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MESOBLAST PROVIDES UPDATE ON CLINICAL PROGRAMS OF PROCHYMAL® FOR CROHN'S DISEASE AND ACUTE GRAFT VERSUS HOST DISEASE

New York, USA; 29 April and Melbourne, Australia; 30 April 2014: Regenerative medicine company Mesoblast Limited (ASX:MSB; USOTC:MBLTY) today provided an update on its clinical programs using the product Prochymal®, which was acquired as part of the entire culture-expanded mesenchymal stem cell (MSC) business of Osiris Therapeutics (NASDAQ:OSIR) by the Mesoblast Group.

A key aspect of the strategic rationale for the acquisition of the culture-expanded MSC assets was the potential for early and significant revenue streams using Prochymal®, the world's first approved allogeneic stem cell therapeutic and the only allogeneic stem cell therapeutic designated by the United States Food and Drug Administration (FDA) as both an Orphan Drug and Fast Track product. Major drivers for this transaction were Mesoblast's evaluation of the use of Prochymal® for inflammatory diseases of the bowel, including patients with Crohn's disease who have failed other biologic agents and patients with potentially life-threatening Graft Versus Host Disease (GVHD) involving the gut and liver after a bone marrow transplant.

Mesoblast will meet with the United States Food and Drug Administration (FDA) shortly to discuss potential pathways for accelerated Prochymal® product approvals in the United States for the treatment of steroid-refractory acute GVHD, a disease with inflammatory etiology and a significant gastrointestinal component. In Japan, Mesoblast collaborator, JCR Pharmaceuticals, is expanding its manufacturing facility in preparation for its commercial launch of its MSC product, JR-031. This product was granted JR-031 orphan drug status in December 2013 and as a result it will be subject to an expedited review. JCR has confirmed it will launch its product as scheduled in 2015.

A recently-completed internal review of the Crohn's disease program reinforced Mesoblast's intention to complete the ongoing Phase 3 trial in adult patients with Crohn's Disease refractory to treatment with steroids, classic immunosuppressives and biologic therapy. The Company expects to have a readout by the end of the year on whether the primary endpoint of day 28 remission in biologic-refractory patients has been achieved, whether there is evidence of efficacy in high-risk groups such as those with fistulizing disease, and whether repeat dosing can result in longer-term maintenance of effect.

As a result of the acquisition of the culture-expanded mesenchymal stem cell (MSC) assets, Mesoblast expects during 2014 to have active products based on proprietary Mesenchymal Precursor and Stem Cell technologies in Phase 3 clinical trials in all four core major therapeutic areas of focus: cardiovascular medicine (congestive heart failure), inflammatory/immune diseases (Crohn's Disease), orthopedics (spinal disc disease) and oncology (acute Graft Versus Host Disease, and cord blood expansion in bone marrow transplantation).

Prochymal® for Crohn's Disease

Prochymal® is an intravenous preparation of MSCs using MSCs isolated from the bone marrow of healthy young adult donors. They are grown in culture and expanded, permitting large-scale production with potentially thousands of doses produced from a single donation.

Prochymal® has demonstrated immunomodulatory properties to regulate T-cell mediated inflammatory responses by inhibiting T-cell proliferation and down-regulating the production of the pro-inflammatory

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cytokines, tumor necrosis factor-alpha (TNF-alpha) and interferon gamma.More critically, mesenchymal lineage stem cells have been shown to be capable of effective down-regulation of Th17 cells, reduction in IL-17 levels, and induction of FoxP3 regulatory T cells. These inflammatory pathways are central to the pathogenesis of Crohn's Disease and inflammatory bowel diseases.

In 2006, Osiris Therapeutics announced positive results from a pilot Phase 1/2 study.using Prochymal® for the treatment of patients with moderate to severe Crohn's disease who had failed to respond to standard treatments such as steroids and infliximab (Remicade(R)). The trial was a prospective, randomized, open label trial, conducted at 4 leading centers in the United States. Patients with moderate to severe Crohn's disease, defined as having a Crohn's Disease Activity Index (CDAI) of at least 220, who had previously failed treatment with steroids and other immunosuppressive agents, were given two infusions of Prochymal® seven days apart.

