Proteostasis Therapeutics Announces a New Class of Agents for Cystic Fibrosis Called CFTR Amplifiers and Selects PTI130 as a Development Candidate

Amplifiers to Be Developed Complementing Emerging Standard of Care and Delivering Even Greater Benefit to CF Patients

CAMBRIDGE, MA--(Marketwired - February 04, 2015) - Proteostasis Therapeutics, Inc. (PTI), a company developing novel therapeutics to treat diseases of protein folding, trafficking and clearance, today unveiled a new class of agents, CFTR AMPLIFIERS, for the treatment of cystic fibrosis (CF). CFTR amplifiers represent a new drug class able to enhance the effect of known cystic fibrosis transmembrane conductance regulator (CFTR) modulating agents, such as potentiators and correctors. The amplifiers are effective across CFTR mutation classes and form the basis for Proteostasis' strategy to develop a broad acting combination therapy able to serve CF patients with most mutations.

Proteostasis Therapeutics also announced today that it has nominated PTI130 as a clinical development candidate for the treatment of CF. PTI130, an amplifier, was found to have excellent pharmacologic properties amenable for oral dosing. Fourteen-day, non-GLP preclinical toxicology studies testing multiple dose groups of PTI130 in two different animal species demonstrated a favorable safety and tolerability profile for clinical development.

PTI130 is fully owned by Proteostasis Therapeutics and was internally discovered through the Company's proprietary Disease-Relevant Translation, DRT™ platform. DRT™ utilizes functionally pertinent phenotypic assays and disease relevant models to identify highly translatable therapies associated with the modulation of protein homeostasis pathways within the cell. PTI130 was derived from medicinal chemistry optimization of hits from the Company's internal compound library based on its impressive ability to double the efficacy of CFTR modulating agents such as correctors and potentiators, in the HBE (human bronchial epithelial) cell Ussing functional assay. These data provide a basis for the clinical exploration of adding PTI130 on to the emerging standard of care (corrector/potentiator combination) to deliver even greater benefit to CF patients. The discovery of PTI130 was partially funded by research grants from Cystic Fibrosis Foundation Therapeutics Inc., the nonprofit affiliate of the Cystic Fibrosis Foundation.

Proteostasis Therapeutics is expected to file an IND for PTI130 with the US FDA and the molecule will enter the clinic in phase I trials by the end of 2015.

"We are proud of our drug discovery platform that has allowed us to identify molecules with novel mechanisms of action such as CFTR amplifiers," said Meenu Chhabra, President and Chief Executive Officer. "We believe that PTI130 places amplifiers on the vanguard of the rapidly evolving CF treatment paradigm and may prove to be the lynchpin for maximizing benefit for all CF patients regardless of the underlying CFTR mutation class."

About Cystic Fibrosis

Cystic fibrosis is the most common genetic disorder affecting approximately 70,000 people worldwide. Improvement in disease management protocols and approval of new drugs to treat the symptoms have extended the life expectancy for CF patients and is now approaching 40 years of age. However, CF remains an incurable disease that leads to death. Recently, CFTR mutation specific disease modulators such as correctors and potentiators, have shown the ability to restore CFTR function in selected genotypes.

About Proteostasis Therapeutics

Proteostasis Therapeutics is developing disease-modifying therapeutics for diseases of protein folding, trafficking and clearance. By combining the DRT™ platform with state of the art medicinal chemistry tools, PTI generates highly selective drug candidates. The Company's proprietary Disease-Relevant Translation, DRT™ platform utilizes functionally pertinent phenotypic assays and disease relevant models to identify highly translatable therapies associated with the modulation of proteostasis pathways within the cell. PTI has multiple wholly owned programs in cystic fibrosis. PTI collaborates with Biogen Idec to research and develop therapeutic candidates for neurodegenerative disease based on the inhibition of Usp14, which may result in total payments of up to $200M plus royalties. In addition, PTI has a collaboration with Astellas Inc. based on the Unfolded Protein Response (UPR) pathway where PTI is eligible to earn up to $1.2B in development milestones.

For more information visit www.proteostasis.com.

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