



Eiger BioPharmaceuticals Announces Positive Results in Phase 2 PREVENT Study of Avexitide Targeting GLP-1 in Post-Bariatric Hypoglycemia (PBH)

- Primary and Secondary Endpoints Achieved with Statistical Significance**
- Avexitide Treatment Reduces Hypoglycemia and Hyperinsulinism**

PALO ALTO, Calif., Oct. 16, 2018 /PRNewswire/ -- Eiger BioPharmaceuticals, Inc. (Nasdaq:EIGR), focused on the development and commercialization of targeted therapies for rare diseases, today announced positive results from the Phase 2 PREVENT study. PREVENT is a multi-center, placebo-controlled study investigating the safety and durability of effect of 28-day dosing of subcutaneous (SC) avexitide (formerly known as exendin 9-39) in post-bariatric surgical patients who experience dangerously low, postprandial blood glucose levels known as post-bariatric hypoglycemia (PBH). Avexitide is a first in class glucagon-like peptide-1 (GLP-1) antagonist in development for PBH as a convenient, novel liquid formulation for SC administration. PBH is an orphan disease with a high unmet medical need and no approved pharmacologic therapy.

Eighteen patients with refractory, severe PBH were enrolled across five U.S. academic centers and dosed as outpatients in the PREVENT study. All patients received placebo subcutaneous (SC) injections for 14 days in a single-blinded manner followed by avexitide SC 30 mg twice daily (BID) injections for 14 days and 60 mg once daily (QD) injections for 14 days, for a total of 28 days active dosing, in a double-blinded to dose, cross-over design.

The primary efficacy endpoint of improved postprandial glucose nadir during mixed meal tolerance testing (MMTT) was achieved with statistical significance with avexitide 30 mg BID (57.1 vs 47.1 mg/dL; $p = 0.001$) and 60 mg QD (59.2 vs 47.1 mg/dL; $p = 0.0002$), with fewer participants requiring glycemic rescue during each of the active dosing regimens than during placebo dosing.

The secondary endpoint of reduced postprandial insulin peak during MMTT was also statistically significant with avexitide 30 mg BID (349.5 vs 454.5 mIU/mL; $p < 0.03$) and 60 mg QD (357.2 vs 454.5 mIU/mL; $p = 0.04$).

Metabolic and clinical improvements were also monitored during each patients' daily routine in the outpatient setting and assessed by electronic diary and continuous glucose monitoring (CGM). Patients experienced fewer episodes of hypoglycemia (hypoglycemia symptoms confirmed by self-blood glucose monitor (SBGM) concentrations of <70 mg/dL) and severe hypoglycemia (neuroglycopenic symptoms confirmed by SBGM concentrations <55 mg/dL) during both dosing regimens of avexitide as compared to placebo. These results were corroborated by CGM data.

Avexitide was well-tolerated. There were no treatment-related serious adverse events and no participant withdrawals. Adverse events were typically mild to moderate in severity. The most common adverse events were injection site bruising, nausea, and headache, all of which occurred with lower frequency during avexitide dosing periods than during the placebo dosing period.

Co-lead Investigators Helen Lawler, MD, Assistant Professor of Medicine in Endocrinology at University of Colorado at Denver School of Medicine and Marilyn Tan, MD, Clinical Assistant Professor of Medicine in Endocrinology at Stanford University School of Medicine commented on PREVENT results. "Targeted blockade of GLP-1, which is known to be elevated in patients suffering from PBH, significantly reduced postprandial insulin peaks and increased postprandial glucose nadir levels in both once daily and twice daily dosing regimens of avexitide," said Dr. Lawler. "PREVENT results are promising for patients suffering from post-bariatric hypoglycemia, a growing and debilitating complication of bariatric surgery for which an effective treatment is urgently needed," said Dr. Tan.

"We are very pleased by the results from PREVENT, our first outpatient study of avexitide in patients suffering from PBH," said Lisa Porter, MD, Chief Medical Officer of Metabolic Diseases at Eiger. "Avexitide treatment led to clinically meaningful improvements consistently throughout 28-days of treatment, reducing postprandial hyperinsulinemic hypoglycemia and associated signs and symptoms. We look forward to meeting with regulatory authorities, both FDA and EMA, to discuss next steps."

Avexitide is a first in class, GLP-1 antagonist in development as a convenient, novel liquid formulation for SC administration for PBH. Eiger has now generated positive results from 4 separate proof of concept clinical studies in 54 PBH patients treated with avexitide, demonstrating that pharmacologic blockade of GLP-1 with avexitide prevents hypoglycemia in post-bariatric surgical patients.

About the PREVENT Study

The PREVENT study is a Phase 2, multicenter, randomized, single-blind, placebo-controlled cross-over study to assess the efficacy and safety of 28-day dosing of avexitide in patients with post-bariatric hypoglycemia (PBH). A total of 18 patients were

enrolled and treated with two dosing regimens (once daily and twice daily) of avexitide for 28 days. All patients participated in three 14-day treatment periods, involving placebo subcutaneous (SC) injections, once-daily avexitide SC injections, and twice-daily avexitide SC injections. Patients self-administered injections in an outpatient setting. Participants underwent in-clinic mixed meal tolerance test (MMTT) provocations with concomitant blood draws and symptom assessments following each treatment period.

