

MESOBLAST PHASE 2 TRIAL RESULTS SHOW EARLY AND DURABLE EFFECTS OF SINGLE MESENCHYMAL PRECURSOR CELL INFUSION IN BIOLOGIC REFRACTORY RHEUMATOID ARTHRITIS PATIENTS

Trial Results Over 52 Weeks Presented At 2017 American College Of Rheumatology Annual Meeting

New York, USA; and Melbourne, Australia; November 10, 2017: Mesoblast Limited (ASX: MSB; Nasdaq: MESO) today announced that results from the randomized, placebo-controlled Phase 2 trial of its proprietary allogeneic mesenchymal precursor cells (MPCs) over 52 weeks in patients with biologic refractory rheumatoid arthritis (RA) were presented at the 2017 American College of Rheumatology (ACR) Annual Meeting held this week in San Diego, CA.

The abstract was submitted for peer review by the trial's lead investigators, Dr. Suzanne Kafaja, Assistant Clinical Professor, and Dr. Daniel E. Furst, Professor of Medicine in the Division of Rheumatology, Department of Medicine, at the University of California at Los Angeles (UCLA). The ACR Annual Meeting is attended by approximately 16,000 delegates from more than 100 countries.

Dr. Kafaja said: "The clinical responses in this Phase 2 trial, together with the safety profile, position MPC-300-IV to become an early treatment option in rheumatoid arthritis patients who are resistant to or intolerant of anti-TNF or other biologic agents."

The Phase 2 trial recruited a total of 48 patients with active RA who were on a stable regimen of methotrexate and had an inadequate prior response to at least one anti-TNF agent. Of the 48 patients, 30 (63%) had previously received 1-2 biologic agents. Patients were randomized to a single intravenous infusion of 1 million MPCs/kg (1M/kg, n=16), 2 million MPCs/kg (2M/kg, n=16) or placebo (n=16).

The primary objective of the study was to evaluate safety and tolerability of a single intravenous MPC infusion in these biologic refractory RA patients through a 12-week primary endpoint. Additional objectives were to evaluate clinical efficacy at the 12-week endpoint and to assess the durability of effects and safety profile through the full 52-week study.

Pre-specified efficacy endpoints included the following: ACR composite clinical response, which is an endpoint used in RA clinical trials to measure improvement in signs and symptoms of the disease in terms of 20%, 50% or 70% improvement from baseline; ACR-N which measures the mean or median magnitude of benefit using an ACR composite for a typical patient; the health assessment questionnaire-disability index (HAQ-DI), a standardized measure of functional status; the short-form health survey (SF-36), an assessment of health-related quality-of-life; and the measure of disease activity in 28 joints (DAS28) composite measurement of disease activity; no adjustment for multiplicity was performed as these efficacy endpoints were exploratory and the trial was not powered for efficacy.

Additionally, continuous variables ACR-N, HAQ-DI and DAS-28 were evaluated in a pre-specified manner since the use of endpoints sensitive to change provide better discriminatory power for dose-response assessment, in line with the FDA Guidance For Industry Rheumatoid Arthritis: Developing Drug Products For Treatment, May 2013.

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Analyses were performed for the whole study population and for the pre-specified exploratory subgroups based on whether the subjects had previously received 1-2 biologic agents or more than 2 biologic agents.

Key findings:

