



Proteostasis Therapeutics Licenses Novel Protein Clearance Targets, Compounds from Harvard University

- Technologies Broaden the Drug Discovery Platform for Developing Disease-modifying Therapeutics to Treat Neurodegenerative and Orphan Diseases -

April 26, 2011, Cambridge, Mass. - [Proteostasis Therapeutics](#) announced today that it has acquired two exclusive licenses from Harvard University to technologies for enhancing the activity of a key cellular protein clearance mechanism, the ubiquitin-proteasome pathway. The technologies, which include novel targets and small molecule compounds, contribute to the company's innovative approaches to developing therapeutics for neurodegenerative diseases, such as Alzheimer's, Parkinson's, and Huntington's, as well as orphan diseases, such as cystic fibrosis and lysosomal storage diseases. Financial terms were not disclosed.

The licenses cover technologies that arose from research in the laboratories of three leading researchers, all of Harvard Medical School, of the biology of the ubiquitin-proteasome pathway: [Daniel Finley, Ph.D.](#), Professor of Cell Biology; [Randall King, Ph.D., M.D.](#), Associate Professor of Cell Biology; and [Alfred Goldberg, Ph.D.](#), Professor of Cell Biology.

"Protein clearance mechanisms, along with cellular pathways governing protein folding and trafficking, are the cornerstones of the Proteostasis Network that maintain proper protein function," said Peter Reinhart, Ph.D., President and Chief Scientific Officer of Proteostasis. "Proteostasis is building a novel drug discovery platform for discovering and developing disease-modifying therapeutics that regulate the Proteostasis Network. These licenses from Harvard provide us with multiple novel targets and compounds that complement our existing programs, which are focused on other pathways within the Proteostasis Network." Dr. Reinhart noted that the company also has pre-development programs aimed at altering folding and trafficking pathways to treat a number of diseases, including Parkinson's, Alzheimer's, Huntington's, and cystic fibrosis.

The ubiquitin-proteasome pathway is an essential mechanism for protein clearance that regulates many activities within cells. Through this pathway, proteins are first tagged by ubiquitin molecules and then degraded in the proteasome complex. Drs. Finley and King have identified a cellular enzyme, Usp14, which removes ubiquitin tags, inhibiting the breakdown of ubiquitin-targeted proteins. They further identified small molecule inhibitors of Usp14 that accelerate the degradation of several neurodegenerative disease-related proteins, such as tau, TDP-43 and ataxin-3, which are linked to Alzheimer's disease, frontotemporal dementia, amyotrophic lateral sclerosis and polyglutamine

expansion diseases such as Huntington's disease. Their research was published in September 2010 in the journal *Nature*. Research by Drs. Goldberg and David Smith has led to the discovery of novel targets and small molecules that affect the proteasome's gating mechanism. The development of compounds that regulate proteasome gating may result in therapeutics that increase the protein degradation capacity of disease-relevant proteins, such as tau and α -synuclein, which have been linked to Alzheimer's disease and Parkinson's disease.

"We're delighted to place Harvard-originated technology with a strong licensing partner such as Proteostasis," said Isaac T. Kohlberg, Harvard's Chief Technology Development Officer and head of its Office of Technology Development. "It provides yet another positive linkage between leaders in academia and industry to progress potentially groundbreaking research from the lab to the clinic, and exemplifies Harvard's commitment to cooperate with industry in ways that will progress translational science and, hopefully, impact the practice of clinical medicine--which advances our core mission to serve the public interest."

About Proteostasis Therapeutics

Proteostasis Therapeutics is developing "Proteostasis Regulators" (PRs), small molecule drugs that restore proper protein function or remove misfolded and aggregated proteins to treat neurodegenerative, metabolic, genetic and inflammatory disorders. The Proteostasis Network is the cellular machinery responsible for protein folding, trafficking and clearance, and can become imbalanced by the cumulative effects of aging, disease, genetics, and environmental factors. PTI was founded by leading scientists who discovered a pioneering approach for treating disease by restoring protein network homeostasis. www.proteostasis.com

About Harvard University's Office of Technology Development

The Harvard Office of Technology Development (OTD) is responsible for all activities pertaining to the evaluation, patenting and licensing of new inventions and discoveries made at Harvard University and Harvard Medical School. OTD also serves to further the development of Harvard technologies through the establishment of sponsored research collaborations with industry. OTD's mission is to promote the public good by fostering innovation and translating new inventions made at Harvard into useful products available and beneficial to society.

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