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PRESS RELEASE

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Key data on economic impact of BOS presented at ISHLT 2021

- Research finds that Bronchiolitis Obliterans Syndrome (BOS), which represents a high physical and emotional burden on patients, significantly increases the cost of care of lung transplant patients, as the condition leads to higher rates of hospitalizations and ICU stays
- Zambon also presented two posters on organ shortage in the US and insights into approaching BOS clinical trials during COVID-19 pandemic

Zambon, a multinational pharmaceutical company focused on innovating cure and care to improve people's health and the quality of patients' lives, is pleased to announce research presented at the International Society for Heart and Lung Transplantation (ISHLT) Annual Meeting 2021.

BOS is a common complication of lung transplantation and a significant barrier to long-term survival, affecting nearly 50% of lung transplant recipients who survive five years after transplantation and nearly 80% of those who survive ten years after transplantation. BOS represents a very high physical, emotional and economic burden on patients, their caregivers and the healthcare system.

A presentation, titled *Bronchiolitis Obliterans Syndrome after Lung Transplantation: Economic Burden*, explored the impact of Bronchiolitis Obliterans Syndrome (BOS) on healthcare resource use and associated costs which is not well understood. BOS is the leading cause of death for patients who survive at least one year after a lung transplant. The goal of the study was to quantify the economic burden of BOS in the US using real-world data. The research found that patients diagnosed with BOS saw annual costs of care reach as high as almost $67,000, driven primarily by an increase in the number/length of hospitalizations and ICU stays. The researchers suggest that early diagnosis and therapies aimed at slowing disease progression may reduce the economic burden associated with BOS.

Zambon also presented two posters at the meeting that provided additional insights on the challenges posed by BOS for those living with the condition as well as for healthcare systems. The first poster, *Development in lung transplantation, organ shortage, Bronchiolitis Obliterans and overall survival in the US, 2011-2018*, highlights that while the number of lung transplantations increased between 2011-2018, the waiting list for lung transplants remains long and improvements in treating BOS, which could have benefits on long-term survival of lung-transplant patients, have been nominal.

The second poster, *Ensuring patient safety and data integrity in clinical trials for the treatment of Bronchiolitis Obliterans Syndrome (BOS) during the COVID-19 pandemic*, concerns the various BOS studies:

- BOSTON-1 and BOSTON-2 – phase III, prospective, multicenter, randomized, controlled clinical trials aimed at demonstrating the efficacy and safety of inhaled liposomal

cyclosporine A (L-CsA-i) in patients with chronic lung allograft dysfunction BOS following single (BOSTON-1) or double (BOSTON-2) lung transplantation
- BOSTON-3 – an open label extension trial for patients who have completed the 48-week treatment period in BOSTON-1 and BOSTON-2 trials

The poster details how BOS clinical trials were adapted during the COVID-19 pandemic to ensure the safety of this vulnerable patient population and provide continued access to care. Strategies deployed include remote visits and inclusion of remote spirometry assessments with home portable spirometers.

"*Our activities at ISHLT demonstrate our commitment to serving the undertreated area of severe respiratory diseases. These are diseases that continue to have significant impacts on patient outcomes and healthcare systems. The presentation and posters at ISHLT 2021 speak to the urgency to find a solution for one such disease – BOS. We have seen research showing the significant economic burden associated with BOS but also unfortunately seen that the development of BOS within 5-years post-transplantation remains high. Such findings reiterate the importance of the work we are doing in the ongoing BOSTON studies – and our other programs in severe respiratory diseases – to deliver meaningful treatments to patients whose options are currently limited,*" said **Paola Castellani, CMO and R&D Head** at Zambon.

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Bronchiolitis Obliterans Syndrome (BOS)
Bronchiolitis obliterans syndrome (BOS) is the most common form of chronic lung allograft dysfunction (CLAD) after lung transplantation (also referred to as chronic rejection). In BOS, an uncontrolled immune reaction to the transplanted lung or lungs leads to chronic inflammation of the small airways of the lungs. This causes scarring and narrowing of the airways that continues to worsen over time, limiting an individual's ability to breathe. Up to 50% of lung transplant patients develop BOS within five years post-transplant.[1] BOS usually leads to respiratory failure and death within 2 to 4 years after diagnosis.[2] There is currently no approved treatment indicated for BOS.[3] BOS commonly affects people following lung or allogeneic hematopoietic stem cell transplant (alloHSCT), although it is also associated with autoimmune diseases and exposure to environmental contaminants.

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

2. Chambers DC, et al. J Heart Lung Transplant. 2018;37(10):1169–1183.
3. Verleden GM, et al. J Heart Lung Transplant. 2019; 38(5):493-503.

BOSTON Development Program
The BOSTON development program is evaluating Liposomal Cyclosporine A for Inhalation (L-CsA-i) for the treatment of BOS, with the goal of minimizing the decline in lung function. The BOSTON-1 and -2 phase III studies are enrolling BOS patients following lung transplantation in eight countries, including over 20 US clinical sites. BOSTON-3 is an open-label extension study for eligible study participants who complete BOSTON-1 or -2. BOSTON 4 is studying L-CsA-i in adult alloHSCT recipients with BOS. L-CsA-i has received FDA Fast Track and Orphan Disease Designations for the treatment of BOS from the EMA and FDA, reflecting the high unmet need of the disease.

Liposomal Cyclosporine A for Inhalation (L-CsA-i)
L-CsA-i is a novel liposomal formulation of cyclosporine A developed for inhaled delivery to the lungs. Calcineurin inhibitors (CNIs), like cyclosporine A, are highly potent immunosuppressive drugs and a cornerstone of lung transplant medicine. L-CsA-i is administered via a drug-specific Investigational eFlow® Technology nebulizer system (PARI Pharma GmbH). The rationale of inhaled therapy is to deliver sufficient concentrations of drug directly to the site of disease while minimizing systemic exposure.

About Zambon S.p.A.
Zambon is a multinational pharmaceutical company that focuses on innovation and development with the aim to improve patients' lives. Based on a valuable heritage and strongly focused on the future, its goal is to improve people's health through the development of innovative and quality healthcare solutions.
Zambon products are commercialized in 87 countries. The company has 23 subsidiaries in three different continents – Europe, America and Asia – and owns manufacturing units in Italy, Switzerland, China and Brazil. The company today has a strong focus on the treatment of rare diseases and specialties, on top of respiratory, pain management and women's care. Zambon was established in 1906 in Italy and today counts 2,500 employees all over the world. For further information, please visit www.zambon.com

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L-CsA-i and the eFlow® for L-CsA-i are investigational and their safety and efficacy have not been established for the uses described here.