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Contact:

Rebekah Handley
Human BioMolecular Research Institute
San Diego, CA 92121
(858) 458-9305
RHandley@hbri.org

Heather Buschman, Ph.D.
Sanford-Burnham Medical Research Institute
La Jolla, CA 92037
(858) 795-5343
hbuschman@sanfordburnham.org

Scientists Use Dynamic Medicinal Chemistry to Help Cardiac Regeneration

San Diego, Calif. (January 16, 2012) – Scientists at the Human BioMolecular Research Institute (HBRI) in San Diego, CA, and Sanford-Burnham Medical Research Institute (Sanford-Burnham) in La Jolla, CA and ChemRegen, Inc., a San Diego for-profit company focused on developing small-molecule regenerative medicines for human diseases have reported on a new set of small molecules helpful in human cardiomyocyte formation using inhibition of a biochemical signaling pathway called Wnt. The Wnt signaling pathway is a key mediator of cellular development and stem cell differentiation. A paper published online* in the *Journal of Medicinal Chemistry* reports a new class of small molecules that work as Wnt inhibitors that can be used to increase cardiogenesis from human stem cells.

In the United States, curing heart disease is a major unmet medical need. Of the 300,000 individuals suffering from heart disease that need a heart transplant, less than 1 percent will receive one. During a heart attack, heart tissue is irreparably damaged and scar tissue can form around the heart that may eventually lead to heart failure. If regenerative medicine could provide a way to regenerate damaged tissue, it would be a significant benefit to millions of people who are currently living with heart disease. Another application of the technology is to generate large numbers of cardiomyocyte cells for transplantation purposes.

Scientists at HBRI and Sanford-Burnham, in collaboration with ChemRegen, chemically synthesized and tested a large number of small molecules that induce cardiogenic differentiation. In this series of small molecules, they found that the potency of Wnt inhibition highly correlates with the ability of the molecules to cause cardiogenesis. Some of the most promising small molecules identified may be useful for making large numbers of human cardiomyocytes. The most potent Wnt inhibitors discovered have also increased our understanding of the biology underlying the process. One potent small molecule was identified that inhibited transduction of the canonical Wnt response within the cell, showing that Wnt inhibition alone is sufficient for deriving cardiomyocytes from human embryonic stem cells (hESCs) originating from mesoderm cells. This may have practical applications for making large numbers of cells for utility in a biotechnology sense from hESCs because there are currently few ways to readily make large numbers of human heart cells.

The dynamic medicinal chemistry research approach used in these studies represents an exciting new paradigm to discover therapies for heart disease, and may result in drug leads for human cardiac regeneration or practical approaches for producing large numbers of human cardiomyocytes.

About HBRI: The Human BioMolecular Research Institute is a non-profit research institute conducting basic research focused on unlocking biological and chemical principles related to diseases of the human brain, cardiovascular disease and cancer. The Institute conducts fundamental studies of central nervous system disorders, heart disease and cancer including stem cell approaches and translates findings into new drug development to address human illness. In addition, the institute promotes scientific learning through community service and public access by disseminating information and sharing research with collaborators, colleagues and the public. For more information, visit www.HBRI.org.

About Sanford-Burnham: Sanford-Burnham Medical Research Institute is dedicated to discovering the fundamental molecular causes of disease and devising the innovative therapies of tomorrow. Sanford-Burnham, with operations in California and Florida, is one of the fastest-

growing research institutes in the country. The Institute ranks among the top independent research institutions nationally for NIH grant funding and among the top organizations worldwide for its research impact. From 1999 – 2009, Sanford-Burnham ranked #1 worldwide among all types of organizations in the fields of biology and biochemistry for the impact of its research publications, defined by citations per publication, according to the Institute for Scientific Information. According to government statistics, Sanford-Burnham ranks #2 nationally among all organizations in capital efficiency of generating patents, defined by the number of patents issued per grant dollars awarded.

Sanford-Burnham utilizes a unique, collaborative approach to medical research and has established major research programs in cancer, neurodegeneration, diabetes, and infectious, inflammatory, and childhood diseases. The Institute is especially known for its world-class capabilities in stem cell research and drug discovery technologies. Sanford-Burnham is a nonprofit public benefit corporation. For more information, please visit www.sanfordburnham.org.

About ChemRegen Inc.: ChemRegen is a for-profit company doing research directed at identifying small molecules of use for addressing human diseases. The approach is to develop regenerative medicines to work in conjunction with human embryonic stem cells to cure major human diseases including heart disease, cancer and other diseases. For more information, visit www.ChemRegen.com.

*M Lanier, D Schade, E Willems, M Tsuda, S Spiering, J Kalisiak, M Mercola and JR Cashman. (2012) Wnt Inhibition Correlates with Human Embryonic Stem Cell Cardiomyogenesis: A Structure−Activity Relationship Study Based on Inhibitors for the Wnt Response. *J. Med Chem.* January 12 (Epub ahead of print).