BOSTON Studies – Information for Patients

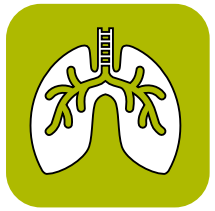
INNOVATING CURE & CARE TO MAKE PATIENTS' LIVES BETTER

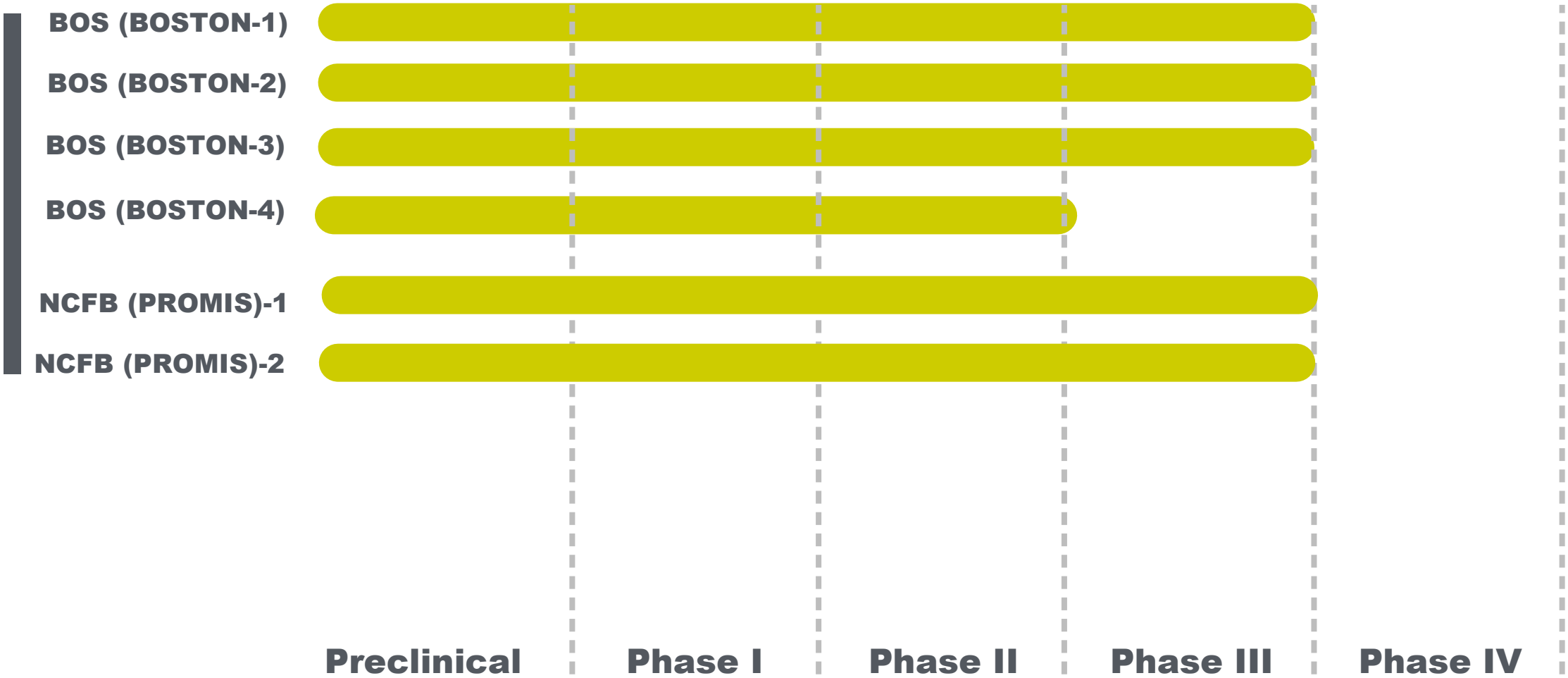
Zambon is a multinational pharmaceutical company that focuses on innovation and development with the aim to improve **patients' lives**.
Based on a valuable heritage and strongly focused on the future, its goal is to **improve people's health** through the development of innovative and quality healthcare solutions. Zambon products are commercialized in **87 countries**.

Zambon has a precise business development plan: further **internationalization**, maximization of **core products**, and investment in **research** in specialized areas such as Parkinson's Disease, **Severe Respiratory Diseases** and Women's Health.

