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Title: SPARTA: Efficacy and safety assessment of two regimens of alpha$_1$-proteinase inhibitor in emphysema due to alpha$_1$-antitrypsin deficiency

Mark 5342 Forshag Mark.Forshag@grifols.com MD [1], Sandra 5343 Camprubi sandra.camprubi@grifols.com [2], Rhonda 5344 Griffin Rhonda.Griffin@Grifols.com [1], Junliang 5345 Chen Junliang.chen@grifols.com [1], Jaume 5346 Ayguasanosa Jaume.Ayguasanosa@grifols.com MD [2] and Susan 5347 Sorrells susan.sorrells@grifols.com [1]. [1] Clinical Development, Grifols Therapeutics, Research Triangle Park, NC, United States and [2] Clinical Development, Instituto Grifols SA, Barcelona, Spain .

Body: Introduction: Alpha$_1$-Antitrypsin Deficiency (AATD) is a hereditary condition characterized by low serum levels of alpha$_1$-proteinase inhibitor (alpha$_1$-PI) and an increased risk of emphysema. The approved dose for augmentation therapy is 60 mg/kg/wk, associated with raising trough levels to approximately 11 µM. However, the normal lower limit in the nondeficient population is 20 µM. To date, no prospective randomized controlled trial has conclusively proven the clinical efficacy of augmentation therapy. Goal: To assess the effect of augmentation therapy on emphysema progression in AATD assessed by lung computed tomography (CT) densitometry, dosed to approximate trough levels of 11 µM or 20 µM, vs placebo. SPARTA will be the largest randomized trial with the longest duration of exposure, and the first to compare two active augmentation arms. Design: Prospective, double-blind, randomized, placebo-controlled

Arms	60 mg/kg/wk vs 120 mg/kg/wk of intravenous alpha$_1$-PI, vs placebo
Duration	3 years
Primary Endpoint	Lung loss via whole lung CT densitometry (15th percentile point) in each active arm vs placebo
Other Endpoints	- Severe COPD exacerbations
	- Basal lung CT densitometry
	- Forced expiratory volume in 1 sec
	- Quality of life
Sample Size	Total of 339 subjects (80% power at 0.025 level with an assumed 20% dropout)

Discussion: SPARTA will be the first prospective, randomized controlled trial of augmentation to assess two active doses, including one designed to achieve population based normal trough levels, vs

placebo.Enrollment is anticipated to commence in September 2013 and should allow analyses of a number of secondary endpoints and subject subpopulations.