Elixir Pharmaceuticals Researchers Publish New Data Validating Ghrelin as a Key Metabolic Regulator

Compelling Evidence in Knockout Model Provides Further Support for Elixir's Oral Ghrelin Antagonist

Cambridge, MA – May 28, 2008 – Elixir Pharmaceuticals, Inc., today announced publication in a peer-reviewed journal of new data that further establish ghrelin, a potent, naturally occurring hormone, as a master regulator of metabolism. The data describe an array of physical and metabolic improvements in mice genetically engineered to lack the receptor for ghrelin (“knockout” mice), despite their having been fed a high-fat diet. These findings provide additional support for Elixir’s small molecule, oral ghrelin antagonist as a potential treatment for type 2 diabetes and other metabolic diseases.

This publication highlights the improved metabolic profile of the knockout mice (lacking the ghrelin receptor) compared to a matched set of normal mice, which have all been placed on a high-fat diet:

- The knockout mice have significantly lower levels of hemoglobin A1c (HbA1c) as well as lower levels of fasting plasma glucose. HbA1c is the most widely accepted measure of long-term blood sugar control in diabetic patients. In the study, the lower plasma glucose levels were a result of a marked increase in insulin sensitivity. Increased insulin sensitivity is a key goal in controlling type 2 diabetes.

- Although the animals in both groups ate an equivalent high-fat diet, the knockout animals had a 19 percent lower body weight. The vast majority of the weight difference was due to a reduced amount of white fat. Importantly, there was no difference in lean body mass or brown fat resulting in improved overall body composition. While these knockout mice had lower levels of white fat throughout the body, there was dramatically less fat particularly in the livers of the knockouts when compared to normal mice. A contributing factor to the lower weight and lower amount of white fat in the knockout mice was that they demonstrated lower rates of intestinal fat absorption.

- The knockout mice fed a high-fat diet displayed a wider range in respiratory quotient (RQ) indicating greater metabolic flexibility. This phenomenon characterizes a healthy state reversing a key dysfunction of the disease states encompassed by the term ‘metabolic syndrome’. Normal mice fed a high-fat diet demonstrated reduced metabolic flexibility.

- Total cholesterol was approximately 20% lower on average in the knockout animals as compared to normal animals.
Dr. Peter S. DiStefano, Chief Scientific Officer of Elixir Pharmaceuticals and an author of the paper, stated, “Our positive results in this knockout model are perhaps the most important validation to date of the potential value of pharmacologic inhibition of ghrelin receptor signaling. Indeed, knockout models are the gold standard, accurately gauging the efficacy of the 100 best-selling drugs. The fact the knockout mice in our research are healthy and show an interesting phenotype provides additional, compelling support of our program to advance a product into clinical testing.”


**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) later this year. Based on this timeline, the Company anticipates initiating a phase I clinical trial by the end of 2008.

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, in which the stomach takes too long to empty its contents because muscles of the stomach are not functioning normally. 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 (Glinsuna™ (mitiglinide) and Metgluna™, combining metformin 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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