- Infusions were well-tolerated and there were no treatment-related serious adverse events reported during the 52-week period, with the safety profile over 52 weeks comparable among the placebo and two MPC treatment groups.
- A single intravenous MPC infusion in biologic refractory RA patients resulted in dose-related improvements in clinical symptoms, function, disease activity and patient-reported outcomes. Efficacy signals were observed for each of ACR 20/50/70, ACR-N, HAQ-DI, SF-36 and DAS-28 disease activity score.
- The 2 million MPC/kg dose showed the greatest overall treatment responses. Onset of treatment responses occurred as early as 4 weeks, peaked at 12 weeks, were maintained through 39 weeks, and waned by 52 weeks.
- Greatest benefits over 52 weeks were seen in patients who had failed less than 3 biologics (1-2 biologic sub-group) prior to MPC treatment, identifying this as a potentially optimal target population.
- The following statistically significant outcomes were observed over the 52-week study period:
 - At 4 weeks:
 - the MPC 2M/kg group had significantly better outcomes than placebo for improvement in pain, as measured by the ACR domain for subjective assessment of pain ($p=0.04$) and the SF-36 domain for bodily pain ($p=0.014$)
 - the MPC 2M/kg group had significantly better outcomes than placebo for improvement in physical function, as measured by the SF-36 physical component summary score ($p=0.015$) and physical function score ($p=0.002$), as well as the HAQ-DI mean change from baseline ($p=0.043$)
 - At 12 weeks:
 - the MPC 2M/kg group had significantly better outcomes than placebo for both the composite ACR70 response ($p=0.043$) and the overall ACR-N Area Under the Curve, AUC ($p=0.05$)
 - the MPC 2M/kg group had significantly better outcomes than placebo for the ACR domains of subject's assessment of pain ($p=0.039$) and subject's assessment of disease activity ($p=0.04$)
 - the MPC 2M/kg group had significantly better outcomes than placebo for proportion of patients achieving minimally important improvement in HAQ-DI function score ($p=0.003$) as well as the HAQ-DI mean change from baseline ($p=0.018$)
 - the MPC 2M/kg group had significantly better outcomes than placebo for several domains of the SF-36 composite score, including physical component summary score ($p=0.018$), bodily pain ($p=0.03$), and role physical ($p=0.014$)

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- At 12, 39 and 52 weeks:
 - the MPC 2M/kg group significantly outperformed placebo at every time point for ACR-N Area Under the Curve (AUC) (p=0.05 at 12 weeks, p=0.004 at 39 weeks, and p=0.008 at 52 weeks), indicating a robust, durable and consistent clinical effect of this MPC dose.

Mesoblast Chief Medical Officer Dr. Donna Skerrett said: “We are very pleased with the results of this Phase 2 trial, which identified a dose-related treatment effect, the earliest onset of the effect, and the durability from a single dose. Given the excellent safety profile, we intend to evaluate whether higher MPC doses can achieve even greater rates of low disease activity or remission within the first 12 weeks and beyond. We also plan to evaluate whether the observed durable treatment responses can be maintained for the longer term using repeat dose therapy.”

About Rheumatoid Arthritis

RA is a chronic autoimmune disease of unknown etiology, affecting approximately one percent of the global population. The disease is attributed to chronic inflammation affecting the synovial membrane of multiple joints, which eventually leads to cartilage and bone destruction. The health-related quality of life in patients with RA is significantly impaired by pain, fatigue, and decline in musculoskeletal function. RA is associated with an increased risk of cardiovascular disease and mortality.

Major advances in the treatment of RA using biologic agents have resulted in a \$19 billion global market in 2016, the majority of which is due to use of anti-TNF agents. The RA population resistant to anti-TNF agents, which constitutes about one-third of patients treated with anti-TNF agents, is the fastest growing branded market segment within the global RA biologics market, and is set to grow further as multiple anti-TNF biosimilars become available. There are approximately 6 million prevalent cases in the United States, Japan, and EU5, with 2.9 million in the United States alone in 2016.^{1,2}

Standard criteria established by the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) are used to assess the effectiveness of RA treatments. The ACR20/50/70 response is a composite measure based on achieving 20%/50%/70% improvement in tender joint counts (TJC) or swollen joint counts (SJC) plus improvement in three of the following:

- Patient global assessment
- Physician global assessment
- Patient pain assessment
- Physical function/disability questionnaire (HAQ-DI)
- Acute phase reactant (sedimentation rate or high-sensitivity C-reactive protein)

The patient and physician global assessments and pain assessment are measured using a visual analogue scale on a scale of 0-100. The ACR-N provides a single number that characterizes the percentage of improvement or deterioration from baseline that a patient has experienced in analogy to ACR20, ACR50, and ACR70 responses. The ACR-N is defined operationally as the lowest of 3 values (the percent change in the SJC, the percent change in the TJC, and the median of the other 5 measures in the ACR core data set). The ACR-N can be used to measure improvement at specific time points in a landmark analysis and expressed as the mean or median ACR-N achieved, or to compare the area under the curve (AUC) by patient over time. This approach may substantially increase the power to detect small differences between treatment arms.

