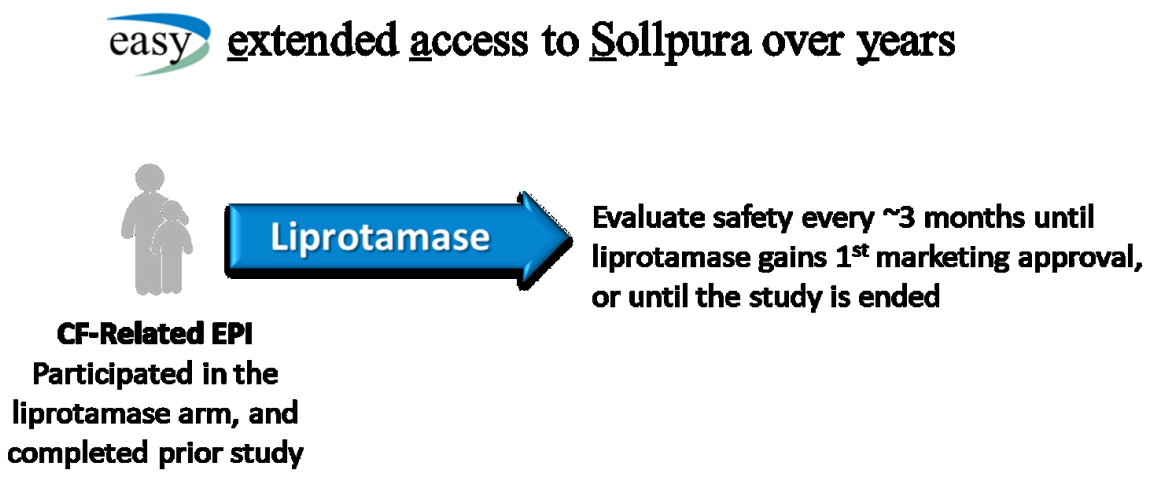
PROTOCOL SYNOPSIS

Sponsor:	Anthera Pharmaceuticals, Inc.
Product Name:	Liprotamase
Indication:	Cystic Fibrosis-Related Exocrine Pancreatic Insufficiency
Protocol Title:	An Open-Label Study Evaluating the Efficacy and Safety of Liprotamase in Subjects with Exocrine Pancreatic Insufficiency due to Cystic Fibrosis
Study Name:	**EASY**: **E**xtended **A**ccess to **S**ollpura over **Y**ears
Planned Study Centers:	Centers having participated in Study AN-EPI3331 or participating in Study AN-EPI3333
Treatment Duration:	Until the first commercial authorization of liprotamase or until the Sponsor discontinues the study.
Number of Subjects:	Approximately 50: Subjects with a diagnosis of Cystic Fibrosis-Related EPI who completed Study AN-EPI3331 or Study AN-EPI3333 and were receiving liprotamase may be eligible to enroll.
Objectives:	To evaluate the safety of long-term use of liprotamase in the management of Cystic Fibrosis-Related Exocrine Pancreatic Insufficiency (EPI)
Study Schematic:	



Study Design:	• This is a multi-center, open-label study in which subjects who received liprotamase and completed Study AN-EPI3331 (the SOLUTION Study) or who completed AN-EPI3333 (the RESULT Study) at a lipase-CLEC dose of >10,000 U lipase-CLEC/kg/day and CFA of at least 80% may continue to receive liprotamase to evaluate the safety of long-term use of liprotamase in the management of EPI due to CF. • Subjects will be assessed approximately every 3 months throughout this study for safety and control of nutritional status. • Throughout this study, subjects should continue to receive the pre-study background medications for treatment of CF, including approved potentiators or modulators of the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR), and gastric acid suppression medication. • Upon enrollment into the EASY Study, all subjects will receive liprotamase at the dose they were receiving in the prior study. Subsequent dose adjustments are allowed at any time based on Investigator assessment of nutritional status, food consumption, age, weight, fat intake, and clinical signs of malabsorption, as long as the protocol-defined maximum dose is not exceeded. The maximum allowed doses of study drug are defined as follows: o For all subjects regardless of age, dose increases up to 10,000 U lipase-CLEC/kg/day and 2,500 U lipase-CLEC/kg per meal or snack can be made irrespective of pre-study lipase dose, per CFF guidelines. o For subjects who enrolled from the RESULT Study, their final, optimized liprotamase dose from the RESULT Study is their maximum allowed dose in the EASY study. • The liprotamase dose may be adjusted, within the above constraints, at any time during the EASY Study by the Investigator based on clinically-observed symptoms of malabsorption or as-reported by the subject and/or parent/caregiver. It is recommended that all subjects enrolled in this study follow the nutritional recommendations from the Cystic Fibrosis Foundation (*Stallings 2008, Borowitz 2009*).
Inclusion Criteria:	Subjects are eligible for enrollment if they meet the following inclusion criteria: 1. Male or female subjects who received liprotamase and completed Study AN-EPI3331, or who completed Study AN-EPI3333 at a liprotamase dose >10,000 U lipase-CLEC/kg/day and CFA ≥80% 2. Signed informed consent by subject and/or subject's legally authorized representative

