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Metabolic Solutions Development Company announces publication of data describing potential for new drugs to maintain pancreatic β -cells in treating diabetes

mTOT Modulators may provide a new tool for preserving β -cell function in patients with type 2 diabetes

KALAMAZOO, Mich., May 29, 2013 - Metabolic Solutions Development Company, LLC ([MSDC](#)) announced today the publication of data in a recent issue of the scientific journal PLOS ONE (<http://dx.plos.org/10.1371/journal.pone.0062012>) on the effects of a new drug for type 2 diabetes in restoring insulin sensitivity and insulin content in human beta- (β -) cells. Researchers at Washington University in St. Louis, led by Michael McDaniel, PhD, and Nidhi Rohatgi, PhD, found this next generation insulin sensitizer may provide physicians with a new tool for the treatment of diabetes that relieves insulin resistance in human islets, thereby preserving the survival and function of human β -cells.

β -cells are produced in regions in the pancreas referred to as “islets”. Their function is to produce, store and release insulin, a hormone essential to the efficient utilization of glucose, a type of sugar that comes from carbohydrate foods and that is the body’s main source of energy.¹ In patients with type 2 diabetes, β -cell death is increased and the number of β -cells is reduced. In addition, their function may have declined by as much as 80 percent by the time treatment is initiated,² resulting in lower insulin levels and higher glucose levels. In this laboratory study, researchers found that direct treatment of cultured human islets with a new drug for the treatment of type 2 diabetes, MSDC-0160, produced a unique modulation of nutrient sensors that restored normal cell communication mechanisms and enabled the survival and preservation of human β -cell function, including insulin content.

Diabetes is an undertreated global epidemic affecting an estimated 340 million people worldwide, with a rapidly increasing incidence throughout the developed and developing world. In the United States alone, nearly 26 million adults and children live with the disease. An additional 79 million have pre-diabetes, placing them at increased risk for developing type 2 diabetes. Recently published [research](#) by the American Diabetes Association estimates the total costs of diagnosed diabetes have risen to \$245

billion in 2012 from \$174 billion in 2007, when the cost was last examined. This figure represents a 41 percent increase over a five-year period.

MSDC-0160, a prototype mTOT modulator developed by MSDC, exerts its insulin sensitizing effects through a recently identified mitochondrial protein complex called mTOT™ (mitochondrial target of thiazolidinediones).³ Data suggest mTOT functions as a molecular sensor switch that coordinates carbohydrate, lipid, and amino acid metabolism with cell function. In addition to preserving β -cell function as observed in human islets, mTOT modulators have been shown in animal models of type 2 diabetes to improve insulin signaling, decrease calorie-storing “white fat,” and increase levels of calorie burning “brown fat.”

Recently published Phase 2b clinical data from a study⁴ in 258 type 2 diabetic patients further demonstrate modulating mTOT could constitute a new approach for the discovery and development of potentially more useful and novel insulin sensitizers.

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 type 2 diabetes.

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¹ <http://diabetes.webmd.com/blood-glucose>.

² DeFronzo, RA. *Diabetes*, Vol. 58, April 2009, pp. 773-795.

³ <http://dx.plos.org/10.1371/journal.pone.0061551>: “Identification of a Mitochondrial Target of Thiazolidinedione Insulin Sensitizers (mTOT) - relationship to newly identified mitochondrial pyruvate carrier proteins.”

⁴ Colca, *et al.* Clinical Proof-of-Concept Study With MSDC-0160, a Prototype mTOT-Modulating Insulin Sensitizer. *Clinical Pharmacology & Therapeutics* doi:10.1038/clpt.2013.10 .