**Study Rationale**

- Eryaspase is an investigational drug product that is produced by encapsulating L-asparaginase, an asparagine-catabolizing enzyme, inside donor-derived erythrocytes.
- Asparagine is a non-essential amino acid that many cancer cells are unable to produce in large enough quantities to support their aberrant metabolism; therefore, they are sensitive to asparagine depletion.
- L-asparaginase, in its native, non-encapsulated form, has been used as an anti-cancer agent for decades; however, its use has been associated with toxicities such as hypersensitivity reactions, coagulopathy, as well as hepatic and pancreatic toxicities, particularly in solid tumors.1,2
- The encapsulation approach has been shown to prolong the activity and reduce the toxicity of native enzymes.3
- Pancreatic cancer is predicted to become the second most lethal malignancy in the United States, and additional treatment options remain a significant unmet need.4
- Pancreatic ductal adenocarcinoma (PDAC) is characterized by extensive metastases and poor overall survival.5
- Studies have demonstrated promising anti-cancer effects for L-asparaginase against human pancreatic tumor cells.6

**Previous Phase 2 Study Experience in Pancreatic Cancer**

- In a recent randomized phase 2 study in patients with advanced PDAC whose disease progressed following first-line treatment (NCT02195188), the addition of eryaspase to chemotherapy significantly prolonged median overall survival (mOS) with an acceptable safety profile.8
- These results provided a rationale for initiating this ongoing confirmatory phase 3 pivotal trial (Trybeca-1, NCT03665441).

**Study Design**

**Study Participants (N=≈500):**
- **Stage IV Pancreatic Cancer**
  - First Relapse
  - Performance Status of 0/1

**Key Eligibility Criteria**

- **Eighteen (18) years of age or older**
- **Histologically confirmed pancreatic ductal adenocarcinoma**
- **Stage IV disease**
  - Received only one prior line of systemic chemotherapy with or without targeted agents, immunotherapy, or radiotherapy for treatment of advanced PDAC
  - Radiological evidence of disease progression following most recent prior treatment
  - ECOG PS of 0 or ECOG PS of 1 and score of ≥80 on Karnofsky Performance Status Scale

**Secondary Objectives**

- To determine the pharmacokinetics of eryaspase in combination with gemcitabine or FOLFOX as second-line treatment of pancreatic cancer compared to chemotherapy alone

**Primary Objective**

- To determine whether the addition of eryaspase to chemotherapy improves mOS in second-line treatment of pancreatic cancer compared to chemotherapy alone

**Treatment Administration**

- Eryaspase will be given every two weeks, intravenously (IV) via a standard pathway through approximately 60 minutes, followed by chemotherapy
- Chemotherapy will be administered according to local practice
- Patients may receive gemcitabine + albumin-bound paclitaxel or an irinotecan-based chemotherapy regimen, depending on the previous treatment received

**Statistical Plan**

- Patients are stratified based on choice of chemotherapy, and time since diagnosis of advanced disease
- The interim analysis for efficacy will take place once 67% of events have occurred
- Life expectancy of >12 weeks

**Trial Design**

- 1L Gemcitabine-based Chemotherapy
- 2L FOLFIRI/NALIRI +/- eryaspase
- 1L Fluoropyrimidine-based Chemotherapy
- 2L Gemcitabine/ Abraxane +/- eryaspase

**Key Outcomes**

- Treatment and disease progression
- Overall survival

**Study Progress**

- This is a global trial that will enroll patients in several European countries and the United States
- CTA approvals in UK, Spain, France, Italy, Czech Republic, Sweden, Austria, and Denmark
- 10% of patients are currently treated with advanced pancreatic cancer; you may refer to second-line treatment to the Trybeca-1 investigational center at: trybeca-protocolo@erytech.com

**References**

2. Liu, et al., Targeting the novel GTPase Arl6 in ovarian cancer Cancer Res 77 (2017)
5. References to all data are provided in the paper. The data were retrieved from various sources, including clinical trials, academic journals, and other reputable medical sources. The data presented are intended for educational and research purposes only.
6. The authors wish to thank the patients and their families, all investigators, and site personnel for their participation in the study. This study was supported in part by Eli Lilly and Company and Erytech Pharma Inc., Cambridge, MA.

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**Contact Information**

- For more information, please visit: trybeca1.com

**Contact Information**

- Telephone: +1 866-469-0255
- E-mail: info@trybeca1.com

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