Zambon

Our Specialty Respiratory Pipeline





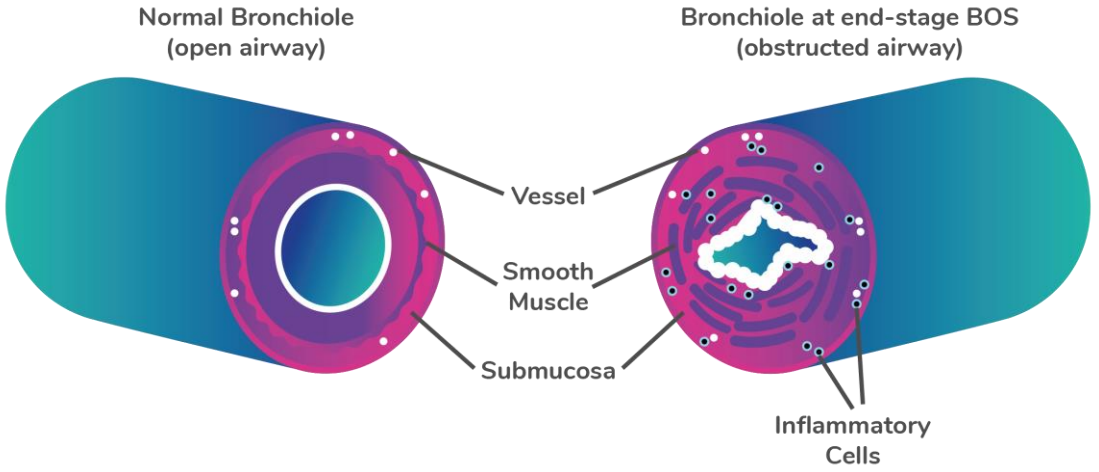
Chronic Lung Allograft Dysfunction (CLAD) – Bronchiolitis Obliterans Syndrome (BOS)

- Chronic Lung Allograft Dysfunction is a severe lung disease where the immune system attacks the airways of the lungs. There are various types, the most common is called BOS.[1] This condition is also called chronic rejection.
- BOS may be diagnosed through pulmonary function tests. The Forced Expiratory Volume at 1 second (FEV_1) is measured for decline after lung transplantation. Chest x-ray, computerized tomography (CT) scan, and lung biopsy are other methods used to diagnose BOS, or in the alternative, to exclude BOS because of other potential causes for the decline in FEV_1, such as infection.

- Lung tissue shows inflammation, scarring and narrowing of the airways

  → **<u>Sadly, nearly 50% of patients develop BOS within 5 years of transplant</u>**

- There are no approved therapies indicated for the treatment of BOS[2]



1. Verleden, G.M. (2019). Chronic lung allograft dysfunction: Definition, diagnostic criteria, and approaches to treatment—A consensus report from the Pulmonary Council of the ISHLT. The Journal of Heart and Lung Transplantation 38, 11.
2. Meyer KC, et al. Eur Respir J 2014; 44: 1479–1503 2. Barker et al., NEJM 2014; 370:1820-8

Idea Behind the Therapy

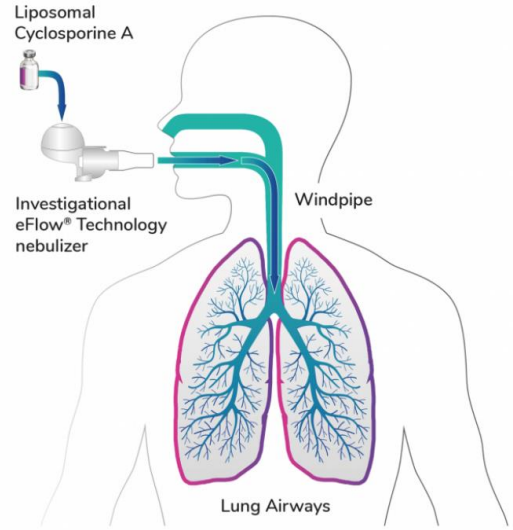
- Cyclosporine A is an immunosuppressant drug used to prevent and treat organ rejection after a transplant
- Liposomal Cyclosporine A (L-CsA) is an investigational formulation of cyclosporine A that is enclosed within tiny droplets called liposomes

→ *Liposomes are known drug delivery systems that may help carry difficult to dissolve medication into the lungs*

