Nontuberculous Mycobacteria (NTM)

Where does it comes from?

- More than 150 species recognized
- Acquired by inhalation from the environment
- Water thought to be the main source
- Warmer climates have higher infection rates
- Patient to patient transmission possible

Who is at risk?

- Underlying lung disease and/or genetic predisposition
- Cystic Fibrosis patients
- COPD (chronic obstructive pulmonary disease)
- Bronchiectasis patients
- Immunosuppressive therapy



* Data: www.ntmfacts.com, FDA

Market Dynamics: NTM

There is no competition in MABSC and limited competition in MAC

Median survival for MAC is 13 years while for non-MAC NTM it is 4.6 years ****

20% - 25% of all NTM cases in a South Korean database are MABSC***

Over 180k NTM cases were estimated for 2014 in the United States*

NTM costs estimated at $1.7b* with MABSC costs > 2x MAC costs

37% of NTM confirmed Cystic Fibrosis patients in the US are MABSC**

AIT is initially targeting NTM abscessus (MABSC), the most aggressive and difficult to treat form of NTM. AIT will seek approval in NTM MAC (mycobacterium avium complex) following MABSC approval

* Strolloet al. The Burden of Pulmonary Nontuberculous Mycobacterial. Pub 27-July-2015 ** Data presented at ATS 2017 (Derek Low et al, Medical University of South Carolina) *** Data presented at ATS 2017 (Keun Burn Chung et al, Seoul National University College of Medicine) **** Kotilainen, H. et al. "Clinical Findings in Relation to Mortality in Non-Tuberculous Mycobacterial Infections: Patients with Mycobacterium Avium Complex Have Better Survival than Patients with Other Mycobacteria." European Journal of Clinical Microbiology & Infectious Diseases 34.9 (2015)

NO Used to Treat MABSC in CF patients

Three Patients Have Been Treated Under Compassionate Use, Two in Israel at Rambam Medical Center and One in the United States at the National Heart, Lung and Blood Institute (NHLBI)

- All refractory to standard of care (cocktail of antibiotics recommended by the American Thoracic Society)
- All had significant adverse events associated with standard of care
- NO was added to standard of care
- NO Treatment Regimen: 160 ppm NO 5x/day for 14 days, then 3x/day for the next 7 days
  - One patient received 160 ppm NO 5x/day for 5 days, then 2 or 3x/day for the next 21 days
- ***M. abscessus* bacteria were eradicated in one of three patients at the end of the 21 day treatment period**
- **There were no serious adverse events related to NO therapy**
- **6-minute walk improved in 2 patients (6-minute walk not recorded for one patient) at day 21 vs baseline**
- **FEV1 improved for 2 patients and declined for one patient at day 21 vs baseline**
  - **Each % improvement > % decline**
- **Quality-of-Life improvements were seen at day 21 vs baseline for all patients**

Nitric Oxide for NTM abscessus (NO-NTM abscessus) Phase 2 Trial Design

Single-Arm, Open-Label Trial in Israel

- 9 patients were enrolled with MABSC, who are refractory to standard-of-care
- In addition to standard-of-care, Patients received:
  - 5 treatments of inhaled NO at a concentration of 160 ppm for 30-minutes per day for 14 days in the hospital setting
  - 3 treatments of inhaled NO at a concentration of 160 ppm for 30-minutes per day for 7 days in the ambulatory setting
- PE (primary endpoint): Safety, as measured by NO-related serious adverse events (SAEs), over the 21-day treatment period
- SE (secondary endpoints): 6-minute walk test and MABSC load in sputum at day 21
- SE: Safety (specifically methaemoglobinemia and NO_2 levels) and Tolerability
- Other data to be gathered include 6-min. walk and MASBC load at day 51 and 81

Highlights

- All patients have completed dosing in the trial
- AIT will release data once all patients have reached 30 days post the completion of dosing
- Data are expected in the fourth quarter of 2017