mesoblast

Newsletter

December 2018

Corporate Review from Chief Executive Dr Silviu Itescu

Mesoblast will enter 2019 with the most mature cell therapy product pipeline and technology platform in the regenerative medicine industry. Two commercial products have already been approved and marketed by the Company's licensees JCR Pharmaceuticals Co, Ltd. in Japan and Takeda Pharmaceutical Company in Europe. Mesoblast has one product candidate which has successfully completed Phase 3 and with near-term commercial potential in the United States (U.S.), another product candidate having achieved clinical outcomes in line with the U.S. Food and Drug Administration (FDA) guidance for a registrable clinical indication for market authorization, and two additional Phase 3 assets with blockbuster potential.

Mesoblast has recently entered into a strategic cardiovascular partnership for China with Tasly Pharmaceutical Group, China's leading cardiovascular company, and is in advanced and active discussions with a number of potential global commercialization partners to maximize the value proposition of each of our blockbuster cell therapy candidates.

Mesoblast's royalty income and milestone payments from licensees continues to grow, the Company has sufficient cash to achieve key commercial milestones, and access to additional non-dilutive sources of capital from strategic financial institutions whose extensive due diligence provides further third party validation of the strength of the product portfolio and patent estate.

Below is a summary of the current status of the product portfolio and the developments expected to take place in 2019.

Substantial Commercialization Opportunities

Mesoblast's proprietary immunoselected and culture-expanded allogeneic mesenchymal precursor cells (MPCs) are a homogeneous, well characterized, and highly reproducible cell population that are manufactured to industrial scale for commercial purposes. They express an array of surface receptors that bind pro-inflammatory cytokines and, when placed into a pro-inflammatory microenvironment, release factors that switch off production of these cytokines. Their immunomodulatory mechanism of action makes MPCs uniquely suited to target resistant diseases where inflammation plays a central role.

Acute Graft Versus Host Disease, a Life-threatening Inflammatory Condition

In Q1 2019, the Company plans to initiate the FDA process of filing a Biologics License Application (BLA) for market authorization of remestemcel-L in the U.S., where there are no approved therapies for steroid-refractory acute Graft Versus Host Disease (aGVHD). Underpinning Mesoblast's confidence in the U.S. market access plan is the Japan experience, where Mesoblast's licensee, JCR Pharmaceuticals, markets TEMCELL®[1] HS Inj. for children and adults with aGVHD.

Importantly, TEMCELL has achieved substantial adoption rates in just over 2.5 years, helping inform the view of the product value proposition potential in the U.S. market. With an experienced commercial leadership in place, Mesoblast is establishing a focused sales team that will target the principal U.S. transplant centers, and will be in place on FDA approval to ensure a successful product launch.

Inflammation Due to Left Ventricular Assist Device Implants in End-stage Heart Failure Patients

In the first half of 2019, Mesoblast plans to meet with the FDA to discuss a potential approval pathway following the clinically meaningful outcomes of reduction in major gastrointestinal (GI) bleeding and related hospitalizations seen in the U.S. National Institutes of Health (NIH)-sponsored Phase 2 trial of MPC-150-IM (Revascor) in patients with end-stage heart failure and a left ventricular assist device (LVAD). This potentially life-threatening complication is the most common non-surgical complication in LVAD recipients and occurs in up to 40% of patients.

In the 159-patient trial, a single intra-cardiac injection of Revascor resulted in a 76% reduction in major GI bleeding episodes and in 65% reduction in associated hospitalization events. Reduction in GI bleeding and associated hospitalizations were the basis of the Regenerative Medicine Advanced Therapy (RMAT) designation granted in December 2017 by the FDA for use of Revascor in LVAD patients based on concordant data from the earlier 30-patient Pilot Trial. In a subsequent meeting in 2018, the FDA advised Mesoblast that reduction in major GI bleeding in LVAD patients is considered a clinically meaningful outcome by the FDA and an acceptable endpoint for product approval.

In end-stage heart failure, where intra-cardiac inflammation is greatest, putting a foreign object (the LVAD) in contact with the failing left ventricle results in further activation of intra-cardiac inflammation, which exacerbates pre-existing vascular dysfunction in the peripheral organs. The GI blood vessels respond to vascular dysfunction and reduced flow by generation of abnormal thin-walled, leaky capillaries (angiodysplasia). These pre-dispose LVAD patients to massive and life-threatening GI bleeding.

Mesoblast believes that reduction in major GI bleeding episodes by Revascor is due to reduction in intra-cardiac inflammation and the associated vascular dysfunction in peripheral organs, including the GI vessels. If this is correct, this will have significant read-through to the Phase 3 trial in patients with class II/III heart failure where intra-cardiac inflammation and peripheral vascular dysfunction are thought to directly result in recurrent hospitalizations and terminal cardiac events.