Patients entering this study had suffered from Crohn's Disease for an average of 14.2 years, and 80% of the patients required prior surgical intervention to treat their Crohn's disease. In the study, every patient evaluated reported a reduction in CDAI after receiving two infusions of Prochymal®. Mean Inflammatory Bowel Disease Questionnaire (IBDQ) scores improved significantly from baseline to day 28 (113 to 146, p=0.008). There was a statistically significant decrease in mean CDAI scores of 105 points by day 28 from 341 to 236 (p=0.004). There were no infusional toxicities, nor were there any treatment-related severe adverse events.

On the basis of these positive results, an adaptive Phase 3 trial was initiated to evaluate two dose regimens of Prochymal® in a multi-centered, double-blind, randomized, placebo-controlled trial of patients with moderate to severe Crohn's Disease who are resistant to steroids, immunosuppressants and a biologic therapy. The primary endpoint is the proportion of patients experiencing disease remission within 28 days of treatment with Prochymal®, defined as an absolute CDAI score below 150, compared to those patients receiving placebo.

The clinical program consisted of two linked trials in patients who had failed other available treatments for the disease - one aimed at inducing remission (Protocol 603) and one reviewing impact in the maintenance phase (Protocol 610/611). The program is evaluating patients with severe Crohn's disease not responsive to treatment with steroids, immunomodulators(azathioprine, 6-mercaptopurine, and methotrexate), and biologic agents (Remicade®, Humira®, and Cimzia®. There were no differences in average CDAI scores at entry, which exceeded 350 in all arms prior to treatment, indicating the patients had a very debilitating disease state.

Two interim analyses have been performed in this trial to date, including a pre-determined futility analysis which resulted in temporary cessation of recruitment. The trial remained blinded to permit an interim analysis of all 207 patients enrolled in the study to that stage, of which 148 patients had completed the 28 day primary endpoint assessment. The results showed that the effect size, or difference between the Prochymal® and placebo response rates, of one of the two active dose arms of Prochymal® was consistent with the original statistical assumptions of the protocol and was significantly outperforming placebo.

Following discussions with the FDA about the results of the interim analysis for futility, enrollment resumed in 2010 and continues with the best performing Prochymal® dose arm and the placebo arm, according to the pre-specified adaptive trial design. A new follow-on retreatment trial (Protocol 611) continues to enroll.

About Crohn's Disease
Crohn's Disease is a chronic inflammatory disorder of the gastrointestinal tract, characterized by periods of remission and symptomatic relapse. The cause of this life-long debilitating disease which results in a poor quality of life is unknown. There is some evidence to suggest a genetic predisposition leading to abnormal intestinal T lymphocyte immune response to environmental and dietary agents, particularly to enteric bacteria. The burden of Crohn's disease is substantial, accounting for more than 1 million cases in the seven major pharmaceutical markets in 2012.

According to GlobalData, the United States has the highest prevalence of the disease, with more than 500,000 people afflicted and approximately 20,000 new cases diagnosed each year. GlobalData has estimated that the global CD therapeutics market was worth $4.4 billion in 2012 and is forecast to reach $6.8 billion in 2022, at a compounded annual growth rate of 4.5% per year. Growth is driven by the continued uptake and earlier use of tumor necrosis factor inhibitors and the introduction of new, premium-priced biologics and novel mechanisms of action beginning in 2014.

Although immunosuppressants and tumor necrosis factor-alpha (TNF-alpha) inhibitors are effective maintenance therapies for moderate to severe disease, they seldom result in persistent remission. A treatment to induce rapid remission is highly needed, particularly in high-risk patients such as those with biologic-resistant disease and those with fistulas, a devastating complication of Crohn's Disease which occurs in 20-25% of patients and often requires invasive surgical procedures.

