**CardiAMP™ Heart Failure Trial**

**Randomized Controlled Pivotal Trial of Autologous Bone Marrow Mononuclear Cells Using CardiAMP Cell Therapy in Patients with Post Myocardial Infarction Heart Failure**

**Hypothesis**
Demonstrate treatment superiority in subjects treated using the CardiAMP cell therapy (Treatment Group) showing a statistically significant improvement in Six Minute Walk Distance (6MWD) compared to subjects undergoing a sham procedure, after 12M follow-up.

Secondary hierarchical endpoints include overall survival (non-inferiority), freedom from MACE (non-inferiority), Minnesota Living with Heart Failure Questionnaire, time to first MACE, and survival.

**Study Design**
Prospective, multi-center, randomized (3 Treatment: 2 Sham Control), sham- controlled, patient and evaluator blinded comparing treatment with the CardiAMP cell therapy to a sham treatment in 256 patients with post myocardial infarction heart failure.

**Primary Endpoint**
Comparison of change in distance walked in 6-minutes between the subjects treated with the CardiAMP cell therapy and subjects undergoing a sham control procedure, at 12-months follow-up.

**Secondary Hierarchical Endpoints**
1. Overall survival at 12-months, as a non-inferiority outcome
2. Freedom from Major Adverse Cardiovascular Events at 12-months, as a non-inferiority outcome
3. Change in quality of life as measured by Minnesota Living with Heart Failure at 12-months, as a superiority outcome
4. Time to first MACE at 12-months, as a superiority outcome
5. Overall survival at 12-months, as a superiority outcome

**Inclusion Criteria**
- Greater than (-) 21 and less than (-) 80 years of age
- New York Heart Association (NYHA) Class II or III
- Diagnosis of chronic ischemic left ventricular dysfunction secondary to myocardial infarction (MI) as defined by:
  - Presence of MI (≥ 6M)
  - Treatment with thrombolytic therapy, coronary artery bypass surgery, or percutaneous coronary revascularization
  - Ejection fraction ≤ 35% and ≤ 40% by 2D Echocardiogram and not in the setting of a recent ischemic event
- On stable evidence based medical and device therapy for heart failure or post-infarction left ventricular dysfunction, per the 2013 ACC/AHA Heart Failure guidelines, for at least 3M prior to randomization
  - Pharmacological Therapy (as appropriate)
  - Cardiac Resynchronization Therapy (CRT)
  - Cardiac Resynchronization Therapy Defibrillator (CRT-D)
  - CRT or CRT-D implanted - 3M before randomization
  - Eligible or anticipated to be eligible for CRT or CRT-D ≥ 6M
  - Cell Potency Assay Score of 3, as determined by the Cell Analysis Core Lab results
- Provide written informed consent

**Exclusion Criteria**
- Acute coronary syndrome within 3M
- History of bronchoplastic lung disease, orthopedic, muscular, or neurologic conditions that could limit the ability to perform the 6MWD Test
- Not a candidate for cardiac catheterization
- Require coronary artery revascularization. Patients who require or undergo revascularization procedures would undergo these procedures a minimum of 3M in advance of randomization in this study. Note that patients who later develop a need for revascularization following enrollment will be submitted for this therapy without delay
- Left Ventricular Thrombus, as detected by echocardiography
- Severe mitral regurgitation, as measured by echocardiography
- Severe mitral or tricuspid insufficiency or aortic insufficiency (≤ 2) as assessed by echocardiography
- Presence of aortic stenosis (Sawa > 2 equivalent to an orifice area of 1.5cm2 or less)
- Have a mechanical aortic valve or heart constrictive defect
- Have evidence of a life-threatening arrhythmia
- Have complete heart block or QRS interval >550 ms on screening 12lead ECG
- ACD furing in the past 60 days prior to the procedure
- Have peripheral arterial disease involving the aorta or iliofemoral system that impacts the feasibility or safety of the study intervention
- Have a non-cardiac condition that limits lifespan to ≤ 1 year
- Have a history of drug or alcohol abuse within the past 24M
- Be currently participating (or participated within the past 30 days) in an investigational therapeutic or device trial or participated in the treatment arm of a gene or stem cell therapy trial within the previous 12M
- Unwilling or unable to comply with follow-up

**Optional Roll-in Phases**
- Maximum of 10 subjects

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**References**
- Loffredo FS. Stem cell derived cell therapy stimulates endogenous cardiomyocyte progenitors and promotes cardiac repair. Cell Stem Cell. 2011 April 8; 8:589-598.