mesoblast
the adult stem cell company

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ALLOGENEIC STEM CELLS EFFECTIVELY TREAT EYE DISEASES

Cells highly synergistic with anti-VEGF therapy; combination prevents blood vessel leakage and retinal detachment

KEY POINTS:

- Trial outcomes identify diabetic retinopathy and age-related macular degeneration, the leading causes of blindness in the developed world, as major new market opportunities for the Company's proprietary stem cell technology
- Single injection of proprietary allogeneic, or "off-the-shelf", adult stem cells were safe and highly synergistic with the United States Food and Drug Administration-approved anti-VEGF agent Lucentis for treatment of leaky blood vessels in the eyes of non-human primates
- Combining a single injection of the Company's stem cells with Lucentis resulted in a significantly superior outcome to Lucentis alone in preventing severe blood vessel leakage and preventing disease recurrence
- Combining a single injection of the Company's stem cells with Lucentis prevented the formation of new blood vessels and protected against retinal detachment
- Trial results form the basis of an IND submission to commence a Phase 2 clinical trial of the Company's stem cell therapy for eye diseases.

Melbourne, Australia; 10 July 2008: Australia's regenerative medicine company, Mesoblast Limited (ASX:MSB; USOTC: MBLTY), today announced highly significant preclinical trial results of the adult stem cell technology platform for the treatment of eye diseases associated with abnormal blood vessels. These diseases include diabetic retinopathy and age-related macular degeneration (AMD), the leading causes of blindness in the western world.

The current standard-of-care therapy for AMD is repeated eye injections using an anti-VEGF agent. Two of these agents, marketed under the names Lucentis and Macugen, have been approved by global regulatory bodies and distributed by Genentech, Novartis, and Pfizer. These agents are injected into the eye every 4-6 weeks on an ongoing basis as maintenance therapy to prevent reversal in visual improvement.

The results of the trial in 42 non-human primates, conducted in conjunction with Mesoblast's New York-based sister company Angioblast Systems Inc., indicate that combining an anti-VEGF agent with the company's proprietary stem cells may lead to improved vision and a reduction in the frequency of subsequent anti-VEGF injections into the eyes.

In the United States alone, there are about 1.5 million people suffering from the form of AMD associated with abnormal blood vessels, and over 200,000 new cases per year. An additional 500,000 diabetics suffer from macular oedema caused by abnormally leaky blood vessels, making these disease states a major market opportunity.

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The results of the preclinical trial showed that a single intra-ocular injection of the Company's proprietary allogeneic, or "off-the-shelf", adult stem cells was as effective at reducing blood vessel leakage after laser-induced damage as Genentech's Lucentis, the most effective FDA-approved anti-VEGF agent in use. The trial showed similar effectiveness with each of the three escalating cell doses used, without any significant cell-related adverse events.

More importantly, the trial showed that combining Lucentis with a single injection of the company's stem cells resulted in a highly synergistic, and significantly superior, outcome to Lucentis alone in preventing development of severe blood vessel leakage, preventing disease recurrence, reducing formation of new blood vessels and preventing retinal detachment.

"These are extremely exciting results which raise the prospect that our cells may be able to improve vision in conditions associated with abnormal blood vessels in the eye, while at the same time enabling physicians to reduce the frequency or dosage requirements of intra-ocular injections of anti-VEGF agents such as Lucentis," said Company founder and director, Professor Silviu Itescu.

The results of this primate study, together with earlier preclinical results, will form the basis of an Investigational New Drug (IND) submission to the FDA to commence a Phase 2 clinical trial of the Company's allogeneic stem cells in combination with an anti-VEGF agent, with the objective to show improvement in vision, long-term disease remission, and reduction in frequency of intra-ocular anti-VEGF maintenance injections.

Angioblast intends to form a strategic partnership with a major global health care company in order to rapidly commercialise its stem cell product for the treatment of eye diseases caused by abnormal blood vessels, such as diabetic retinopathy and AMD.

