(hereinafter: the "**Company**" or "**Bonus BioGroup**")

May 27, 2021

To
Israel Securities Authority
www.magna.isa.gov.il

To
Tel Aviv Stock Exchange Ltd. (hereinafter: "**TASE**")
www.tase.co.il

**At the International Society for Cell & Gene Therapy (ISCT) 2021 annual meeting in New Orleans,**

# Bonus BioGroup presented complete success in treating COVID-19 patients with MesenCure, which significantly improved the patients' health

## The Israel Ministry of Health approved the phase II clinical trial for the treatment of life-threatening respiratory distress with Bonus BioGroup's MesenCure therapy

Bonus BioGroup (TASE: BONS) is a clinical-stage Israeli biotechnology company, engaged in research and development of biomedical tissue-engineered and cell therapy products.

Bonus BioGroup is pleased to announce that on May 26, 2021, the company presented at the International Society for Cell & Gene Therapy (ISCT) 2021 annual meeting in New Orleans, the preliminary results of the clinical trial evaluating the safety and efficacy of the cell therapy product MesenCure for the treatment of Covid-19 patients with life-threatening respiratory distress (hereinafter: "the clinical trial for the treatment of respiratory distress"), conducted at the Rambam Health Care Campus, Haifa, Israel.

Dr. Shadi Hamoud, the principal investigator of the clinical trial for the treatment of respiratory distress, is the head of the research unit and deputy director of the department of internal medicine E, at Rambam Health Care Campus, declared: "the results of the treatment with MesenCure, thus far, are very impressive and are significantly better compared to the results achieved with other therapies. All patients treated with MesenCure were in a severe condition, exhibiting acute respiratory distress, with diffuse pneumonia as per chest radiographs, and



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blood parameters indicating the presence of cytokine storm. Moreover, about 90% of the trial participants suffered from comorbidities known as risk factors for increased disease severity, complications and mortality. These patients' prognosis was poor, with low chances of recovery and survival, hasn't it been for MesenCure. However, thanks to the treatment with Bonus BioGroup's MesenCure, the patients demonstrated a significant improvement in the tested parameters, and were released from hospital only one day (median calculation) following treatment end. The treatment with the MesenCure, showed good and surprising results and created great interest among other departments at Rambam Health Care Campus. We hope to treat a large number of patients with this cell therapy, and we will strive to extend its use to other indications as well".

The healed lungs of the patients treated with MesenCure highlighted the superior efficacy of MesenCure, compared to other treatments, and was reflected in a significant ($p < 0.0001$) and rapid reduction in the area of diffuse lung inflammation, as demonstrated by chest radiographs, from a median of approximately 55% of the lung area before treatment, to a median of approximately 15% of the lung area, only five days after starting the treatment, and up to a negligible median of about 1% of the lung area, about a month after treatment initiation.

The improvement in respiratory function of the MesenCure-treated Covid-19 patients was demonstrated in the significant increase ($p = 0.0086$) from the low blood oxygen saturation levels ($O_2$ saturation) caused by acute respiratory distress prior to MesenCure treatment, to blood oxygen saturation levels of about 95% after treatment end.

The alleviation in the severity of the pneumonia and the life-threatening cytokine storm in the MesenCure-treated Covid-19 patients was demonstrated, among others, in a median decrease of about 89% in the blood levels of the inflammatory protein CRP ($p = 0.0039$), in a median increase of about 55% in the blood levels of the lymphocytes ($p = 0.0234$), and the return of these parameters to normal levels, which indicates, among other things, the healing of lymphocytopenia, a common symptom of Covid-19 infection.

The reduction in tissue injury in the MesenCure-treated Covid-19 patients was demonstrated by a median decrease of 22% in the enzyme lactate dehydrogenase (LDH) as well as a median decrease of 72% in the enzyme creatinine kinase (CK), and in their return to normal levels ($p = 0.0039$), which indicated the cessation of tissue destruction.



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In addition to improvements in the objective parameters of the patients treated with MesenCure, an improvement was also noted in all subjective parameters indicative of the patient's health, including their mobility, ability for self-care and performing of routine activities, degree of pain and anxiety ($p = 0.02$), and the patients' own assessment of their overall well-being, which improved by more than 11 points on average ($p = 0.02$), as evident from questionnaires answered by the trial participants prior to treatment and about two weeks after treatment with MesenCure.

The above-mentioned significant improvements were seen in all Covid-19 patients treated with MesenCure, all of which, although hospitalized in a severe condition and with poor prognosis of recovery, were released from hospital as result of MesenCure therapy, only one day (median calculation) after treatment end, without any need for respiratory support; with the exception of one patient whose treatment with MesenCure did improve his parameters related to Covid-19 disease, but unfortunately passed away during follow-up period as a result of a severe comorbidity from which he had suffered prior to getting infected with Covid-19 which resulted in very unfavorable prognosis for survival to begin with. MesenCure treatment was not assessed to be related to this event.

In comparison, according to a meta-analysis of 52 observational studies performed on more than 43,000 severe coronavirus patients with medical condition similar to the participants in the clinical trial for the treatment of respiratory distress, the mortality rate among severe Covid-19 patients was 35.5%[1].

In the clinical trial for the treatment of respiratory distress with MesenCure, conducted at Rambam Health Care Campus, ten severe Covid-19 patients, women and men, aged 45-75 years (average age above 60 years) have been treated thus far.

