



CELLTHERAPY
REGENERATIVE MEDICINE FOR LIFE

Press release (24th June 2015)

Cell Therapy Ltd announces continuing 100% MACE-free survival after two years average follow up in the Heartcel™ clinical trial in advanced heart failure patients at high risk of incomplete revascularization

Cardiff, UK, June 24 2015 – Cell Therapy Ltd (“CTL”), a development stage pharmaceutical company with a portfolio of allogeneic regenerative medicines in clinical trials, reported average 24-month (19-29 months) MACE-free survival for all patients in the Heartcel™ trial studying myocardial regeneration. This means that in these patients, suffering from advanced heart failure, all are still alive after an average of two years vs. up to an expected 70% annual mortality rate, and none have suffered cardiac events such as heart attack or stroke.

Today, at the International Society of Stem Cell Research (ISSCR) Annual Conference in Stockholm, CTL reported follow-on data from the Heartcel™ Phase II clinical trial:

- MACE-free survival in all patients at an average of 24-months (19-29 months)
- 70% Quality of life improvement measured by MLHF

The Heartcel™ Phase II clinical trial studied patients at high risk of incomplete re-vascularization (ICR) undergoing Coronary Artery Bypass Graft (CABG), and investigated a new regenerative cell type, the iMP cell (immuno-modulatory cell), as an adjuvant to mitigate the mortality and morbidity associated with ICR. Heartcel™ has been designed as a cardiac specific cell therapy, and is the first to demonstrate heart regeneration in humans.

At the original 12-month follow up the trial met all study endpoints reporting statistical and clinically significant results: Major Adverse Cardiac Event (MACE)-free survival in all patients, improved Left Ventricular Ejection Fraction (LVEF) of 30%, reduced Left Ventricle (LV) scar size of 40% and improved Quality of Life of 50%.

Today CTL reported average 24-month (19-29 month) follow up results for MACE-free survival and quality of life improvement, unprecedented data for a trial of this kind for patients with advanced heart failure. (See Abstract 2 in notes below).

The iMP cell is a novel regenerative cell discovered by Nobel Prize winner Sir Martin Evans, CTL's Chief Scientific Officer. The iMP cell was presented at the British Society of Cell and Gene Therapy Annual Conference, on 11 June 2015 and forms a novel and distinct family of mesodermal progenitor cell. iMP cells express cardiac-specific and immuno-modulatory phenotype and form the basis of allogeneic or "off the shelf" cellular regenerative medicines. (See Abstract 1 in notes below).

CTL's proprietary platform technology has generated a portfolio of allogeneic tissue-specific regenerative cellular medicines that are in late stage clinical trials including Heartcel™, and cellular therapies for orthopaedic and dermatological conditions.

Professor Stephen Westaby, John Radcliffe Hospital, Oxford, the principal investigator for the Heartcel™ trial, said: *"In the Heartcel™ clinical trial, all patients survived and were free of major adverse events at 19-29 months. SPECT imaging demonstrated the change in hypo-kinetic tissue to functional myocardial at the site of injection. There was an average 30% improvement in heart function, 40% scar size reduction and 50% quality of life improvement. While the study cohort was small, the results were highly clinically relevant and statistically significant."*

Ajan Reginald, Chief Executive Officer of Cell Therapy Ltd., commented: *"Rapid translation of in-house research into meaningful clinic benefit for patients in the Heartcel™ trial exemplifies our mission to develop game-changing regenerative medicines. We delighted all the Heartcel™ patients remain alive and free of major adverse cardiac events for an average of 24 months. Tendoncel™ and Myocardion™ also entering late-stage trials, expands CTL's regenerative medicine pipeline into Tendon repair and moderate heart failure. Regenerative medicine is a disruptive technology and CTL's seems well placed to be at the forefront of this new class of medicines."*

Notes to editors

Abstract 1

"Isolation of Immunomodulatory Progenitor Cells of Mesodermal Lineage"

Authors: Sabena Sultan, Nancy Piouka, Ajan Reginald and Martin Evans

Abstract: Immuno-modulatory progenitor cells or iMP cells, are a novel and distinct mesodermal progenitor cell that *in vitro* exhibit an immune-modulatory (MIC A/B, CD178, CD289, CD99 and EGF-R) and cardiac specific phenotype (CD181, CD126, CD304, CD363 and CD182). iMP cells are not mesenchymal stromal cells (MSC) as defined by the International Society for Cellular Therapy.

Allogeneic iMP cells were used in a Phase II (Heartcel) clinical trial of advanced heart failure patients diagnosed to be at high risk of incomplete re-vascularization (ICR) with coronary artery bypass graft (CABG) surgery. ICR affects ~37% of all CABG patients and is associated with a ~40% increase in mortality and ~49% increase in major adverse cardiac events (MACE). The Heartcel trial completed a mean duration of 24 months post treatment follow up of all patients in Q2 2015 (19 to 29 months range).

Concomitantly with CABG, iMP cells were injected intra-myocardially into the areas of hypo-kinetic myocardium that bypass grafting would not re-vascularise. SPECT imaging was used pre-operatively to identify iMP injection sites and post-operatively to monitor / measure change in viability and contractility.

The study met all endpoints: 100% 1 year MACE-Free survival in all patients, which persists to date

(19-29 months). Clinically and statistically significant mean improvement in left ventricular ejection fraction (LVEF) (30%), LV scar size (40%) and quality of life (50%). The results suggest the potential for *in situ* myocardial regeneration to mitigate the effect of incomplete revascularization.

CD45. Up-regulation of these markers has been reported to show greater functional properties such as immune-modulation and proliferation.

Abstract 2

“Immunomodulatory progenitor cells: a novel allogeneic therapy for patients with ischaemic cardiomyopathy undergoing coronary artery bypass grafting”

Authors: S. Sultan, A. Reginald, M. Evans, K. P. Antonitsis, S. Westaby and K. Anastasiadis

Immuno-modulatory progenitor cells or iMP cells, are a novel and distinct mesodermal progenitor cell that do not meet the International Society for Cellular Therapy mesenchymal stromal cell (MSC) definition but do exhibit an immune-modulatory (MIC A/B, CD178, CD289, CD99 and EGF-R) and cardiac specific phenotype (CD181, CD126, CD304, CD363 and CD182). Thus allogeneic iMP cells were used in a phase II (Heartcel) clinical trial of advanced heart failure patients incompletely re-vascularized (ICR) by Coronary Artery Bypass Graft (CABG). ICR affects ~37% of CABG patients and is associated with a ~40% increase in mortality and ~49% increase in major adverse cardiac events (MACE). The Heartcel trial completed in Q4 2014.

Concomitant with CABG, iMP cells were injected intra-myocardially into the areas of hypo-kinetic myocardium bypass would not re-vascularise. SPECT imaging was used pre-operatively to identify these iMP injection sites and post-operatively to monitor / measure change in viability and contractility. The study met all endpoints: 100% 1 year MACE-Free survival in all patients that persists to date (19-29 months). Clinically and statistically significant mean improvement in LVEF (30%), LV scar size (40%) and quality of life (50%). The results suggest the potential for *in situ* myocardial regeneration to mitigate the effect of incomplete revascularization in heart failure.

About Cell Therapy Ltd

Cell Therapy Limited (CTL) is a Cardiff-based biotechnology focused on the discovery and development of regenerative medicines focused on areas of high unmet patient need. CTL was founded in 2009 by Nobel Laureate Professor Martin Evans and Ajan Reginald, ex-Global Head of Emerging Technologies at Roche, and the team includes world-class scientists and clinicians led by experienced management and an active Board and Scientific advisory committee of world experts.