Proteostasis Therapeutics Presents Promising Preclinical Data at the 27th Annual North American Cystic Fibrosis Conference

Cambridge, Mass., October 18, 2013 -- Proteostasis Therapeutics, Inc., a company developing novel therapeutics that regulate protein homeostasis to improve outcomes for patients with orphan and neurodegenerative diseases, today announced the presentation of data on the Company's lead preclinical candidates and their potential for use as combination therapies for cystic fibrosis (CF) at the 27th Annual North American Cystic Fibrosis Conference in Salt Lake City, Utah.

"These presentations demonstrate the exciting progress being made in our CF program as we work to identify a clinical candidate in 2014," said David Weiner, M.D., Chief Medical Officer of Proteostasis Therapeutics. "Our novel Proteostasis Network (PN) platform has allowed us to identify small molecule proteostasis regulators that modulate protein homeostasis pathways to correct the folding, trafficking, and functional activity of the DF508 Cystic Fibrosis Transmembrane Regulator (CFTR). In these presentations we reported corrector activity for our compounds in human bronchial epithelial (hBE) cells, both as stand-alone therapies, and in combination with existing clinical-stage corrector candidates."

The Company's first poster and oral presentation, titled "Robust Correction of DF508 Using Small Molecule Proteostasis Regulators Alone and in Combination with Clinical-Stage Correctors," were presented by Markus Haeberlein, MSc, Ph.D., Senior Vice President and Head of Research at Proteostasis Therapeutics. The Company has identified multiple novel CFTR corrector series from internal compound library screens using Multiplex Gene Expression with sentinels to pathways within the PN, and a subsequent screen for functional activity in a cystic fibrosis bronchial epithelial cell line. Identified correctors were found to have robust functional activity in DF508/DF508 hBE cells comparable to CFTR correctors currently in clinical development. Importantly, the maximal activity of those clinical-stage CFTR correctors was more than doubled when combined with the Company's correctors, providing a strong foundation for the ongoing development of the program's CFTR corrector candidates, and the potential for combination therapies.

The Company's second poster, entitled "Correcting the DF508 Defective Folding and Trafficking Mutant of CFTR Using Small Molecule Regulators of the Proteostasis Network," was presented by Lawrence Drew, Senior Research Associate at Proteostasis Therapeutics. The data details the Company's broader PN-based approach of identifying small-molecule CFTR correctors, and highlights the enhanced functional activity shown by the Company's correctors in DF508 cellular models and patient-derived hBE cells. Compound induced modulation of PN pathways correlates with functional correction, supporting the role of PN modulation in rescuing the folding/trafficking of this disease-causing protein, and demonstrating proof of concept for the utilization of the PN in treating CF.

About Proteostasis Therapeutics

Proteostasis Therapeutics is developing disease-modifying therapeutics for orphan and neurodegenerative diseases. The Company's lead programs in cystic fibrosis and protein

aggregation diseases such as Parkinson's disease modulate protein chaperone and proteasomal degradation pathways within the cell. These pathways are part of the cellular 'quality control' machinery, called the protein homeostasis network or Proteostasis Network (PN) that regulates protein folding, trafficking, and clearance. By enhancing the function and capacity of the PN, the Company's product candidates correct for imbalances in the PN resulting from the cumulative effects of disease, genetic mutations, environmental factors, and aging. For more information, please visit www.proteostasis.com.

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