Metabolic and clinical improvements were monitored during each patients' daily routines in the outpatient setting and assessed by electronic diary and continuous glucose monitoring (CGM). Outcomes include improvement in plasma glucose nadir levels, reduction in peak insulin concentrations, and the requirement for rescue during MMTT provocation.

About Insulin, GLP-1, and Avexitide

Insulin is the principal physiologic hormone secreted to control high blood glucose levels. Abnormal increases in insulin secretion can lead to profound hypoglycemia (low blood sugar), a state that can result in significant morbidities, including seizures, brain damage, and coma. Glucagon-like peptide-1 (GLP-1) is a gastrointestinal hormone that is released postprandially from the intestinal L-cells. GLP-1 binds to GLP-1 receptors on the beta cells of the pancreas and increases the release of insulin. In patients with PBH, GLP-1-mediated insulin secretion is dysfunctionally exaggerated.

Avexitide (formerly exendin 9-39) is a 31-amino acid peptide that selectively targets and blocks GLP-1 receptors, normalizing insulin secretion by the pancreas, and thereby reducing postprandial hypoglycemia. Avexitide is being investigated as a novel treatment for PBH. Avexitide has been granted orphan designation in the European Union by the EMA for the treatment of non-insulinoma pancreatogenous hypoglycemia syndrome (NIPHS) and orphan designation in the United States by the FDA for the treatment of hyperinsulinemic hypoglycemia. Both of these broad designations include PBH. Avexitide has never been approved or commercialized for any indication. More information on avexitide clinical trials may be found at www.clinicaltrials.gov.

About Post-Bariatric Hypoglycemia (PBH)

Approximately 150,000-200,000 bariatric surgical procedures are performed each year in the United States, and another 100,000 are performed each year in Europe. The estimated prevalence of PBH is approximately 30,000 in the United States and approximately 25,000 in the European Union. As the number of bariatric surgeries to treat obesity and related comorbidities has increased, so too has the number of individuals who experience PBH, with symptoms typically developing one or more years following surgery. PBH can occur with a range of severity in post-bariatric surgery patients. Mild to moderate hypoglycemia may be managed largely through dietary carbohydrate restriction, whereas severe hypoglycemia results in neuroglycopenic outcomes (altered mental status, loss of consciousness, seizures, coma) which are unresponsive to diet modification. Severe PBH can be debilitating with a significant negative impact on quality of life. There is no approved pharmacologic therapy.

About Eiger

Eiger is a clinical-stage biopharmaceutical company focused on the accelerated development and commercialization of targeted therapies for rare and ultra-rare diseases. We innovate by developing well-characterized drugs acting on newly identified or novel targets in rare diseases. Our mission is to systematically reduce the time and cost of the drug development process to more rapidly deliver important medicines to patients. Lonafarnib is our lead compound advancing into Phase 3 with a single, pivotal trial to treat HDV to initiate by the end of the year. Lonafarnib is also advancing toward an NDA for the treatment of Hutchinson-Gilford Progeria Syndrome (HGPS or Progeria) in 2019. For additional information about Eiger and its clinical programs, please visit www.eigerbio.com.

Note Regarding Forward-Looking Statements

This press release contains "forward-looking" statements that involve substantial risks and uncertainties. All statements other than statements of historical facts, including statements regarding our future financial condition, timing for and outcomes of clinical results, business strategy and plans and objectives for future operations, are forward looking statements. These forward-looking statements include terminology such as "believe," "will," "may," "estimate," "continue," "anticipate," "contemplate," "intend," "target," "project," "should," "plan," "expect," "predict," "could," "potentially" or the negative of these terms. Forward looking statements are our current statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our ongoing and planned clinical development, including whether the D-LIVR study will be successful as a single, pivotal study to support registration; the timing of and our ability to initiate or enroll clinical trials, including whether our D-LIVR study can be advanced by the end of this year; the timing for completion and potential filing for registration for our clinical candidates; whether PREVENT Phase 2 study results of avexitide will be repeated in larger, more advanced clinical trials and the timing and costs of such trials; our ability to make timely regulatory filings and obtain and maintain regulatory approvals for lonafarnib as a single agent or in combination, ubenimex, PEG IFN lambda, avexitide and our other product candidates; our intellectual property position; and the potential safety, efficacy, reimbursement, convenience clinical and pharmaco-economic benefits of our product candidates as well as the commercial opportunities, including potential market sizes and segments; our ability to finance the continued advancement of our development pipeline products, including our results of operations, cash available, financial condition, liquidity, prospects, growth and strategies; and the potential for success of any of our product candidates.


Various important factors could cause actual results or events to differ materially from the forward-looking statements that Eiger

makes, including the risks described in the "Risk Factors" sections in the Quarterly Report on Form 10-Q for the quarter ended June 30, 2018 and Eiger's periodic reports filed with the SEC. Eiger does not assume any obligation to update any forward-looking statements, except as required by law.

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