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Proteostasis Therapeutics, Inc. Demonstrates Therapeutic Potential of a Proprietary Triple Combination Therapy for the Treatment of Cystic Fibrosis that Restores Activity of Mutant F508del CFTR protein to 80% of Normal

CAMBRIDGE, Massachusetts, November 20, 2015 – Proteostasis Therapeutics, Inc. (PTI), a company developing small molecule therapeutics to treat diseases caused by defects in protein processing, announced today the expansion of its cystic fibrosis (CF) drug candidate pipeline to include the addition of a novel triple combination therapy of PTI's own CFTR amplifiers, correctors and potentiators. PTI's testing has shown that a triple combination comprising a proprietary corrector and potentiator, currently in late lead optimization stage, and one of PTI's CFTR amplifiers, can restore the activity of mutant F508del CFTR protein to 80% of normal activity in Ussing chamber assays.

The components of the triple combination were developed internally using the Company's proprietary Disease-Relevant Translation, or DRT™, platform. The screening assay was optimized to identify novel CFTR modulators that show functional synergy with the Company's lead drug candidate, PTI-428, which belongs to a novel class of CFTR modulators the Company refers to as "amplifiers", while restoring chloride currents above levels achieved by existing commercially available products. In Ussing chamber assays, one PTI potentiator, PTI-P271, has shown comparable efficacy with Vertex Pharmaceuticals' (Vertex) potentiator, ivacaftor, and did not cause F508del CFTR protein destabilization under chronic administration conditions when combined with a PTI corrector. Also in Ussing chamber assays, one PTI corrector, PTI-C1811, has been shown to restore at least 140% of CFTR functional levels relative to Vertex's corrector lumacaftor, which is currently marketed together with ivacaftor as Orkambi™.

Based on the data generated in the human bronchial epithelial (hBE) cells homozygous for the F508del mutation, the Company believes that the combined use of the three molecules has the potential to restore mutant CFTR function in CF patients homozygous for the F508del mutation to approximately 80% of normal activity. Further, PTI-C1811 and PTI-P271 combined have demonstrated higher levels of CFTR function *in vitro* than Orkambi™.

"The unique screening set-up allowed us to identify novel chemical moieties with corrector and potentiator properties that act synergistically with our CFTR amplifiers across several CFTR mutation classes" said Meenu Chhabra, President and Chief Executive Officer of PTI. "We are very pleased with the rapid advancement of all of our CF programs, and are confident that we will continue to build on our promising amplifier program to expand the range of treatment options for most CF patients."

PTI is advancing its CFTR amplifier PTI-428 as its lead clinical development candidate for the treatment of CF and expects to file an IND with the FDA by the end of 2015. The PTI correctors and potentiators are expected to enter clinical development by the middle of 2017.

About Cystic Fibrosis

Cystic fibrosis is a genetic disorder affecting approximately 70,000 to 100,000 people worldwide. Improvement in disease management protocols and approval of new drugs to treat the symptoms have extended the life expectancy for CF patients. However, CF remains an incurable disease that leads to death.

About Proteostasis Therapeutics

Proteostasis Therapeutics, Inc. (PTI) is developing disease-modifying therapeutics for diseases of protein processing. By combining the DRT™ platform, a phenotypic screening approach based on the use of functionally pertinent cellular assays, with state of the art medicinal chemistry tools, PTI generates highly selective drug candidates that modulate the proteostasis imbalance in the cell. In addition to its multiple wholly-owned programs in CF, PTI has formed collaborations with Biogen Inc. to research and identify therapeutic candidates for neurodegenerative disease and with Astellas Pharma Inc. to research and identify therapies targeting the Unfolded Protein Response (UPR) pathway.

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