As a result of the excellent outcomes in the phase I clinical trial for the treatment of respiratory distress, demonstrating the safety of MesenCure therapy in all treated patients, in all tested parameters, the Israel Ministry of Health (IMOH) approved the continuation of the trial to phase II, which will include up to 50 additional Covid-19 patients, and will be conducted by Prof. Tony Hayek, director of the department of internal medicine E, and the deputy director

[1] https://associationofanaesthetists-publications.onlinelibrary.wiley.com/doi/10.1111/anae.15425



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Dr. Shadi Hamoud, the principal investigator in this clinical trial for the treatment of respiratory distress, which is conducted at Rambam Health Care Campus, a leading medical facility in Israel and specifically in the treatment of Covid-19 patients.

In the phase II clinical trial, the efficacy and safety of MesenCure will be evaluated for the treatment of Covid-19 patients with life-threatening respiratory distress, in comparison to a control group.

During the clinical trial for the treatment of respiratory distress, the experiment group will receive intravenously three doses of MesenCure. The parameters that will be evaluated include, among others: respiratory functions, inflammatory parameters that indicate the attenuation of the cytokine storm characteristic of the disease, general parameters that indicate the course of the disease, the shortening in the hospitalization period, and the increase in patient survival.

The effectiveness of the cell therapy MesenCure stems from the enhancement of the mesenchymal cells in MesenCure by an innovative and unique combination of biological and physical growth conditions, while reducing the overall growth period of the cells and by improving their safety.

The cell therapy MesenCure is intended for the treatment of life-threatening respiratory distress, whether caused by the original Covid-19 strain or any other strain, by another virus, or whether it is caused by a bacterial or other infection. Therefore, Bonus BioGroup estimates that in the immediate term, vaccines will have no significant effect on the market positioning of MesenCure, due to the growing risk for further coronavirus waves as result of the emergence of more violent coronavirus strains[2], and due to a global shortage of vaccines that is expected to last several years, until about 70% of the world's population is vaccinated, which is, according to experts, the minimal requirement for a herd immunity[3].

The company estimates that even after herd immunity is established, millions of incidences of severe coronavirus infections are expected to occur worldwide every year, all of which may be a potential target population for MesenCure therapy. This assessment is based on the experts' opinion published last January in the prestigious scientific journal Nature, who believe that

[2] https://www.usatoday.com/story/news/health/2021/02/16/covid-19-us-fourth-wave-variants-coronavirus/4460958001/

[3] https://www.washingtonpost.com/business/2020/05/11/coronavirus-vaccine-global-supply/



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despite the available vaccines for the coronavirus, the corona plague will become an endemic disease, with a stable incidence[4] similar to influenza, affecting more than 10% of the population each year[5].

In addition, the cell therapy MesenCure may be used to treat a wide range of indications, including lower respiratory tract infections as well as asthma and chronic obstructive pulmonary disease, which together represent a global market expected by 2026 to exceed US$ 43 billion per year[6,7,8], even excluding the expected effect of Corona virus.

Since its establishment, Bonus BioGroup is developing cell-based therapies and tissue-engineered products for bone regeneration. The main component of the viable bone graft are mesenchymal stromal cells isolated from the patient's adipose tissue. During the beginning of the Covid-19 pandemic outbreak, the Company started to study these mesenchymal cells, isolated from the adipose tissue of healthy donors, and their priming in order to enhance their potential to attenuate the inflammatory responses, and especially respiratory inflammations and the hyper-inflammatory response – the cytokine storm prevalent in Covid-19 infection and other inflammatory diseases.

Bonus BioGroup applied in the development of MesenCure a variety of unique technologies and knowledge, some of which are currently in development by the company, and some of which are part of the company's rich intellectual property, which includes six families of patents and patent applications, consisting of twenty-five approved patents and eighteen patent applications in many countries around the world.

The International Society for Cell and Gene Therapy[9] (ISCT) is the world's leading professional organization in the field of the company's activities. Since the outbreak of the Covid-19 pandemic, the ISCT has been encouraging the research and development of cellular therapies for Covid-19 patients, and in particular mesenchymal cell-based therapies, similar to

[4] Phillips, N., The coronavirus is here to stay - here's what that means. Nature, 2021. 590(7846): p. 382-384.
[5] https://www.cdc.gov/flu/about/burden/2018-2019.html
[6] https://www.coherentmarketinsights.com/press-release/global-chronic-obstructive-pulmonary-disease-copd-treatment-market-to-surpass-us-218-billion-threshold-by-2026-1411
[7] https://www.bloomberg.com/press-releases/2019-06-13/global-asthma-therapeutics-market-to-surpass-us-20-4-billion-by-2026-coherent-market-insights
[8] https://www.reportsanddata.com/report-detail/acute-respiratory-distress-syndrome-ards-market
[9] https://isctglobal.org/page/AboutUs



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MesenCure. At the pinnacle of ISCT's activities is its annual meeting, which attracts thousands of scientists, physicians, and opinion leaders from around the world, as well as other experts and executives from industry, academia and health services, engaged in the safe and effective implementation of cell therapies.

**Company estimations regarding forward-looking statement**

Bonus BioGroup's assessments regarding the therapeutic effect of MesenCure and/or its marketing potential, the company's ability to continue the development of the drug product, including the conduction of clinical trials, and the attaining of a drug product that can be medically applied in humans, for the time periods expected to conduct any stages in any trial, are a forward-looking statement, as defined by the in the securities law 1968, which is based on the Company's estimates and on the information in its possession at the time of reporting.

There is no certainty that these information will be realized, in whole or in part, among others, due to dependence on third parties actions that are not under the control of the company, the possibility of delay in obtaining relevant regulatory approvals and/or a change in the relevant conditions and/or feasibility studies that the Company may conduct, and/or delay in conducting of studies and/or the need for further studies and/or failure of studies and/or technological changes and/or development and marketing of similar and/or more effective competing products and/or lack of availability of resources and/or realization of any of the risk factors related to research and/or trials and/or its results.

Sincerely,

Bonus BioGroup



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