About Breath Therapeutics – a Zambon Group Company

BREATH is dedicated to developing inhaled therapies for rare lung diseases

• Breath Therapeutics – a Zambon Group Company has offices in Germany and the US
• Research focused on inhalation therapies for rare respiratory diseases
• Leadership team with expertise in drug formulation and aerosol delivery, clinical development, respiratory diseases and commercialization
What is Bronchiolitis Obliterans Syndrome?

Bronchiolitis Obliterans Syndrome is a severe lung disease where the immune system attacks the airways of the lungs.

- Bronchiolitis Obliterans Syndrome (BOS) is also known as:
  - Obliterative Bronchiolitis
  - Chronic Rejection (in lung transplant)
  - Pulmonary graft-versus-host disease (in allogenic Hematopoietic Stem Cell Transplantation {alloHSCT})
  - Constrictive Bronchiolitis (in environmental exposure)

- BOS is diagnosed by decline in FEV₁ in high risk patients or by lung biopsy in other patients.

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

- Nearly 50% of patients develop BOS within 5 years following lung transplantation¹

2. Barker et al., NEJM 2014; 370:1820–8
Who Develops BOS?

Current estimated number of people with BOS in the US, EU and Japan

- **~ 21,500 Cases** following lung transplantation
- **~ 8,500 Cases** following allogeneic hematopoietic stem cell transplantation (alloHSCT)

- BOS affects about 30,000 lung transplant and alloHSCT recipients, including approximately 2,000 pediatric patients.
- Other causes of BOS may include autoimmune disease and due to certain environmental exposures but the total number of patients are less clear.

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1 Company internal research based on country-specific reports for lung transplants and stem cell transplantations for the US, EU, and Japan.
Current Research at Breath Therapeutics

L-CsA-i is an investigational medicine being studied to treat BOS

- L-CsA-i stands for Liposomal Cyclosporine A for inhalation
- L-CsA-i is an inhaled medicine given by a drug-specific Investigational eFlow® Nebulizer System (PARI Pharma), designed for home-inhalation
- Inhaled approach allows L-CsA-i to be delivered to the lungs, site of BOS lung disease
- The safety and efficacy of L-CsA-i to treat BOS is currently being evaluated in the BOSTON clinical studies
BOSTON Clinical Studies

The BOSTON clinical studies are designed to evaluate the safety and efficacy of Liposomal Cyclosporine A for Inhalation (L-CsA-i) for the treatment of BOS

- **BOSTON-1**: L-CsA-i for BOS following single lung transplant (Initiated Q1 2019)
- **BOSTON-2**: L-CsA-i for BOS following double lung transplant (Initiated Q1 2019)
- **BOSTON-3**: Extension trial of BOSTON-1 and BOSTON-2
- **BOSTON-4**: L-CsA-i for BOS following alloHSCT*
- **BOSTON-5**: L-CsA-i for pediatric patients with BOS

*The safety and efficacy of L-CsA-i has not been demonstrated for the investigational uses described here

*Allogenic Hematopoietic Stem Cell Transplantation (alloHSCT)*
BOSTON-1 and -2: Clinical Studies of L-CsA-i in Patients with BOS following Lung Transplantation

BREATH is currently conducting two studies at approximately 35 sites in the US and in Europe

- Two phase 3 studies in BOS following lung transplantation; one in single lung transplant and one in double lung transplant
- Designed to evaluate if L-CsA-i is safe and effective for the treatment of BOS in people who have had a lung transplant
- Study participants will be randomized (like flipping a coin) to one of two groups
- One group will be given the study medication in addition to their usual medications and the other group will be given their usual medications alone. Your usual medications refer to the ones that your doctor already has prescribed for you.
BOSTON-1, BOSTON-2 & BOSTON-3 Studies

The BOSTON-1 and BOSTON-2 studies are currently enrolling patients

BOSTON-1 & BOSTON-2
- Randomized studies
  - 55 pts usual medications + L-CsA-i
  - 55 pts usual medications
  - 55 pts usual medications + L-CsA-i

BOSTON-3
- Open label extension study
  - Usual medications + L-CsA-i

110 Single Lung Transplant Pts*
110 Double Lung Transplant Pts*

* Pts – abbreviation for patients
What is the BOSTON-3 study?

The BOSTON-3 study is a planned extension study of BOSTON-1 & BOSTON-2

- Designed to look at long-term safety and efficacy of L-CsA-i for the treatment of BOS after lung transplantation
- All patients that participate in BOSTON-3 will receive L-CsA-i in addition to their usual medications
- Only patients who complete BOSTON-1 and BOSTON-2 can enroll in the BOSTON-3 study, if they are eligible
- The study will follow patients for up to 3 years
How do I enroll into BOSTON-1 or BOSTON-2?

Talk with your lung transplant doctor or study coordinator

• Your doctor will determine if you are eligible to participate in one of the studies
• Your doctor will review the study details with you
• You are encouraged to thoroughly read the informed consent document and discuss all questions with your doctor
• If you meet the eligibility criteria and agree to participate in one of the studies, your doctor and the study team will schedule you for a Screening Visit
• If your transplant center is not a study site, you can participate if your physician refers you to an active study site
Where can I learn more?

- https://clinicaltrials.gov/ct2/show/NCT03657342?term=NCT03657342&rank=1
- https://clinicaltrials.gov/ct2/show/NCT03656926?term=NCT03656926&rank=1
- https://clinicaltrials.gov/ct2/about-studies/learn
People living with rare lung diseases are at the center of everything we do

CONTACT:
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