Oral Presentation 21
Session: *Brown adipose tissue and mitochondria*
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Metabolic Solutions Development Company presents new brown fat research at the European Association for the Study of Diabetes

Novel insulin sensitizers that increase brown fat in a PPAR-independent manner may have important implications for the development of new therapies to treat type 2 diabetes

LISBON, September 13, 2011 – Metabolic Solutions Development Company, LLC (MSDC) presented results today demonstrating its novel insulin sensitizers, MSDC-0160 and MSDC-0602, stimulate progenitor cells within subcutaneous fat tissue to become brown-like fat cells instead of white fat cells. Brown fat, which diminishes with age, burns calories while white fat stores calories. The mechanism of action by which MSDC-0160 and MSDC-0602 cause these effects is independent of the activation PPARγ, a factor that drives the expansion of white fat. These findings suggest the potential for minimizing weight gain normally associated with currently marketed insulin sensitizers, and may result in weight loss in longer duration clinical studies. The data were presented in an oral presentation at the 47th European Association for the Study of Diabetes (EASD) Annual Meeting in Lisbon, Portugal.

MSDC-0160 and MSDC-0602 are novel insulin sensitizers that are selective for mTOT, a mitochondrial molecular target that functions as a “switch” connecting mitochondrial

metabolism to important cell functions. Previous studies have shown the PPAR-independent pharmacology of each of these compounds results in improved insulin action, preservation of beta cell function, and generation of brown fat. The amount of brown fat is inversely proportioned to body weight (and white fat).

“Given the novel mechanism of action of our compounds, we expect to see weight control over longer duration treatments with these new clinical candidates as a result of the “browning” of adipose or fat stores,” said Jerry Colca, Ph.D., president and Chief Scientific Officer of MSDC. “These results in the preclinical setting have important mechanistic implications for developing future therapies and provide a framework for further defining the mTOT biochemical pathway.”

Study Methodology and Key Results

In this *in* vitro study, progenitor cells from axillary adipose depots (fat tissue located in the armpit region) were isolated from mice and placed in tissue culture under defined conditions. Treatment of these cells with micromolar concentrations of the MSDC compounds elicited a time- and dose-dependent differentiation of the progenitor cells into brown-like adipose cells. The brown-like adipose cells express UCP1 message and protein in a process that includes increased mitochondrial biogenesis. These effects were not attenuated by the potent PPARγ antagonists, T0070907 and GW9662, confirming the PPAR-independent pharmacology of the MSDC compound. Importantly, the cells from axillary adipose depots also secreted the insulin-sensitizing hormone adiponectin in response to the MSDC compounds. These results show that novel insulin sensitizers that increase brown fat could have important implications for the development of new therapies to treat type 2 diabetes.

About Metabolic Solutions Development Company

Metabolic Solutions Development Company (www.msdrx.com) is a drug discovery and development company investigating novel molecular targets and new therapies for metabolic diseases associated with mitochondrial dysfunction, especially insulin

resistance and type 2 diabetes. The company has raised more than $55 million to support development of its lead compounds MSDC-0160 and MSDC-0602.

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