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Cardiovascular Disease

Cardiovascular Disease and Regenerative Medicine

A heart attack, known formally as myocardial infarction (MI), occurs when blood supply to the heart is interrupted, causing heart cells to die from lack of oxygen. Several companies are developing regenerative medicine technologies to rescue, replace and help repair these damaged heart tissues and revascularize heart tissue in and around areas of infarct. Several ARM members are looking into using single or mixed populations of cells, both autologous (self to self) and allogeneic (other to self) to target the effects of cardiovascular disease. Other organizations are developing advanced biologics, gene therapies and small molecule approaches that focus on the cell cycle or other pathways which may allow the regeneration of lost heart cells and tissue.

Aastrom is developing an autologous ixmyelocel-T cell therapy, a patient specific, expanded multicellular therapy that selectively amplifies mesenchymal cells, monocytes and macrophages. They are currently conducting Phase 2 trials for dilated cardiomyopathy.

Amorcyte (a NeoStem company) is developing an autologous, bone marrow derived, CD34 positive selected stem cell product, AMR-001, to treat damaged heart tissue following acute myocardial infarction. A Phase 2 trial has been initiated to evaluate the potential of AMR-001 to improve perfusion, preserve cardiac function and improve clinical outcomes.

Athersys Inc.'s allogeneic product, MultiStem, is a therapy that consists of a special class of stem cells obtained from bone marrow and other non-embryonic tissue sources. One year follow-up data from a Phase 1 study confirmed and extended the previous clinical observations at four months, showing a consistent safety

Overview

Cardiovascular disease (CVD) refers to a broad range of diseases that affect the cardiovascular system, which includes the heart and blood vessels. CVD is highly prevalent among the general population and represents the leading causes of death and disability in the United States. CVDs include coronary heart disease, cerebrovascular disease, peripheral arterial disease, rheumatic heart disease, congenital heart disease, deep vein thrombosis and pulmonary embolism. The most recent studies completed by the American Heart Association (AHA) estimate that over one-third of Americans currently suffer from some form of CVD, and that 40,400,000 of those are over the age of 60.¹

Often there are no symptoms of underlying disease to the heart and blood vessels until the acute events or symptoms of a heart attack. Patients with these conditions and diseases frequently need life-changing treatments, ranging from daily medications to surgical interventions such as pacemakers, stents, angioplasty or heart transplants.² Patients with heart disease, especially those who have survived acute events, often suffer from long-term disabilities, loss of productivity and diminished quality of life.

profile, and meaningful improvement in multiple clinical parameters.

Capricor is focusing on using cells from the heart tissue including concentrated cardiac stem and other supporting cells. Capricor successfully completed a Phase 1 clinical trial of their cardio-sphere-derived autologous stem cell product to reverse ventricular dysfunction. A second clinical study began in the fall of 2012, this time using allogeneic heart stem cells to potentially achieve myocardial regeneration.

Cytomedix is developing ALD-201, a population of autologous pluripotent stem cells isolated from the patients' bone marrow using Cytomedix's proprietary Bright Cell technology. In a Phase 1 ischemic heart failure clinical trial, ALD-201 was well-tolerated and the study provided initial evidence of improved blood flow and improved clinical status.

Cytori Therapeutics' cell-based technology includes adult stem cells, endothelial progenitor cells, leucocytes, endothelial cells and vascular smooth muscle cells found in adipose tissue taken from the patient's own body fat (known as adipose-derived stem and regenerative cells or ADRCs) to target cardiovascular disease. They are currently conducting clinical trials to evaluate the use of these ADRCs in cardiovascular disease, after pre-clinical trials showed promising signs of restoration of heart function following the use of ADRCs.

Juventas Therapeutics' biologic product, JVS-100, utilizes stromal cell-derived factor-1 (SDF-1), a cytokine belonging to the chemokine family, which is shown to protect and repair tissue following ischemic injury by recruiting the body's own stem cells to the injury site to prevent cell death and promote angiogenesis. JVS-100 has an ongoing Phase 2 clinical trial to test efficacy in heart failure.

Mesoblast's technology platform is based on the use of their allogeneic mesenchymal precursor cells (MPCs) to repair tissue damaged in cardiovascular disease and induce sustainable large blood vessel formation. The company is currently working with partner Teva and the FDA on the trial design for a Phase 3 study in congestive heart failure.

Beyond cell therapy, companies such as **VentriNova** are developing small molecules and gene therapies that stimulate heart cells to re-enter the cell cycle, therefore regenerating lost heart tissue. VentriNova's lead product targets the Cyclin-A2 gene to induce cellular proliferation of cardiomyocyte, and is in the preclinical stage of development. The company is hoping to receive IND approval to begin clinical trials in 2013.

Clinical progress in any of these areas could have a meaningful impact on improving clinical outcomes, cost of care and quality of life for those patients disabled by heart disease.

Cardiovascular Disease: Economic Impact



\$71.2 Billion

2005 total inpatient hospital cost for CDV care; approximately 25% of the total cost of hospital care in the United States.³



\$316 Billion

Overall medical cost of significant medical intervention over time, for healthcare services, medications and lost productivity of those afflicted with CDV.

¹ *Heart Disease and Stroke Statistics—2012 Update: A Report from the American Heart Association* available at circ.ahajournals.org/content/early/2011/12/15/CIR.0b013e31823ac046.full.pdf (published online in *Circulation: Journal of the American Heart Association*, December 15, 2011)

² Mayo Clinic, "Heart Disease: Treatments and Drugs," Mayo Clinic website, www.mayoclinic.com/health/heart-disease/DS01120/DSECTION=treatments-and-drugs

³ *Heart Disease and Stroke Statistics—2008 Update: A Report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee* available at circ.ahajournals.org/content/117/4/e25.short (published online in *Circulation: Journal of the American Heart Association*, December 17, 2007)