About Mesoblast
Mesoblast Limited (ASX:MSB; USOTC:MBLTY) is committed to the rapid commercialisation of a unique adult stem cell technology aimed at the regeneration and repair of bone and cartilage. Our focus is to progress through clinical trials and international regulatory processes necessary to commercialise the technology in as short a timeframe as possible. Mesoblast has the worldwide exclusive rights for a series of patents and technologies developed over more than 10 years and which relate to the identification, extraction and culture of adult Mesenchymal Precursor Cells (MPCs). The Company has also acquired 39% of Angioblast Systems Inc., an American company developing the platform MPC technology for the treatment of cardiovascular diseases including repair and regeneration of blood vessels and heart muscle. Mesoblast and Angioblast are jointly funding and progressing the core technology. Mesoblast's strategy is to maximise shareholder value through both corporate partnerships and the rapid and successful completion of clinical milestones.

For further information, please contact:

Julie Meldrum
Corporate Communications Director
Mesoblast Limited
T: + 61 (03) 9639 6036 M: +61 (0) 419 228 128
E: julie.meldrum@mesoblast.com

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Appendix

A preclinical trial was performed by Angioblast Systems Inc. in 42 non-human primates, 36 of whom received laser photocoagulation to the back of the eye to induce choroidal neovascularization. The study objectives were to evaluate the safety and effectiveness of a single intravitreal injection of the company's proprietary allogeneic Mesenchymal Precursor Cells (MPC) alone and in combination with a single intravitreal injection of the FDA-approved anti-VEGF agent Lucentis at 0.5mg. Fluorescein angiography was performed at days 15, 28, 35 and 42 to assess and grade the degree of vessel leakage following laser damage.

The trial results showed that each of the three escalating cell doses used were as effective as Lucentis in this model of blood vessel leakage after laser-induced damage, without any significant cell-related adverse events. However, the combination of Lucentis with a single injection of the company's stem cells was significantly superior in outcome to Lucentis alone in preventing development of severe blood vessel leakage, preventing progression of mild to severe vessel leakage, preventing disease recurrence, and preventing retinal detachment.

In comparison to Lucentis alone, combining the drug with a single injection of allogeneic stem cells reduced the mean blood vessel leakage score by approximately 25% by the trial's end at day 42 ($p=0.03$), **figure 1**. This was due to approximately a 50-90% reduction in the number of high-grade leaky vessels throughout the entire trial period and approximately a 29-42% increase in the number of low-grade leaky vessels, suggesting that the combination therapy prevented progression of low-grade to high-grade leaky vessels.

While Lucentis alone prevented the most severe (grade 4) vessel leakage compared with controls at day 15, after this timepoint disease recurrence was seen and sole Lucentis therapy was ineffective relative to controls beyond day 15, **figure 2**. In contrast, adding a single injection of allogeneic stem cells completely eliminated the most severe (grade 4) leakiness throughout the entire 42-day trial period, **figure 2,** indicating that the combination prevented disease recurrence.

Thirdly, adding a single injection of allogeneic stem cells to Lucentis significantly reduced the formation of abnormal new blood vessels. As shown in **figure 3,** the mean severity score for formation of a fibrovascular membrane was over two-fold higher in Lucentis treated eyes than in eyes treated with the combination of Lucentis and allogeneic MPC. ($p=0.001$).

Finally, in comparison to Lucentis alone the incidence of retinal detachment throughout the trial was reduced by approximately 85% when a single injection of the allogeneic stem cells was added. Whereas retinal detachment occurred in 37/72 (51%) laser-treated eyes without combination therapy, it was seen in only 1/12 (9%) eyes receiving the combination therapy ($p<0.01$), **figure 4**.