Phase 3 Trial in Moderate to Advanced Chronic Heart Failure, a Progressive Disease of Cardiac Inflammation

Mesoblast expects to complete patient recruitment in the Phase 3 trial evaluating Revascor in patients with moderate-to-severe advanced chronic heart failure very shortly. In the U.S. alone, there are more than 1.3 million patients with New York Heart Association (NYHA) class III chronic heart failure who have high rates of morbidity and mortality despite existing therapies. The major unmet medical need in these patients represents a potential multi-billion dollar market opportunity for Mesoblast.

The primary endpoint for this Phase 3 trial is the ability of Revascor to reduce recurrent non-fatal heart failure-related major adverse cardiac events (HF-MACE) in patients with left ventricular dysfunction. The key secondary endpoint is to delay or prevent terminal cardiac events (TCEs), defined as death, left ventricular assist device implantation, or heart transplant.

It is important to note that in the Phase 2 LVAD trial patients with ischemic cause of their heart failure showed the greatest benefits after being treated with Revascor and these patients closely resemble the majority of patients enrolled in the ongoing Phase 3 trial of patients with moderate to advanced heart failure. If the mechanism of action by which Revascor improved GI bleeding is indeed reduction of intra-cardiac inflammation and reversal of impaired functioning of blood vessels (endothelial dysfunction), a known primary cause of morbidity, exercise intolerance, and mortality in heart failure and a proven mechanism of action for many drugs in early heart failure, one would expect to see a reduction in HF-MACE and mortality in this Phase 3 trial.

Chronic Low Back Pain Due to Inflammatory Degenerative Disc Disease

In the U.S., the declared opioid public health emergency and significant associated mortality has brought additional attention to Mesoblast's product candidate, MPC-06-ID, with the Phase 3 trial completing enrollment of 404 patients in 2018. More than half of the prescriptions for opioids are for people seeking relief from chronic low back pain. There is a desperate need for a therapy that can offer both a durable reduction in pain and improvement in function without the risk of opioid addiction.

Underpinning Mesoblast's confidence that MPC-06-ID may meet this medical need are the Phase 2 data outcomes that supported the ongoing Phase 3 trial which showed that a single intra-discal injection of MPC-06-ID alleviated pain and improved function for up to three years in patients whose symptoms were not adequately treated with current standard of care therapies.

The patient population suffering from chronic low back pain due to intervertebral disease is estimated at more than 3.2 million patients in the U.S. alone. Mesoblast's objective is to select and secure the ideal strategic partner to maximize the value creation potential inherent in MPC-06-ID.

Upcoming Milestones

Remestemcel-L for Acute Graft Versus Host Disease

- FDA meetings and BLA filing (Early CY19)

Revascor for End-Stage Heart Failure

- Meet with FDA to discuss the clinically meaningful GI bleeding Phase 2 trial data for potential BLA filing (1H CY19)

Phase 3 Events-driven Trial in Advanced Heart Failure

- Complete recruitment (Q4 CY18/Q1 CY19)
- Cardiovascular partner Tasly Pharmaceuticals to meet with National Medical Products Administration to discuss the regulatory approval pathway in China (Q1 CY19)
- Establish global partnership

MPC-06-ID for Chronic Low Back Pain

- Establish global partnership

About Mesoblast

Mesoblast Limited (Nasdaq:MESO; ASX:MSB) is a world leader in developing allogeneic (off-the-shelf) cellular medicines. The Company has leveraged its proprietary technology platform to establish a broad portfolio of late-stage product candidates with three product candidates in Phase 3 trials – acute graft versus host disease, chronic heart failure and chronic low back pain due to degenerative disc disease. Through a proprietary process, Mesoblast selects rare mesenchymal lineage precursor and stem cells from the bone marrow of healthy adults and creates master cell banks, which can be industrially expanded to produce thousands of doses from each donor that meet stringent release criteria, have lot to lot consistency, and can be used off-the-shelf without the need for tissue matching. Mesoblast has facilities in Melbourne, New York, Singapore and Texas and is listed on the Australian Securities Exchange (MSB) and on the Nasdaq (MESO). www.mesoblast.com

1. TEMCELL® HS Inj. is the registered trademark of JCR Pharmaceuticals Co. Ltd.

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 timing, progress and results of Mesoblast's preclinical and clinical studies; Mesoblast's ability to advance product candidates into, enroll and successfully complete, clinical studies; the timing or likelihood of regulatory filings and approvals; 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.