aTyr, The Hong Kong University of Science and Technology, The Scripps Research Institute and Stanford University Join in the Discovery of a New Class of Human Proteins

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Publication in Science Unveils Novel, Diverse and Separate Biological Functions That Can Be Harnessed Therapeutically to Mediate a Wide Range of Human Disease

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SAN DIEGO and HONG KONG

SAN DIEGO and HONG KONG, July 17, 2014 /PRNewswire/ -- aTyr Pharma, an innovative rare disease therapeutics enterprise, and its subsidiary in Hong Kong, Pangu Biopharma (aTyr), announced the discovery of a new class of human proteins with therapeutic relevance for a wide range of diseases. The findings unveiled today in a publication in *Science* further supplies the basis for aTyr's ongoing clinical studies in the areas of rare diseases and represents an entirely new and unmined area of human biology for therapeutics.

Scientists from aTyr, The Hong Kong University of Science and Technology (HKUST), The Scripps Research Institute (TSRI) and Stanford University reported for the first time that an entire enzymatic gene family can generate novel splice variants that possess non-enzymatic, extracellular activities. Using deep sequencing, mass spectroscopy, protein purification techniques and parallel cell-based assays, the team found nearly 250 new proteins with previously unidentified activities spanning from stem cell biology to immunology. The vast majority of these novel proteins, called Physiocrines, lacked catalytic domains from the gene family, thereby creating new cellular functions.

The aminoacyl tRNA synthetase gene family is required for life as an essential component of protein synthesis, from bacteria to fruit flies to rodents to humans. Over the course of evolution, new roles developed for this gene family, which are outside protein synthesis, and which reveal a deep new layer of previously unknown and unexplored biology.

"We believe this work will enable us to harness the regulating power of these proteins to heal disease states where human physiology is dysregulated," said John Mendlein, Ph.D., CEO and Executive Chairman of aTyr and co-author of the study. "During evolution this ancient gene family played a critical role in cellular life - catalysis of protein synthesis. Our international effort to understand this enzymatic gene family now leads us to a completely new horizon for all of human physiology - the alternate use of a gene family for non-catalytic regulation of basic physiological processes of humans, such as stem cell biology, immune pathways, vascularization and metabolism. We feel very privileged to have completed the work with our colleagues from HKUST, Stanford University and TSRI and the visionary influence of Dr. Paul Schimmel, Ernest and Jean Hahn Professor of Molecular Biology and Chemistry at The Scripps Research Institute (California and Florida) who also holds an appointment at the Institute for Advance Study (IAS) at The Hong Kong University of Science and Technology."

Professor Mingjie Zhang, IAS Senior Fellow and Kerry Holdings Professor of Science, Division of Life Sciences, who is also a co-author, said, "This breakthrough finding uncovers a vast new area of biology and provides opportunities to develop protein-based therapeutics. This work marks a successful collaboration between scientists at HKUST, TSRI, aTyr Pharma and Pangu Biopharma. It serves as a wonderful example showing close connections between basic research and biotechnology therapeutic development."

The paper, "Human tRNA Synthetase Catalytic Nulls with Diverse Functions," was published in the July 18, 2014 issue of *Science*, doi: 10.1126/science.1252943.

About Physiocrines
Among their various homeostatic functions, some Physiocrines act as extracellular signaling molecules to orchestrate immuno-homeostasis in response to stress and other physiological changes. Physiocrines comprise naturally occurring proteins derived from tRNA synthetases that play fundamental roles in the function of human physiology and restoring pathophysiological states to a healthier state. aTyr is currently focused on Physiocrines that act as endogenous modulators of our immune and regenerative systems. Physiocrines offer the opportunity for modulating biological pathways through newly discovered naturally occurring mechanisms, many of which may provide multiple therapeutic advantages, including improved efficacy and reduced side effect profiles compared to many existing therapeutics.

About aTyr Pharma
aTyr Pharma is developing a pipeline of therapeutic products based on Physiocrine biology. To protect these products aTyr built a dominant intellectual property estate comprising over 200 patent applications and patents. aTyr's key programs are currently focused on rare disorders where the immune system is imbalanced. These diseases are serious, potentially life-threatening rare diseases, for which there are currently no effective, safe, long-term treatments. The privately held biotech was founded by The Scripps Research Institute Professor Paul Schimmel, a leading aminoacyl tRNA synthetase scientist, and is backed by top life sciences investors Alta Partners, Cardinal Partners, Domain Associates and Polaris Partners. For more

information, please visit http://www.atyrpharma.com.

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