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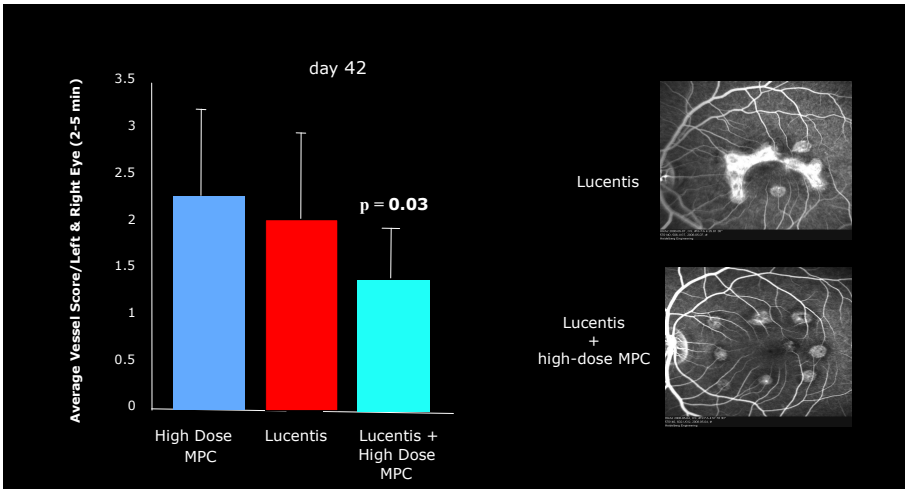

Figure 1. Allogeneic MPC are synergistic with anti-VEGF for preventing vessel leakage

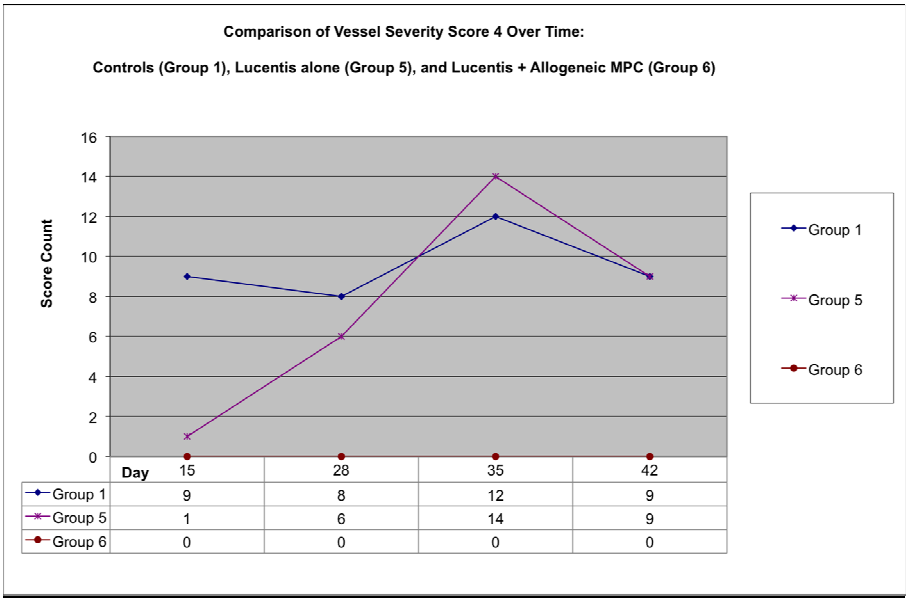

Figure 2.Combination of allogeneic MPC + anti-VEGF prevents Stage 4 disease relapse seen with anti-VEGF alone after day 15.

