PRESS RELEASE

Zambon Receives U.S. FDA Breakthrough Therapy Designation for CMS I-neb® in Patients with Non-Cystic Fibrosis Bronchiectasis (NCFB)

- CMS I-neb® is an investigational treatment being developed as a potential first-in-class inhaled therapy for adult patients with NCFB colonized with *P. aeruginosa*; NCFB is a chronic, progressive, and irreversible respiratory disease
- Breakthrough designation validates registrational path for CMS I-neb® in NCFB and facilitates potentially expedited development and review

MILAN, Italy and Boston, MA, April 21, 2022 — Zambon, a multinational pharmaceutical company focused on innovating cure and care to improve people's health and the quality of patients' lives, today announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation to *colistimethate sodium* powder for nebulization solution (CMS I-neb®) for the reduction in the incidence of pulmonary exacerbations in adult patients with non-cystic fibrosis bronchiectasis (NCFB) colonized with *P. aeruginosa*. NCFB is a chronic, progressive, and irreversible respiratory disease. There are no approved inhaled treatments currently available for patients with bronchiectasis and chronic *P. aeruginosa* colonization.

The Breakthrough Therapy Designation is supported by data from the Phase 3 PROMIS - I study, which showed that CMS I-neb® significantly reduced the annual rate of exacerbations in patients with NCFB and *P. aeruginosa* chronic infection, the primary endpoint of the trial. In addition, the trial met important secondary endpoints, including reduction of severe exacerbations and prolongation of time to first exacerbation compared to placebo, and also improvement in Quality of Life (QoL). The treatment was demonstrated to be well tolerated with adverse events similar between groups. Data from the Phase 3 trial were most recently presented at the European Respiratory Society (ERS) International Congress in September 2021.

"*With no approved drugs for patients with NCFB colonized by P. aeruginosa anywhere in the world, the Breakthrough Therapy Designation by FDA marks an important step forward in support of our mission to develop and provide treatment options for people with rare and severe respiratory diseases*," said **Roberto Tascione, CEO at Zambon**. "*We are proud that the FDA has recognized the importance of CMS I-neb® and the urgent need to develop innovative treatments for these patients*."

Breakthrough Therapy Designation from the U.S. FDA is granted to accelerate the development and regulatory review of investigational drugs that are intended to treat

serious or life-threatening ailments. Investigational therapies with this designation have shown preliminary clinical evidence that indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints.[i]

"*This FDA Breakthrough Therapy Designation reinforces our confidence in CMS I-neb®, which, if approved, would be the first inhaled treatment for people with NCFB and chronic P. aeruginosa infection. CMS I-neb® is a unique inhaled investigational therapy designed to deliver targeted concentrations of drug directly to the site of disease while aiming to minimize systemic exposure that can cause toxicity and side effects. We look forward to working with the FDA over the coming months as we advance the development of CMS I-neb® with the hope of bringing much needed benefit to patients whose lives are severely impacted by this disease,*" commented **Paola Castellani, CMO and Head of R&D at Zambon.**

In patients with NCFB, lung infection with *P. aeruginosa* is associated with frequent pulmonary exacerbations and admission to hospital for treatment, reduced quality of life, and increased mortality[ii].

About NCFB

Non-cystic fibrosis bronchiectasis (NCFB) is a chronic lung disease characterized by recurrent infection, inflammation, persistent cough, and production of sputum and its prevalence is increasing worldwide. NCFB has a progressive course primarily determined by the rate of exacerbations, many of which are related to *P. aeruginosa*. Consequently, research efforts directed to treat infection by *P. aeruginosa* and its associated acute exacerbations remain a clinical priority.

The objectives of treatment in bronchiectasis are to prevent exacerbations, reduce symptoms, improve quality of life, and stop disease progression. Cough and sputum production, along with breathlessness are the most frequent symptoms but rhinosinusitis, fatigue, hemoptysis, and thoracic pain are also common.

About Colistimethate sodium (CMS)

Colistimethate sodium (CMS) is a pro-drug (the form used for inhalation therapy) of the antibiotic colistin. Colistin is a polymyxin antibiotic derived from *Bacillus polymyxa var. colistinus*. The polymyxin antibiotics are surface active agents and act by binding to and changing the permeability of the bacterial cell membrane, causing bacterial cell death.

Colistin is an active agent against aerobic Gram-negative pathogens that can cause life-threatening infections, an example being *P. aeruginosa*. Colistin remains one of the few active antimicrobial agents against multi drug resistant Gram-negative bacteria and is currently considered one of the last therapeutic options for infections such as carbapenem-resistant *P. aeruginosa*.

About I-neb®

The I-neb® is a third-generation nebulizer for Adaptive Aerosol Delivery (AAD). The I-neb® is a small, battery powered, lightweight and silent drug delivery device, delivering a precise, reproducible dose of the drug.

The AAD technology ensures optimal drug delivery by only delivering medication when the patient inhales, (not continuously as in other nebulizers). This gives the medication the best opportunity to reach deep into the lungs and greatly reduces waste to the environment. AAD delivers the right amount of medication, regardless of breath size or breathing pattern.

I-neb® generates a fine-particle low-velocity aerosol, by forcing the liquid medication through a fine mesh. Faster than conventional jet or ultrasonic nebulizers, I-neb® support shorter treatment times (usually 3 to 4 minutes) and precise drug delivery.

About Zambon S.p.A.

Zambon S.p.A. is a global pharmaceutical company established in 1906 in Vicenza, Italy, and built on the values of an Italian family committed to innovating cure and care to improve patients' lives. With innovative quality products commercialized in 87 countries, Zambon has a global presence with 2,400 employees across Europe, America, and Asia, including production facilities in Italy, Switzerland, China, and Brazil. Alongside its three historical therapeutic areas of focus, which are diseases of the respiratory system, urinary tract infections, and pain management, Zambon is also focused on developing treatments for Parkinson's Disease and Cystic Fibrosis. Additionally, Zambon is currently advancing its clinical development programs of potentially first-in-class treatments for Non-Cystic Fibrosis Bronchiectasis (NCFB) and Bronchiolitis Obliterans Syndrome (BOS). If approved by regulatory authorities, the Company intends to launch the NCFB and BOS treatments globally, including in the U.S., which is the latest market entry for Zambon as an organization. In Europe, Zambon also plans to market and distribute, upon regulatory approval, an innovative oral formulation of riluzole for patients suffering with Amyotrophic Lateral Sclerosis (ALS). For further information, please visit www.zambon.com.

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[i] U.S. FDA Breakthrough Therapy: https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/breakthrough-therapy (Accessed April 12, 2022)

[ii] Weigt, et al. Semin Respir Crit Care Med. 2013;34(3):336–351.