Exclusion Criteria:	Subjects must NOT meet any of the following exclusion criteria: 1. Any medical, psychological or social condition, or clinical or laboratory abnormality (in the previous study or currently) that, at the discretion of the Investigator, may put the subject at increased risk by participating in this study or confound interpretation of study results. 2. Treatment with any PERT other than study drug, investigational drugs, or devices 3. Females who are nursing, pregnant, intending to become pregnant, or intending to nurse during the time of the study, or who have a positive pregnancy test at Visit Day 1. All sexually-active subjects of reproductive potential are required to remain on a reliable method of birth control. Females and males are required to continue using a reliable method of birth control throughout the study, and for at least 3 months following completion of study therapy. A reliable method of birth control is defined as one of the following: oral or injectable contraceptives, intrauterine device, contraceptive implants, tubal ligation, hysterectomy, or a double-barrier method (diaphragm with spermicidal foam or jelly, or a condom), abstinence or vasectomy. Periodic abstinence (calendar, symptothermal, or post-ovulation methods) is not an acceptable method of contraception. The preferred and usual lifestyle of the subject must also be evaluated in determining if sexual abstinence is a reliable method of birth control. 4. Known hypersensitivity to the study drug and/or the excipients.
Test Product, Dose and Mode of Administration:	Liprotamase is taken orally with meals and snacks. Each dose of liprotamase contains 3 digestive biotechnology-derived enzymes formulated at a fixed ratio of lipase:protease:amylase activities of 1.0 : 1.0 : 0.15, respectively. Liprotamase will be supplied as capsules at 2 dosage strengths: • Oral Capsule: 40,000 U Lipase cross-linked enzyme crystals (CLEC), 40,000 U Protease, 6,000 U Amylase. • Oral Capsule: 10,000 U Lipase-CLEC, 10,000 U Protease, 1,500 U Amylase. Subjects who have completed Study AN-EPI3331 will continue to receive open-label liprotamase, initially at the same dose which they were receiving at the time they completed the prior liprotamase study. The Investigator may subsequently adjust the dose for any subject if judged clinically appropriate up to 10,000 U lipase CLEC/kg/day. For subjects who have completed Study AN-EPI3333 (RESULT), doses will remain the same during the EASY study, with the exception that they may be adjusted on an absolute (lipase Unit) basis to accommodate for changes in body weight. Instructions on dosing of liprotamase are provided in the Pharmacy Manual.

Endpoints:	The primary endpoint analysis will evaluate the long-term safety of liprotamase in qualifying adults and pediatric subjects from Studies AN-EPI3331 and AN-EPI3333. Safety will be evaluated based on adverse events (AEs) and serious AEs (SAEs); including but not limited to abnormal laboratory results, abnormal findings in physical examinations and abnormal vital signs deemed clinically significant by the Investigator. The secondary endpoints will include: • Change in weight, height, and BMI from baseline. • Changes in measures of growth including weight, height, and BMI relative to population anthropomorphic measures. • Signs and symptoms of malabsorption including stool frequency, stool consistency, bloating, steatorrhea, abdominal pain, and flatulence compared with baseline. For efficacy analyses of change from baseline, baseline will be defined as the first observation in this study.
Sample Size and Statistical Methods:	No formal statistical hypothesis testing will be performed
Procedures:	Refer to Schedule of Assessments (Appendix A).