

The Current State of Chronic Heart Failure

CHRONIC HEART FAILURE OVERVIEW

Chronic heart failure (CHF) is a chronic condition affecting 5.7 million people in the United States alone¹ and a leading cause of death, accounting for greater than 55,000 deaths per year in the United States². Chronic heart failure is a condition when the heart becomes unable to pump enough blood to meet the needs of the body. The heart becomes weakened and pumping function is severely decreased. Over time, multiple negative effects occur from the heart becoming overworked such as high blood pressure, narrowed arteries, fatigue, shortness of breath due to blood accumulating in the chest and fluid accumulation around the abdomen and feet, and a loss of mobility.³

CURRENT TREATMENTS

Although CHF can be treated with good results, the condition cannot be reversed. The current standard of care for the disease involve a combination of devices, ACE inhibitors, beta blockers, angiotensin receptor blockers and/or diuretics, yet these drugs have many limitations. Many cardiologists have expressed a need for drugs having a new mechanism of action that does not only treat the effects of heart failure, but to potentially reverse gradual damage to the heart and heart muscle itself.

NEUCARDIN™ — TREATING THE HEART OF THE DISEASE

After nearly two decades of no new breakthroughs in CHF therapies, Neucardin™ (Neuregulin-1) features a brand new mechanism of action that repairs heart muscle structure and improves diastolic and systolic pumping function. Zensun has filed a New Drug Application (NDA) in China to obtain accelerated market approval and anticipates to conduct a Phase 3 trial in the US following discussion with FDA.

Neucardin™ works by binding to receptors on the outside of cardiac muscle cells. Once bound, many key molecules that are involved in cardiac muscle cell structure and contractile function restoration are activated in the cell, strengthening the heart and optimizing pumping function. Neucardin™ has the potential to increase heart function in the acute setting as well as restore blood flow, reduce heart muscle damage (reverse ventricular remodeling), improve exercise capacity and reduce all-cause mortality in patients living with CHF.

CLINICAL STUDIES

Over 1,200 people were involved in clinical trials of Neucardin™ in China, Australia and the United States. Phase 2 clinical studies in all countries demonstrated that Neucardin™ increases heart function in people with heart failure for up to 3 months following treatment, reduces left ventricular end systolic volume, and has a significant survival benefit compared with placebo in an enriched heart failure population 1 year after treatment. Side effects of Neucardin™ are minimal, but include gastrointestinal disorders such as nausea, vomiting and diarrhea. Some subjects also suffer from headaches and other nervous system disorders. Importantly, side effects are alleviated after cessation of Neucardin™ administration.

¹ Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, Borden WB, et al. Heart disease and stroke statistics—2012 update: a report from the American Heart Association. *Circulation*. 2012;125(1):e2-220.

² Kochanek KD, Xu JQ, Murphy SL, Miniño AM, Kung HC. Deaths: Final Data for 2009. *National vital statistics reports*. 2011;60(3).

³ Mayo Clinic. (2011, December 23). Heart failure. Retrieved from <http://www.mayoclinic.com/health/heart-failure/DS00061>

A table summarizing how current therapies work compared with Neucardin™

DRUG	MECHANISM OF ACTION
Angiotensin-converting enzyme (ACE) inhibitors	ACE inhibitors are vasodilators, widening blood vessels to lower blood pressure, improve blood flow and decrease the workload on the heart.
Angiotensin II receptor blockers	Angiotensin II receptor blockers help relax the blood vessels, lowering blood pressure and making it easier for the heart to pump blood.
Beta blockers	Beta blockers slow the heart rate and reduce blood pressure, while limiting some of the damage to the heart.
Diuretics	Diuretics cause urination and keep fluid from collecting in the body. They also work to decrease fluid in the lungs, improving breathing.
Neucardin™ (in development)	Neucardin™ (Neuregulin-1) repairs heart muscle and improves Ca ⁺ uptake for better contraction and relaxation (pumping) efficiency.

Four completed Phase 2 clinical studies in both China and Australia demonstrate that a 10 day intravenous infusion of Neucardin™ for 10 hours a day to patients with New York Heart Association (NYHA) class II-III heart failure increased cardiac function, reversed ventricular remodeling (left ventricular end systolic volume and end diastolic volume), and reduced circulating NT-proBNP levels for up to three months after administration (all independent long-term predictors of mortality and morbidity). A survival trial in China showed that Neucardin™ reduced death from CHF by 60 % compared with placebo in patients that have NYHA class III heart failure or have blood levels of NT-proBNP that are less than 4000 fmol/ml before treatment.