Prochymal® for Graft Versus Host Disease (GVHD)

Prochymal® is being used for the investigational treatment of steroid-refractory acute GVHD – a near-term revenue opportunity based on potential for product launches in major first-world markets.

Prochymal® has already received conditional approval in Canada and New Zealand for the treatment of children with acute GvHD, and is available in the United States under an Expanded Access Program for treatment of acute GVHD in children. Prochymal® has also generated promising Phase 3 data in adults with acute GvHD at high risk of death due to inflammatory gut or liver complications.

Mesoblast intends to seek FDA marketing approval for use in both pediatric and adult patient populations. Additionally, JCR Pharmaceuticals in Japan is aiming for product launch of its MSC-based product for steroid refractory GVHD in children and adults in Japan next year.

About Graft Versus Host Disease
Acute GVHD is a potentially life threatening complication that arises in approximately 50% of all patients who receive a hematopoietic stem cell transplant (HSCT). According to the Center for International Blood and Marrow Transplant Research, there are approximately 25,000 HSCTs globally per year. Nearly 50% of these develop acute GVHD and a fraction of these will progress to severe GVHD which is steroid refractory. In patients that fail to respond to steroids, mortality can reach 85%. There are no approved therapies for acute GVHD. Standard of care is corticosteroids as a first line agent.

Allogeneic HSCTs are used for the treatment of diseases including hematological malignancies, certain forms of anemia, and immunological deficiencies. The transplant is derived from donated bone marrow, cord blood, or peripheral blood. GVHD occurs when immune cells in the donated cell population attack the recipient cells because the recipient cells are seen as "foreign". Organs that are mainly affected by the immunological attack are the gastrointestinal (GI) tract (upper and lower), skin, and liver.

A peer-reviewed article in the November 2013 scientific journal Biology of Blood and Marrow Transplantation reported that use of Prochymal® resulted in a significant survival benefit among responding pediatric bone marrow transplant recipients with refractory acute GVHD. Of the 75 children with acute severe GVHD, 61% responded to Prochymal® and 76% of these were alive at day 100. The study was the largest prospective study of its kind in pediatric patients with severe, multi-line refractory acute GVHD.

Acute GVHD with liver or low gut involvement is a life-threatening complication of HSCT with a poor prognosis. A Phase 3 trial showed significant improvements in response rates in the difficult to treat liver and lower gut GVHD subgroup. In patients with liver GVHD, Prochymal® improved response by 76% versus 47% in controls (p=0.026, n=61) and durable complete response in 29% versus 5% (p=0.046).

GlobalData estimates that the global GVHD therapeutics market was worth $261.6m in 2010 and is forecast to grow at a Compound Annual Growth Rate (CAGR) of 11.3% to reach $615.1m by 2018.

Mesoblast Limited
Mesoblast Limited (ASX:MSB; USOTC:MBLTY) is a world leader in the development of biologic products for the broad field of regenerative medicine. The Company's proprietary technologies include its highly purified, immunoselected Stro-1/Stro-3 positive Mesenchymal Precursor Cells (MPCs), culture-expanded Mesenchymal Stem Cells (MSCs), Dental Pulp Stem Cells (DPSCs), and expanded Hematopoietic Stem Cells (HSCs). Mesoblast's protein technologies are based on factors derived from its proprietary cellular platforms, including Stromal Derived Factor-1 (SDF-1). Mesoblast's allogeneic or 'off-the-shelf' regenerative medicine products are being developed for the treatment of conditions with significant unmet medical needs. Product development focus is in four major and distinct areas - systemic diseases with an underlying inflammatory and immunologic etiology; cardiac and vascular diseases; orthopedic diseases of the spine; and improving outcomes of bone marrow transplantation associated with oncology or genetic conditions. www.mesoblast.com

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