



## VistaGen Therapeutics and Duke University Publish Results on Production of Functional 3D Human Heart Tissue

May 7, 2013

### Living Heart Muscle Derived From Human Stem Cells Is Closest Man-Made Approximation of Natural Human Heart Muscle to Date

SOUTH SAN FRANCISCO, CA -- (Marketwired) -- 05/07/13 -- VistaGen Therapeutics, Inc. (OTCQB: VSTA), a biotechnology company applying stem cell technology for drug rescue, predictive toxicology and drug metabolism assays, announced that its high-quality, human pluripotent stem cell-derived cardiomyocytes (heart cells) were used by collaboration partner Duke University to grow a revolutionary three-dimensional (3D) human heart muscle. An abstract of the original research article published in *Biomaterials*, an international journal covering the science and clinical application of biomaterials, can be found online at: <http://www.sciencedirect.com/science/article/pii/S0142961213004705>.

Researchers at Duke University combined VistaGen's human stem cell-derived heart cells with innovative tissue engineering and cardiac electrophysiology technologies to grow what is being called a "heart patch," which mimics the natural functions of native human heart tissue. This heart patch technology is being developed to aid in a better understanding of the biology critical to cardiac tissue engineering, for applications in regenerative cell therapy for heart disease, and as predictive in vitro assays for drug rescue and development.

H. Ralph Snodgrass, PhD, VistaGen's President and Chief Scientific Officer, stated, "The developed contractile forces and other functional properties of these cardiac tissues are remarkable and are significantly higher than any previous reports. The achievement of successfully growing a human heart muscle from cardiomyocytes derived from human pluripotent stem cells not only expands the scope of our drug rescue capabilities, but also reflects the advanced nature and potential of our collaboration with the skilled biomedical engineers at Duke Medical Center."

"VistaGen's human cardiomyocytes produced engineered cardiac tissues that exhibited structural and functional properties superior to those previously reported," said Dr. Nenad Bursac, Associate Professor in the Departments of Cardiology and Biomedical Engineering at Duke University. "This is the closest man-made approximation of natural human heart muscle to date."

Achieving this capability represents a significant breakthrough in heart cell-based therapies and in testing new medicines for potential heart toxicity and potential therapeutic benefits impacting heart disease. The following are among several key development points from the study:

- The optimized 3D environment of a cardiac tissue patch yields advanced levels of structural and functional maturation of human cardiomyocytes that produce expected responses to drugs;
- Human cardiomyocyte maturation in an optimized 3D patch environment is enhanced relative to that found in industry standard 2D cultures;
- No genetic modifications were used to produce, purify, or mature cardiomyocytes suggesting potential for future therapeutic applications;
- Cardiac tissue patches generated using VistaGen's cardiomyocytes exhibited 2.2-180 fold higher contractile force generation compared to previous studies;
- Based on a force per cardiomyocyte metric, cardiac tissue engineering methodology that used VistaGen's cardiomyocytes exhibited 4-700-fold higher efficiency than previously reported; and
- Cardiac tissue patches generated using VistaGen's cardiomyocytes exhibited velocities of electrical signal propagation 5-fold higher compared to previous reports in human engineered cardiac tissues.

The original research article also will be published in print in *Biomaterials*.

#### *About VistaGen Therapeutics*

VistaGen is a biotechnology company applying human pluripotent stem cell technology for drug rescue, predictive toxicology and drug metabolism screening. VistaGen's drug rescue activities combine its human pluripotent stem cell technology platform, Human Clinical Trials in a Test Tube™, with modern medicinal chemistry to generate novel, safer chemical variants (Drug Rescue Variants) of once-promising small molecule drug candidates. These are drug candidates discontinued by pharmaceutical companies, the U.S. National Institutes of Health (NIH) or university laboratories, after substantial investment in discovery and development, due to heart or liver toxicity or metabolism issues. VistaGen uses its pluripotent stem cell technology to generate early indications, or predictions, of how humans will ultimately respond to new drug candidates before they are ever tested in humans, bringing human biology to the front end of the drug development process.

VistaGen's small molecule prodrug candidate, AV-101, has completed Phase 1 development for treatment of neuropathic pain. Neuropathic pain, a serious and chronic condition causing pain after an injury or disease of the peripheral or central nervous system, affects millions of people worldwide.

Visit VistaGen at <http://www.VistaGen.com>, follow VistaGen at <http://www.twitter.com/VistaGen> or view VistaGen's Facebook page at <https://www.facebook.com/VistaGen>.

#### *About Dr. Bursac, Duke University*

Dr. Bursac, Associate Professor in the Department of Biomedical Engineering and Faculty of Cardiology at Duke University, is a leader in the field of

cardiac tissue engineering and cell-based therapies in which different cells, either alone or in combination with therapeutic molecules or biomaterials, can be transplanted into the human body to restore function of damaged or diseased organs. Dr. Bursac's research has additional applications in the fields of cardiac electrophysiology and development of microphysiological systems for in vitro toxicology studies and drug screening. Over the last five years, Dr. Bursac's lab has developed and validated novel bioengineered model systems and experimental tools that are providing a more detailed understanding of normal and abnormal heart and skeletal muscle development and function, the intricate processes of myogenesis and the potential of stem cell-based tissue engineering therapies for the treatment of different heart and skeletal muscle diseases, cardiac infarction and arrhythmias.

*Cautionary Statement Regarding Forward-Looking Statements*

The statements in this press release that are not historical facts may constitute forward-looking statements that are based on current expectations and are subject to risks and uncertainties that could cause actual future results to differ materially from those expressed or implied by such statements. Those risks and uncertainties include, but are not limited to, risks related to the success of VistaGen's stem cell technology-based drug rescue, predictive toxicology and metabolism screening activities, further development of stem cell-based bioassay systems, and potentially improved cell therapies, for human blood system disorders or other diseases or conditions, clinical development and commercialization of AV-101 for neuropathic pain or any other disease or condition, its ability to enter into strategic predictive toxicology, metabolism screening, drug rescue and/or drug discovery, development and commercialization collaborations and/or licensing arrangements with respect to one or more drug rescue variants, regenerative cell therapies or AV-101, risks and uncertainties relating to the availability of substantial additional capital to support its research, drug rescue, development and commercialization activities, and the success of its research and development plans and strategies, including those plans and strategies related to any drug rescue variant or cell therapy identified and developed by VistaGen, or AV-101. These and other risks and uncertainties are identified and described in more detail in VistaGen's filings with the Securities and Exchange Commission (SEC). These filings are available on the SEC's website at [www.sec.gov](http://www.sec.gov). VistaGen undertakes no obligation to publicly update or revise any forward-looking statements.

For more information:

Shawn K. Singh, J.D.

Chief Executive Officer

VistaGen Therapeutics, Inc.

[www.VistaGen.com](http://www.VistaGen.com)

650-244-9990 x224

[Investor.Relations@VistaGen.com](mailto:Investor.Relations@VistaGen.com)

Mission Investor Relations

IR Communications

Atlanta, Georgia

[www.MissionIR.com](http://www.MissionIR.com)

404-941-8975

[Investors@MissionIR.com](mailto:Investors@MissionIR.com)

Source: VistaGen Therapeutics, Inc.

Released May 7, 2013