

European Respiratory Society Annual Congress 2012

Abstract Number: 7132

Publication Number: P1476

Abstract Group: 8.2. Transplantation

Keyword 1: Bronchiolitis **Keyword 2:** Infections **Keyword 3:** Transplantation

Title: Results of a phase 2b multi-center trial of ALN-RSV01 in respiratory syncytial virus (RSV)-infected lung transplant patients

Amy 433 Simon asimon@alnylam.com MD ¹, Dr. Verena 876 Karsten vkarsten@alnylam.com ¹, Dr. Jeff 877 Cehelsky ccehelsky@alnylam.com ¹, Ms. Shaily 878 Shah sshah@alnylam.com ¹, Dr. Jared 879 Gollob ggollob@alnylam.com MD ¹, Dr. Rachel 880 Meyers rmeyers@alnylam.com ¹, Dr. Akshay 881 Vaishnav avaishnav@alnylam.com MD ¹, Dr. Allan 882 Glanville aglanville@stvincents.com.au MD ², Dr. Martin 883 Zamora marty.zamora@ucdenver.edu MD ³, Dr. John 884 DeVincenzo jdevince@uthsc.edu MD ⁴, Dr. Selim 886 Arcasoy sa2059@columbia.edu MD ⁵, Dr. Michael 887 Musk michael.musk@health.wa.gov.au MD ⁶, Dr. Urte 888 Sommerwerk Urte.Sommerwerck@ruhrlandklinik.uk-essen.de MD ⁷ and Dr. Jens 889 Gottlieb Gottlieb.Jens@mh-hannover.de MD ⁸. ¹ Research and Development, Alnylam Pharmaceuticals, Cambridge, MA, United States ; ² Thoracic Medicine, St. Vincent's Hospital, Darlinghurst, Australia ; ³ Pulmonary and Critical Care, University of Colorado Hospital, Denver, United States ; ⁴ Pediatrics and Infectious Disease, University of Tennessee Health Science Center, Memphis, United States ; ⁵ Pulmonary, Columbia University Medical Center, New York, United States ; ⁶ Respiratory Disease, Royal Perth Hospital, Wembley, Australia ; ⁷ Respiratory Medicine, Westdeutsches Lungenzentrum am Universitaetsklinikum, Essen, Germany and ⁸ Respiratory Medicine, Medizinische Hochschule, Hannover, Germany .

Body: ALN-RSV01 is a small interfering RNA targeting RSV replication. A Phase 2a randomized, controlled trial in 24 RSV-infected lung transplant patients administering nebulized ALN-RSV01 or PBO daily for 3 days was previously conducted in which ALN-RSV01 led to a significant decrease in new or progressive bronchiolitis obliterans syndrome (BOS) at Day 90 ($p=0.027$). We have now performed a Phase 2b multi-center, randomized, double-blind, PBO controlled trial in 87 RSV-infected lung transplant patients to examine the impact of ALN-RSV01 on the incidence of new or progressive BOS at Day 180. RSV positive subjects were randomized (1:1) to receive nebulized ALN-RSV01 or PBO daily for 5 days, alongside the institution's standard-of-care. Patients were prospectively stratified for: 1) days from symptom onset to treatment; and 2) pre-infection BOS grade. Of the 3,985 patients prescreened, 218 were RSV positive, of which 45 were randomized to receive ALN-RSV01 and 42 to receive PBO [intent-to-treat (ITT) population]. Ten patients were without confirmed RSV by central laboratory testing, thus a total of 77 patients (ALN-RSV01, $n=44$; PBO, $n=33$) comprised the ITTc (ITT central RSV+) population. Baseline viral load was balanced between both treatments. ALN-RSV01 was generally safe and well tolerated. There was a decrease in new or progressive BOS at Day 180 in ALN-RSV01-treated patients compared to PBO in the ITTc population (13.6% vs 30.3%, $p=0.058$), which was statistically significant by prospectively defined Last Observation Carried Forward ($p=0.028$) and Per-Protocol ($p=0.025$) analyses. ALN-RSV01 had a treatment

effect of 54-65% in all of the pre-specified populations.