Potential Benefits of Participation

- Bardoxolone methyl has a novel mechanism of action and therefore may provide a new approach to pulmonary hypertension therapy.
- Preliminary data indicate that bardoxolone methyl:
  - Increases 6 minute walk distance (6MWD) after 16 weeks of treatment in pulmonary hypertension patients already receiving background therapies.
  - Improved 6MWD in pulmonary hypertension patients who typically do not respond as well to other therapies, including those with connective tissue disease and higher 6MWD (> 450 m).
- Your participation may help other patients who have been diagnosed with pulmonary hypertension by contributing to medical research.

Potential Risks of Participation

- There is no guarantee that bardoxolone methyl will work for you.
- Although bardoxolone methyl has been well-tolerated in pulmonary hypertension patients, you may experience side effects from the study drug that are not currently known.
- The following are the side effects more commonly reported in bardoxolone methyl-treated pulmonary hypertension patients as compared to placebo:
  - Nausea
  - Dyspnea (shortness of breath)
  - Upper respiratory tract infection
  - Muscle spasm
  - Dizziness
  - Epistaxis (nose bleeds)
- You may receive a placebo instead of bardoxolone methyl, and your condition could get worse. Approximately 25% of participants will receive placebo.

Phases of Participation in LARIAT

Screening — Up to 4 weeks prior to Randomization

- Meet the study team
- Review detailed information about the study with your doctor
- Review medical history
- Physical Exam
- Electrocardiogram
- Blood draws
- 6 Minute Walk Test
- Echocardiogram
- Other assessments

Randomization — Day 1

- Begin daily dosing of bardoxolone methyl or placebo
- Physical exam
- Blood draws
- Other assessments

Treatment — Weeks 1 Through 16

- Daily dosing of bardoxolone methyl or placebo
- Visits to doctor's office
- Telephone calls
- Physical exams
- Electrocardiograms
- Blood draws
- 6 minute walk tests
- Other assessments

Patients completing the 16 week treatment period are eligible to continue into the extension period.

Extension — Weeks 16 Through 128

- Daily dosing of bardoxolone methyl or placebo
- Visits to doctor's office
- Telephone calls
- Physical exams
- Electrocardiograms
- Blood draws
- 6 minute walk tests
- Other assessments

End of Study — Approximately Week 20 OR 132

- Final study visit
- Physical Exam
- Electrocardiogram
- Blood draws
- 6 minute walk test
- Other assessments

Study participation is complete at approximately week 20, or after the extension period.

LARIAT

For more information, or to see if you may qualify for this study, contact:

Name: _____

Phone: _____

Email: _____

This study is being sponsored by Reata Pharmaceuticals.

www.clinicaltrials.gov (NCT02036970)

Version 1.0—24 September 2015

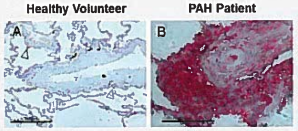
LARIAT

A clinical study in patients with pulmonary hypertension

Understanding Pulmonary Hypertension

Pulmonary hypertension is characterized by narrowing of the blood vessels in the lungs, thereby increasing pressure on the right side of the heart and increasing the chances of heart failure. Researchers have recently shown that the pulmonary arteries of pulmonary hypertension patients often have considerable inflammation, which likely contributes to disease progression through multiple pathways. Additionally, abnormal mitochondria in pulmonary hypertension limit energy production in skeletal muscle, which contributes to fatigue and muscle weakness in the disease.

Inflammation (Red Staining) is Increased in PAH Patients



Current Treatments for Pulmonary Hypertension

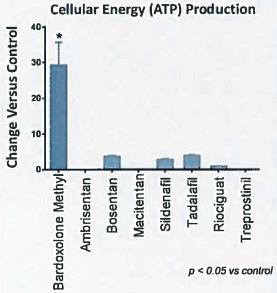
There are four types of treatments for pulmonary hypertension on the market: prostacyclins, endothelin receptor antagonists, phosphodiesterase-5 (PDE-5) inhibitors, and soluble guanylyl cyclase (sGC) modulators. All of these drugs are similar in that they promote the opening up of the arteries in the lung to increase the flow and oxygenation of the blood. However, none of these therapies directly target inflammation or mitochondrial dysfunction in pulmonary hypertension.

About Bardoxolone Methyl

Bardoxolone methyl is a new investigational drug, and closely related drugs have shown activity in animal studies of pulmonary hypertension. Bardoxolone methyl targets pulmonary hypertension at the source of inflammation, so it may treat aspects of the disease in both the lungs and the muscle.

Additionally, available evidence suggests that bardoxolone methyl improves metabolism and mitochondrial function. Impaired energy production in pulmonary hypertension remains unaddressed by available therapies. In cultured muscle cells, bardoxolone methyl improves mitochondrial parameters, including cellular energy (ATP) production while approved PAH therapies have no significant effects on these parameters. Thus, bardoxolone methyl may increase energy production and functional capacity in pulmonary hypertension patients.

Cellular Energy (ATP) Production



p < 0.05 vs control

The LARIAT Study

Researchers are assessing the recommended dosage for bardoxolone methyl, as well as the safety and tolerability of treatment, in adult men and women who have pulmonary hypertension. The types of pulmonary hypertension studied in LARIAT include pulmonary arterial hypertension (PAH) and pulmonary hypertension (PH) due to the following interstitial lung diseases: connective tissue diseases (CTD), idiopathic pulmonary fibrosis (IPF), non-specific interstitial pneumonia (NSIP), and sarcoidosis.

Cohort 3 PAH		Cohort 4 PH Interstitial Lung Disease			
Cohort 3a CTD	Cohort 3b Non-CTD	Cohort 4a CTD-ILD	Cohort 4b IPF	Cohort 4c NSIP	Cohort 4d Sarcoidosis

The LARIAT study will help researchers further explore these ideas and better understand how bardoxolone methyl may be used to treat pulmonary hypertension.

Eligible patients will receive either bardoxolone methyl capsules or placebo capsules, once daily for 16 weeks. All patients who complete treatment in Part 1 of the study are then eligible to participate in Part 2 of the study. Patients may participate in the extension period as long as desired or until the Sponsor ends the study.

If you are between 18 and 75 years of age and have pulmonary hypertension, you may be eligible to participate. Other eligibility criteria will apply. The investigational drug and study-related procedures and doctor visits will be provided at no cost to you. Your participation could last approximately 28-32 months, including screening, study treatment and follow-up. If you decide to participate in this study, your study team will review details of the study, including potential risks, and you will be asked to sign an informed consent document.