TREATMENT OF SYSTOLIC DYSFUNCTION

CROSS-REFERENCE TO RELATED APPLICATIONS

[001] This application claims priority from United States Provisional Patent Application 62/849,936, filed May 19, 2019, and United States Provisional Patent Application 62/852,739, filed May 24, 2019. The disclosures of these priority applications are incorporated by reference herein in their entirety.

BACKGROUND OF THE INVENTION

[002] Heart failure (HF) is a global pandemic affecting about 26 million people worldwide. It is the most rapidly growing cardiovascular condition globally, with substantial morbidity, mortality, and cost burden to healthcare systems (Ponikowski et al., *ESC Heart Fail*. (2014) 1(1):4-25; Savarese and Lund, *Card Fail Rev*. (2017) 3(1):7-11). HF is the most common cause of hospitalization in patients older than 65 years (Ponikowski, *supra*; Savarese and Lund, *supra*; and Shah et al., *J Am Coll Cardiol*. (2017) 70(20):2476-86). The five-year mortality rate after HF hospitalization is about 42%, comparable to many cancers (Benjamin et al., *Circulation* (2019) 139:e56–e528).

[003] Heart failure is a clinical syndrome in which a patient's heart is unable to provide an adequate supply of blood flow to the body to meet the body's metabolic needs. For some patients with heart failure, the heart has difficulty pumping enough blood to support other organs in the body. Other patients may have a hardening and stiffening of the heart muscle itself, which blocks or reduces blood flow to the heart. Those two conditions result in inadequate blood circulation to the body and congestion of the lungs. Heart failure can affect the right or left side of the heart, or both sides at the same time. It can be either an acute (short-term) or chronic (ongoing) condition. Heart failure can be referred to as congestive heart failure when fluid builds up in various parts of the body. Symptoms of heart failure include, but are not limited to, excessive fatigue, sudden weight gain, a loss of appetite, persistent coughing, irregular pulse, chest discomfort, angina, heart palpitations, edema (e.g., swelling of the lungs, arms, legs,