Proteostasis Therapeutics Presents Data at Two Scientific Conferences for Lead Programs in Cystic Fibrosis and Parkinson's Disease

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Cambridge, Mass., October 18, 2012 — Proteostasis Therapeutics, Inc., a company developing novel therapeutics that regulate protein homeostasis to improve outcomes for patients with neurodegenerative and orphan diseases, announced today that company scientists made presentations at two premier scientific conferences. These presentations highlighted progress with the Company's lead programs in cystic fibrosis (CF) and Parkinson's disease (PD) and demonstrated the potential of its differentiated approach to developing disease modifying therapeutics.

"At the North American Cystic Fibrosis Conference, we presented data that show how our Proteostasis Network drug discovery platform can identify proteostasis regulators that function as correctors of ΔF508 CFTR, the most common genetic mutation leading to CF. Our data at the Society for Neuroscience Annual Meeting show how the modulation of proteasome activation through the inhibition of Usp14, a deubiquitinase enzyme, stimulates the degradation of α-synuclein, a misfolding- and aggregation-prone protein that can accumulate in the brains of PD patients," commented Peter H. Reinhart, Ph.D., President and Chief Scientific Officer of Proteostasis Therapeutics. "We are planning to begin clinical trials for both programs in 2014 and are very encouraged by the data we have generated to date."

- **26th Annual North American Cystic Fibrosis Conference (NACFC) in Orlando, FL**: The Company presented a poster entitled "Small Molecule Regulators of the Proteostasis Network Enhance CFTR Protein Function" on Thursday, October 11, 2012. This poster showed how the Company's Proteostasis Network platform can be utilized to perform high-throughput screens for the identification and characterization of proteostasis regulators (PRs) with therapeutic potential as ΔF508 CFTR correctors. These data also show that different chemical series of PRs are associated with distinct Proteostasis Network profiles, suggesting they may act through distinct mechanisms which may be important for identifying compound combinations that have additive or synergistic effects. Furthermore, it was shown that one of the mechanisms identified involves regulation of histone deacetylase enzymes supporting a role for this class of enzymes as drug targets for therapeutic intervention.
- **Society for Neuroscience (SfN) 42nd Annual Meeting in New Orleans, LA**: The Company made a nanosymposium presentation entitled "Proteolytic degradation and clearance of misfolded proteins associated with neurodegenerative diseases by small molecule inhibition of Usp14" on Wednesday, October 17, 2012. The data show recent advances in the discovery of efficacious compounds that lower neurotoxic protein aggregates in cells. It was shown that modulating proteasome activity through the inhibition of Usp14, a deubiquitinase enzyme, stimulates the degradation of specific proteins including α-synuclein, a protein linked to the progression of PD. These findings demonstrate the Company's progress on advancing compounds towards lead nomination for this disease. Furthermore, the data presented show evidence for Usp14 inhibition enhancing the degradation of additional aggregation-prone proteins, suggesting that Usp14 inhibitors may be efficacious in other protein aggregation diseases such as Alzheimer's disease (AD), Amyotrophic Lateral Sclerosis (ALS), Spinocerebellar Ataxia (SCA), and Frontotemporal Dementia (FTD).

About Proteostasis Therapeutics

Proteostasis Therapeutics is developing disease-modifying therapeutics for orphan and neurodegenerative diseases. The Company's lead programs in cystic fibrosis (CF) and protein aggregation disorders such as Parkinson's disease (PD) 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 the Company's website at www.proteostasis.com.

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