News Release

Metabolic Solutions Development Company novel insulin sensitizer meets Phase 2b study endpoints and affirms new mechanism of action

Breakthrough understanding may have significant implications for the discovery and development of new therapeutics to treat the root cause of type 2 diabetes

PHILADELPHIA, June 9, 2012 - Metabolic Solutions Development Company, LLC (MSDC) presented Phase 2b results for MSDC-0160 today at the 72nd Scientific Sessions of the American Diabetes Association. The data showed this novel once-a-day oral insulin sensitizer, the first in a new class of therapeutic agents called mTOT Modulators™, met the study's primary endpoint of significantly reducing fasting plasma glucose (FPG) in patients diagnosed with type 2 diabetes, and significantly reduced hemoglobin A1c (HbA1c).

Of particular importance, the data showed that changes in body weight, hemoglobin, and an important biomarker linked to production of white fat were significantly less in type 2 diabetic patients treated with MSDC-0160 than in patients treated with a comparator drug, pioglitazone 45 mg.

"These results affirm our hypothesis that insulin sensitization is controlled through a newly defined, mitochondrial protein complex we have identified as mTOT™," said Jerry Colca, PhD, MSDC's co-founder, president and chief scientific officer. "We believe this new understanding may have significant implications for the discovery and development of new mTOT Modulators to treat insulin resistance without the side effects attributed to currently approved insulin sensitizers."

In a separate presentation at this meeting (ADA Abstract #1096-P), MSDC researchers discussed their discovery of a newly identified mitochondrial protein complex, which they refer to as the mitochondrial Target of Thiazolidinediones (TZDs), or mTOT™. mTOT functions as a molecular "sensor switch" connecting mitochondrial metabolism to important cellular activities, such as carbohydrate, lipid, and amino acid metabolism, that are out of balance in patients with type 2 diabetes.

Importance of mTOT Discovery to Future Development of Anti-Diabetic Drugs

MSDC researchers have long hypothesized that lowering of plasma glucose can be achieved without having to activate a nuclear receptor called PPARγ. Previously, it was believed that both the activity and the side-effects of the only approved class of drugs used to treat insulin resistance -- the core problem for persons diagnosed with type 2 diabetes -- were mediated through PPARγ. However, it is now generally accepted that over-activation of PPARγ drives the unwanted and often unacceptable side effects associated with the currently approved anti-diabetic insulin sensitizers, which are PPARγ agonists.

Data from studies in obese mice[1], as well as Phase 2 clinical studies of MSDC-0160 and a second oral anti-diabetic investigational drug, MSDC-0602, affirm the company's hypothesis that improvement in insulin sensitivity can occur independent of the activation of PPARγ.

About the MSDC-0160 Phase 2b Study

This study was a 90-day, randomized, double-blind, comparator- and placebo-controlled, multi-dose study in 266 patients with type 2 diabetes. The study compared three doses of MSDC-0160 (50 mg, 100 mg and 150 mg) to maximum dose Actos (pioglitazone) (45 mg) or placebo taken orally once daily for 12 weeks. All treatments were well tolerated. There were no serious adverse events attributed by investigators to the MSDC drug.

Key top-line data from this study include the following:

- Both 100 mg/day and 150 mg/day of MSDC-0160 significantly lowered fasting plasma glucose (primary study endpoint).
- Both 100 mg/day and 150 mg/day of MSDC-0160 lowered hemoglobin A1c similar to 45 mg/day pioglitazone.
- MSDC-0160 produces significantly less volume expansion than pioglitazone at any dose. There was a statistically significant difference between MSDC-0160 and pioglitazone in the effects the compounds on circulating hemoglobin and red blood cells.
- No dose of MSDC-0160 was able to increase adiponectin as much as pioglitazone, supportive of less effect on calorie storing white adipose tissue (i.e., white fat).

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[1] **Insulin resistance and metabolic derangements in obese mice are ameliorated by a novel peroxisome proliferator-activated receptor g-sparing thiazolidinedione**. *Journal of Biological Chemistry*, published online May, 2012; http://www.jbc.org/content/early/2012/05/23/jbc.M112.363960.

- The 100 mg dose of MSDC-0160 was effective with significantly less weight gain. Moreover, given the differential effects on adiponectin, pioglitazone weight gain may involve more increase in white adipose tissue than any dose of MSDC-0160.

About Metabolic Solutions Development Company

Metabolic Solutions Development Company (www.msdrx.com) is a drug discovery and development company investigating novel molecular targets and developing new therapeutics to treat metabolic diseases associated with age-related mitochondrial dysfunction, especially insulin resistance and type 2 diabetes. The company was founded in 2006 by former researchers of The Upjohn Company and has raised more than $55 million to support development of its lead compounds MSDC-0160 and MSDC-0602.

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