MESOBLAST DISC REPAIR RESULTS HIGHLIGHTED AT KEY ORTHOPAEDIC CONFERENCE

Melbourne, Australia; 15 September 2009: Mesoblast’s successful preclinical disc repair trial was featured at the World Congress on Osteoarthritis held in Montréal, Canada, over the weekend.

More than 1,000 specialists in orthopaedics and rheumatology, as well as pain doctors and clinical scientists attended the prestigious congress conducted by the OsteoArthritis Research Society International (OARSI).

Internationally recognised cartilage expert, Professor Peter Ghosh, discussed how a single low-dose injection of Mesoblast’s allogeneic or "off-the-shelf" adult stem cells into severely damaged intervertebral discs resulted in dramatic reversal of the degenerative process, regrowth of disc cartilage, and sustained normalisation of disc pathology, anatomy and function. Professor Ghosh’s presentation is attached.

Mesoblast will continue to ensure that its achievements are highlighted and recognised at respected international conferences and meetings attended by key opinion leaders.

About Mesoblast
Mesoblast Limited (ASX:MSB) is committed to the development of novel treatments for orthopaedic conditions, including 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 relating to the identification, extraction and culture of adult Mesenchymal Precursor Cells (MPCs). The Company has acquired 38.4% of Angioblast Systems Inc., an American company developing the platform MPC technology for the treatment of cardiac, vascular and eye 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
W: www.mesoblast.com
INJECTION OF ALLOGENEIC IMMUNOSELECTED STRO-3+ MESENCHYMAL PRECURSOR STEM CELLS INTO LUMBAR INTERVERTEBRAL DISCS ATTENUATES DEGENERATION AND PROMOTES THE RESTORATION OF THE DISC EXTRACELLULAR MATRIX. AN EXPERIMENTAL STUDY IN AN OVINE MODEL OF DISC DEGENERATION

Peter Ghosh, Silviu Itescu, Robert Moore, Barrie Vernon-Roberts, Tony Goldschlager, Andrew Zannettino, Stan Gronthos, Chris Little, James Melrose, Cindy Shu

Presented at the World Congress on Osteoarthritis held in Montreal Canada September 10-14 2009.
Prevalence of Anatomical Sources of Chronic Back Pain

220 Million Adults

100 million Experience Low Back Pain

12.5 million Experience Chronic Low Back Pain

80% Neurological & Imaging Studies

20% Other

Discogenic Nerve Blocks & Discography

Discogenic 4 million
Facet Joint 3 million
Sacroiliac Joint 1.5 million
Other 1.5 million
Disc Herniation, Spondylolisthesis, DDD, Stenosis, VCF, Tumor 2.5 million

Downside of spinal fusion

Accelerated degeneration!
Sheep model to evaluate the reconstitution of degenerate discs by injections of MPC + hyaluronan (HA)

For personal use only

For personal use only

Un-injected control

Inject Chondroitinase-ABC (loss of GAGs)

Inject Chondroitinase-ABC (loss of GAGs)

Inject Chondroitinase-ABC (loss of GAGs)

3 MONTHS LATER
METHODS of ASSESSMENT

- X-RAY determination of disc height (DHI)
- MRI Scoring of Disc Degeneration
- Histopathology Scoring of disc sections
- Biochemical composition of Fixed disc tissues
MRI determination of Disc Degeneration

T2 Weighted MRI, sagittal midline view of normal ovine lumbar intervertebral disc

Structure component of Pfirrmann grading system, sagittal T2 Weighted MRI

Distinction between annulus fibrosus and nucleus pulposus component of Pfirrmann grading system, sagittal T2 Weighted MRI
DISC HISTOPATHOLOGICAL GRADE 1 (Normal)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Annulus fibrosus</th>
<th>Nucleus pulposus</th>
<th>Cartilage end-plate</th>
<th>Margins/subchondral bone</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Intact lamellae</td>
<td>Homogeneity</td>
<td>Uniform thickness</td>
<td>Even thickness of BEP</td>
</tr>
<tr>
<td></td>
<td>Narrow inter-lamellar matrix</td>
<td>Absence of clefting</td>
<td>Intact attachment to bone</td>
<td>Lamellar bone only</td>
</tr>
<tr>
<td></td>
<td>Intact annulus attachment</td>
<td></td>
<td>Uniform calcification &lt;1/5 depth</td>
<td>Distinct junction with</td>
</tr>
<tr>
<td></td>
<td>Vessels only in outer 1/3</td>
<td></td>
<td>Uniform cell distribution</td>
<td>CEP</td>
</tr>
</tbody>
</table>

For personal use only
DISC HISTOPATHOLOGICAL GRADE 2

Grade | Annulus fibrosus | Nucleus pulposus | Cartilage end-plate | Margins/subchondral bone
--- | --- | --- | --- | ---
2 | Minor lamellar splitting and disorganisation. Minor widening matrix. Minor disorganisation of attachment Rim lesion without reparative reaction | Minor clefting Minor cell necrosis Minor posterior displacement of annulus Minor chondrone formation | Minor cartilage thinning Small transverse fissures Irregular thickening calcified zone Few invading vascular channels Small chondrones | Slightly uneven BEP Schmorl’s nodes Minimal remodelling of BEP Small marginal osteophytes
RESULTS

• Disc Height Index (DHI)
Disc Height Index (DHI) 6 months after low dose Mesenchymal Precursor cells (0.5 million) were administered to discs degenerated by Chondroitinase-ABC treatment 3 months earlier

* p < 0.05 relative to control. # p < 0.05 relative to cABC+HA+MPC

By 6 months post treatment DHI for MPC injected discs higher than HA injected discs and equivalent to controls
RESULTS

• MRI Degeneration SCORES
Aggregate MRI Disc Degeneration Scores

# = significantly different from control p < 0.05  Ω = from MPC p< 0.05

At 3 and 6 months post treatment, aggregate MRI disc degeneration scores for MPC injected discs have normalised and are equivalent to controls.
MRI of an ovine spine 6 months after injecting 0.5 million MPC showing similar H$_2$O signal (white) to normal control ovine disc. Note: L4L5 & L5L6 low H$_2$O signal
RESULTS

• HISTOPATHOLOGY SCORES
Aggregate Histopathology Disc Degeneration Scores

# = significantly different from control p < 0.001;  Ω = from MPC p< 0.01

By 6 months post treatment, aggregate histopathological disc degeneration scores for MPC injected discs have normalised and are equivalent to controls.
Photomicrographs of Alcian Blue/Neutral Red stained histological sections of lumbar discs from Sheep #61 (6 mths low MPC). Note the loss of AF structure CEP disruption in discs injected with Chondroitinase ABC+ Hyaluronan (cABC+HA)(Right panel) compared to discs injected with cABC+MPC (Left Panel).
DISC HISTOPATHOLOGY

Photomicrographs of H&E stained histological sections of lumbar discs from Sheep #66 (6 mths low MPC) viewed under fluorescent light ($\lambda$ 540-580 nM) to show the collagen fibre assembly. Note the loss of structural integrity of nucleus pulposus (NP) and annulus fibrosus (AF) of degenerate disc which received Chondoitinase ABC alone compared to the degenerate disc injected with 0.5 million MPC.

Normal Control Disc  Degenerate Disc  Degenerate Disc + MPC

(AF histopath score = 1). Magnificationx20  (AF histopath score = 4). Magnificationx20  (AF histopath score = 1). Magnificationx20
CONCLUSION

Injection of low-dose MPC (0.5 x 10^6) into degenerate discs normalises disc structure, reverses abnormal histopathology, and restores disc height.