- Inhaled L-CsA is delivered directly into lungs using a drug-specific nebulizer system

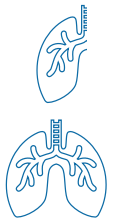
→ *Basis for successful inhalation therapy is direct drug delivery into the small airway of the lungs*

→ *Investigational eFlow® Technology Nebulizer System (PARI Pharma GmbH) is being evaluated*



Phase III Clinical Trials

- **BOSTON-1 and 2** studies are randomized controlled trials
- **BOSTON-1** trial is for CLAD-BOS after single lung transplant
- **BOSTON-2** trial is for CLAD-BOS after double lung transplant



- Study sites are in Austria, Belgium, France, Germany, Spain, UK, Israel and US
- In each trial, approximately 110 patients will be followed for up to 48 weeks
- **BOSTON-3** is an open-label extension study available to patients who participated to BOSTON-1 and -2 studies for 2+ years

Who Can Participate?

- ✓ Individuals who are interested should talk to their doctors about the study
- ✓ These individuals will need to be consented to study, prior to a screening visit. If they qualify, they will be randomized
- ✓ Like flipping a coin, patients will be assigned to one of two groups (50/50 chance)
  - → One group of participants will receive standard of care and the investigational inhaled L-CsA
  - → One group will receive their standard of care regimen only and no study medication

Regardless of the treatment allocation, all participants will continue to receive their standard of care regimen for maintenance of the lung allograft. For evaluation, the two groups will be compared.

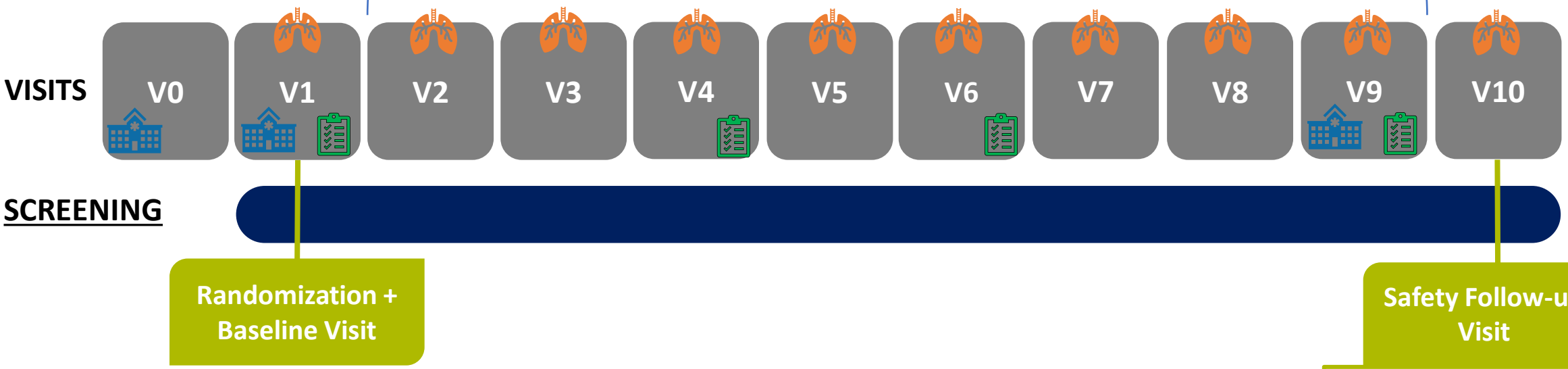
- ✓ Primary study endpoint: Change of FEV_1 over time
- ✓ Secondary endpoint: progression free survival

Patient eligibility criteria for the BOSTON studies, include:

- Are over the age of 18
- Have had a single or double lung transplant
- Have been diagnosed with BOS, per protocol standards
- Are receiving a standard immunosuppression regiment, per protocol
- Willing to commit to study visits with the study doctor for follow up testing

BOSTON-1 & -2 Visit Schedule:

Visits scheduled every 4-8 weeks for a total 48-week treatment period



Mandatory on-site visits

Spirometry Performed

Quality of Life (QoL) Assessment through EQ-5D-5L Questionnaire

For more information

- Study information is available on www.ClinicalTrials.gov, search by keywords
  - BOSTON-1
  - BOSTON-2
  - BOSTON-3
- Inquiries - respiratory.patients@zambongroup.com