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Elixir Pharmaceuticals Announces New Data at the 2008 American Diabetes Association Annual Meeting

Knockout Animal Model Findings Validate Ghrelin's Role as a Key Metabolic Regulator and Demonstrate Potential to Develop New Therapies for Diabetes, Obesity

American Diabetes Association Annual Meeting

CAMBRIDGE, Mass.--([BUSINESS WIRE](#))--Elixir Pharmaceuticals, Inc., today announced new data validating ghrelin, a potent, naturally occurring hormone, as a master regulator of metabolism. The data provides the most advanced evidence to date of the array of metabolic improvements in mice genetically engineered to lack the receptor for ghrelin ("knockout" mice). In particular, the results demonstrated organ-specific improvements that ultimately may have an impact in the treatment of type 2 diabetes and other widespread metabolic diseases.

Results were obtained using the hyperinsulinemic euglycemic clamp, the gold standard in measuring insulin resistance, as well as a newly developed hyperglycemic clamp model. The knockout mice (lacking the ghrelin receptor) demonstrated a greatly improved metabolic profile compared to a matched set of normal mice, whether they were placed on a high-fat diet (HFD) or low-fat diet (LFD). Specifically, the knockout mice showed significant reductions in glucose production in the liver on both diets and a significant increase in glucose uptake in muscle and fat tissue on HFD. The results were consistent with an increase in insulin sensitivity, a key goal in controlling type 2 diabetes.

Dr. Peter S. DiStefano, Chief Scientific Officer of Elixir Pharmaceuticals and an author on the abstract, stated, "These are the first publicly available results demonstrating organ-specific effects of the ghrelin knockout using glycemic clamp technology developed at Elixir. These exciting findings show that blocking ghrelin signaling has a positive effect on metabolically important tissues, including muscle and liver. The results provide key support for Elixir's small molecule, oral ghrelin antagonist which Elixir is advancing as a potential treatment for type 2 diabetes and other metabolic diseases."

The data abstract, titled "Improved Insulin Sensitivity in Ghrelin Receptor Knockout Mice Assessed by Hyperinsulinemic-Euglycemic Clamp" (Abstract # 2600-PO), was published in the American Diabetes Association 2008 Scientific Sessions Abstract book. Contributing authors were as follows: Y. Qi, D. Giuliana, S. Gagne, T. McDonagh, E. Govek, A. Nolan, K. A. Longo, S. Charoenthongtrakul, C. Zou, J. Hixon, J. O. Saunders, P. S. DiStefano, B. J. Geddes. The abstract is available on the American Diabetes Association website.

About Ghrelin

Ghrelin is a naturally occurring hormone secreted by the stomach, which acts primarily at the level of the hypothalamus in the brain. A key metabolic regulator, ghrelin plays a significant role in the regulation of glucose homeostasis, lipid profiles and body composition. It has been shown to stimulate appetite and food consumption, as well as play a central role in metabolism and energy storage. For example, genetically eliminating or "knocking out" ghrelin or the ghrelin receptor results in increased insulin sensitivity, improved triglyceride and cholesterol levels, and overall resistance to obesity in mice fed a high-fat diet.

About Elixir's Ghrelin R&D Programs

Using structure-assisted drug design, a method of creating chemical compounds based on an understanding of the

configuration of the human ghrelin receptor, Elixir has internally discovered and developed a series of potent, small molecule antagonist compounds that block the ghrelin receptor. Oral administration of these compounds in animal models of diet-induced obesity and early diabetes resulted in similarly favorable metabolic effects to those seen in knockout models with respect to improved blood glucose levels, insulin resistance, HbA1c, triglycerides, total cholesterol, liver fat, body weight and white fat when compared to placebo. Elixir is completing selection of a clinical candidate and expects to file an investigational new drug (IND) application with the U.S. Food and Drug Administration (FDA) early in 2009, initiating a phase I clinical trial shortly thereafter.

In addition, the Company has submitted an IND to the FDA for EX-1314, Elixir's novel oral ghrelin agonist. EX-1314 is being developed for the treatment of chronic gastrointestinal disorders, including gastroparesis, a disorder in which the stomach takes too long to empty its contents. EX-1314 will be developed initially for gastroparesis in patients with type 1 diabetes, which is the most common systemic cause of gastroparesis.

About Elixir Pharmaceuticals

Elixir is a pharmaceutical company focused on the discovery, development and commercialization of novel pharmaceuticals for the treatment of metabolic diseases such as diabetes and obesity. The Company's scientific founders identified that modulation of specific genes can slow the aging process and increase longevity. Elixir is developing small molecule drugs that mimic these longevity responses, and these drugs will be used to treat a range of age-related diseases, including the major metabolic diseases.

In addition to oral ghrelin antagonists and agonists, the Company has two late-stage products (Metgluna™ and Glinsuna) for the treatment of type 2 diabetes in a final phase III trial in the U.S., with NDA filing expected in 2009. Further, the Company's SIRT product development program is exemplary of how Elixir continues to use its understanding of the pathways which slow the aging process to identify interesting targets for the development of drugs to treat metabolic disease.

About Metgluna and Glinsuna

For patients with type 2 diabetes not well controlled on metformin alone, Metgluna will provide additional HbA1c reduction through comprehensive glycemic control via two complementary mechanisms of action. Metgluna is a fixed combination tablet of metformin, which helps control fasting plasma glucose by improving insulin sensitivity, and mitiglinide, a product that mimics the body's natural response to glucose by producing a rapid and brief burst of insulin when glucose levels begin to rise to provide for better control of post-meal glucose surges.

The companion product Glinsuna has been studied extensively in human clinical studies in the U.S., Europe, Australia, and Asia. Clinical trial results, including more than 1,500 patients treated in phase III trials, have demonstrated an excellent safety and efficacy profile for mitiglinide as monotherapy or in combination with metformin. An ongoing phase III clinical study enrolled more than 300 patients across 60 sites in the U.S. and was designed to evaluate the efficacy and safety of Glinsuna in combination with metformin in patients whose blood sugar is not adequately controlled by metformin alone.

Elixir in-licensed North and South American rights to mitiglinide from Kissei Pharmaceuticals. Under the terms of the licensing agreement, Elixir has the right to develop and commercialize mitiglinide and any future product combinations, in the U.S., Canada and Latin America.

About Elixir's Sirtuin Development Program

Building upon the Company's knowledge of the regulation of aging and metabolism, Elixir Pharmaceuticals has developed a leadership position in the field of sirtuins, or SIRT, a class of seven naturally occurring human enzymes, known to affect the storage and use of energy in cells. Elixir Pharmaceuticals believes that sirtuin modulators, compounds which increase or decrease the activity or the amount of sirtuin enzymes, may have potential clinical utility in numerous, large pharmaceutical markets with unmet medical needs, such as metabolic disease, cancer and neurodegenerative diseases. Elixir Pharmaceuticals has an extensive intellectual property position with regards to screening, chemical composition of matter and utility claims for sirtuin modulators.

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