The HAQ-DI assesses physical function in performing a variety of activities of daily living and yields a score ranging from 0-3 (lower is better). A reduction in the HAQ-DI score of -0.22 is the minimal clinically important difference. The DAS28 is another validated RA disease activity index based on a 28 joint count. The derived DAS28 scores are comprised of tender joint count; swollen joint count; acute phase reactant (hsCRP or ESR) and the subject’s global assessment of disease but do not include measures of pain or physical function. High disease activity is defined as DAS28 score >5.1; moderate disease activity is defined as DAS28 scores between 5.1-3.2; low disease activity and remission are defined as DAS28 scores of ≤3.2 and <2.6, respectively.

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In line with the FDA Guidance For Industry Rheumatoid Arthritis: Developing Drug Products for Treatment, May 2013, for dose-ranging studies the use of endpoints sensitive to change provide better discriminatory power for dose-response assessment. A clinical endpoint such as the ACR20 response criteria may not be optimal for this purpose, because it is a dichotomous endpoint, and using the proportion of responders in a small group of patients could be unreliable. Continuous variables such as DAS28, HAQ-DI, and ACR-N may be more sensitive to change and provide a more suitable alternative to ACR responder index. For continuous variables where changes from baseline are reported, the Least Squares of the Mean (ANCOVA) is utilized in order to adjust for baseline differences between groups.

1 GlobalData©: Rheumatoid Arthritis Global Forecast 2015-2025 0- January 2017

2 Decision Resources Rheumatoid Arthritis Dec 2015

About Mesoblast

Mesoblast Limited (ASX:MSB; Nasdaq:MESO) is a global leader in developing innovative cell-based medicines. The Company has leveraged its proprietary technology platform, which is based on specialized cells known as mesenchymal lineage adult stem cells, to establish a broad portfolio of late-stage product candidates. Mesoblast's allogeneic, 'off-the-shelf' cell product candidates target advanced stages of diseases with high, unmet medical needs including cardiovascular conditions, orthopedic disorders, immunologic and inflammatory disorders and oncologic/hematologic conditions.

Forward-Looking Statements

This announcement includes forward-looking statements that relate to future events or our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to differ materially from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. Forward-looking statements should not be read as a guarantee of future performance or results, and actual results may differ from the results anticipated in these forward-looking statements, and the differences may be material and adverse. Forward-looking statements include, but are not limited to, statements about: the initiation, timing, progress and results of Mesoblast's preclinical and clinical studies, and Mesoblast's research and development programs; Mesoblast's ability to advance product candidates into, enroll and successfully complete, clinical studies, including multi-national clinical trials; Mesoblast's ability to advance its manufacturing capabilities; the timing or likelihood of regulatory filings and approvals, manufacturing activities and product marketing activities, if any; the commercialization of Mesoblast's product candidates, if approved; regulatory or public perceptions and market acceptance surrounding the use of stem-cell based therapies; the potential for Mesoblast's product candidates, if any are approved, to be withdrawn from the market due to patient adverse events or deaths; the potential benefits of strategic collaboration agreements and Mesoblast's ability to enter into and maintain established strategic collaborations; Mesoblast's ability to establish and maintain intellectual property on its product candidates and Mesoblast's ability to successfully defend these in cases of alleged infringement; the scope of protection Mesoblast is able to establish and maintain for intellectual property rights covering its product candidates and technology; estimates of Mesoblast's expenses, future revenues, capital requirements and its needs for additional financing; Mesoblast's financial performance; developments relating to Mesoblast's competitors and industry; and the pricing and reimbursement of Mesoblast's product candidates, if approved. You should read this press release together with our risk factors, in our most recently filed reports with the SEC or on our website. Uncertainties and risks that may cause Mesoblast's actual results, performance or achievements to be materially different from those which may be expressed or implied by such statements, and accordingly, you should not place undue reliance on these forward-looking statements. We do not undertake any obligations to publicly update or revise any forward-looking statements, whether as a result of new information, future developments or otherwise.

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