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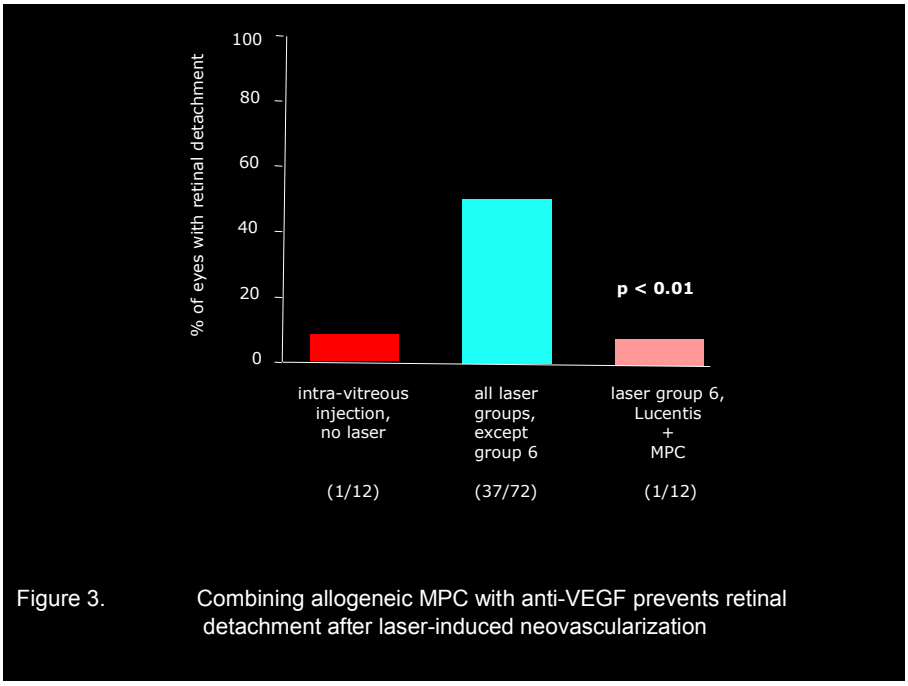

Figure 3. Combining allogeneic MPC with anti-VEGF prevents retinal detachment after laser-induced neovascularization

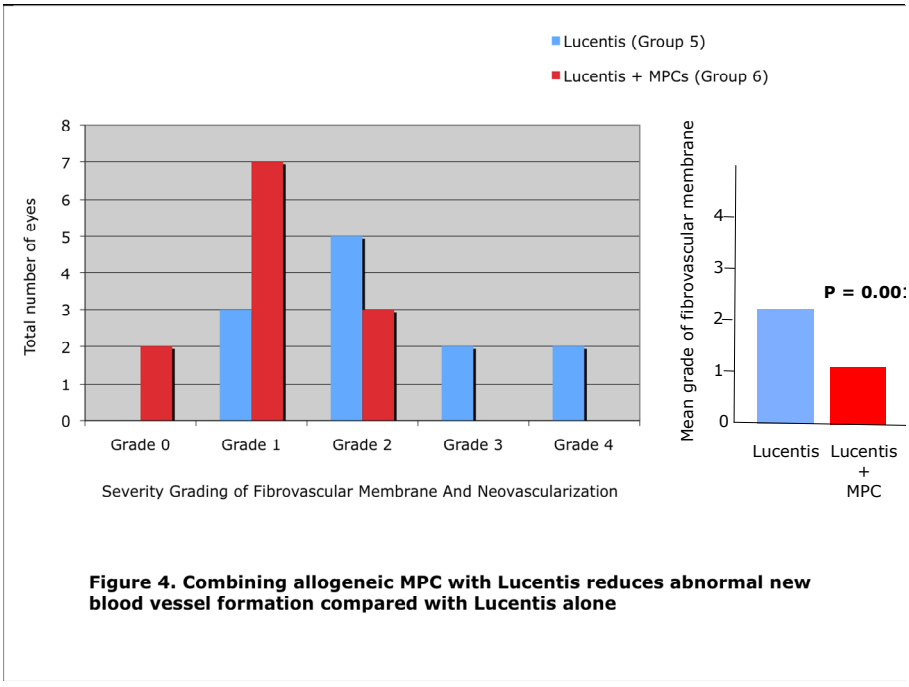

Figure 4. Combining allogeneic MPC with Lucentis reduces abnormal new blood vessel formation compared with Lucentis alone