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**Metabolic Solutions Development Company presents Phase 2a clinical trial results at the
14th International Conference on Alzheimer's Drug Discovery**

Study suggests novel insulin sensitizer may prevent cognitive decline in people with Alzheimer's-related dementia

KALAMAZOO, Mich., /Sept. 9, 2013 - Metabolic Solutions Development Company, LLC ([MSDC](#)) has announced that Jerry Colca, PhD, co-founder and chief scientific officer of MSDC, will present results of a Phase 2a study on September 9 at the 14th International Conference on Alzheimer's Drug Discovery. In people with dementia due to Alzheimer's disease (AD) who were not diabetic, the study found that the mTOT™-modulating insulin sensitizer (MSDC-0160) maintained glucose metabolism in key regions of the brain associated with cognitive decline due to AD, as confirmed by FDG-PET imaging.

Glucose is a major energy source for cells, and alterations in glucose metabolism by nerve cells (neurons) in the brain have been associated with AD pathology.^{1,2} Moreover, reduced brain glucose metabolism is region specific.^{3,4,5} In this study, in participants treated with placebo, the measure of glucose uptake significantly declined in key regions of the brain associated with cognitive decline in persons with dementia due to Alzheimer's disease; however, this did not occur in the subjects treated with MSDC-0160.

"We are in urgent need of new approaches in Alzheimer's drug research because there are currently no approved therapies to halt or even slow progression of the disease," said Howard Fillit, MD, Executive Director and Chief Science Officer of the Alzheimer's Drug Discovery Foundation. "The mitochondrially-targeted insulin sensitizers are an exciting new class of drugs in Alzheimer's disease. The current results provide the basis for further clinical investigation of MSDC-0160 in Alzheimer's patients."

"Evaluation of an mTOT Modulator Insulin Sensitizer as a Treatment for Alzheimer's Disease"

Dr. Colca will present the study findings at 4:45 p.m. EDT Monday, September 9, in a session covering "Mitochondrial Function and Neuroinflammation." The conference, which takes place in Jersey City, NJ, is presented by the Alzheimer's Drug Discovery Foundation (ADDF), which supported the Phase 2a research with grant funding. The study was conducted at Rush Alzheimer's Disease Center, Rush University Medical Center (Chicago). Image data analysis was performed by Abiant, Inc. (Grayslake, IL).

“This study suggests that we should press forward to continue to evaluate this novel class of mitochondrially-targeted insulin sensitizers in AD,” said Dr. Colca. “MSDC is most appreciative of the financial support provided by ADDF, without which completion of this clinical trial would not have been possible.”

Significant Unmet Medical Need

It is estimated that 5.2 million people in the United States have dementia due to AD.⁶ By 2050, the number of individuals worldwide living with dementia due to AD is anticipated to increase from 36 million to 115 million people—with two-thirds living in developing countries. Given the worldwide public health impact of AD, increased efforts are needed to develop new and effective AD interventions which have the potential to be used early in the course of the disease when intervention may have the most impact.

Insulin Sensitizers May Play a Role in Treating Alzheimer’s Disease

AD has been characterized as “[type 3 diabetes](#).”⁷ While the development of AD involves brain cell loss associated with the build-up of abnormal clusters of protein fragments (plaques), and dead and dying nerve cells that contain twisted strands of another protein (tau),⁸ other mechanisms also may play a role. Reduced glucose metabolism associated with AD has been tied with a progressive loss of mitochondrial function^{9,10} and altering mitochondrial dysfunction has been postulated as a target for the treatment of AD together with treatment of insulin resistance—a root cause of type 2 diabetes.^{11,12,13} MSDC has identified a new drug target of insulin sensitizers (mTOT).

MSDC-0160 is a novel mTOT Modulator™

MSDC-0160, a prototype [mTOT modulator](#) developed by MSDC, exerts its insulin-sensitizing effects through a recently identified new drug target located in the inner mitochondrial membrane (mTOT™).¹⁴ 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 islets¹⁵, 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 study¹⁶ 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.

Funding of both preclinical work and the current clinical study by the ADDF has allowed MSDC to test the potential of MSDC-0160 in AD.

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 of aging.

About the Alzheimer's Drug Discovery Foundation

The mission of the Alzheimer's Drug Discovery Foundation (ADDF) (www.AlzDiscovery.org) is to accelerate the discovery of drugs to prevent, treat and cure Alzheimer's disease, related dementias, and cognitive aging. The ADDF has granted more than \$60 million to fund almost 400 Alzheimer's drug discovery programs in academic centers and biotechnology companies in 18 countries.

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¹⁴ Colca JR, McDonald WG, Cavey GS, Cole SL, Holewa DD, et al. (2013) Identification of a Mitochondrial Target of Thiazolidinedione Insulin Sensitizers (mTOT)—Relationship to Newly Identified Mitochondrial Pyruvate Carrier Proteins. PLoS ONE 8(5): e61551. doi:10.1371/journal.pone.0061551.

¹⁵ Rohatgi N, Aly H, Marshall CA, McDonald WG, Kletzien RF, et al. (2013) Novel Insulin Sensitizer Modulates Nutrient Sensing Pathways and Maintains β -Cell Phenotype in Human Islets. PLoS ONE 8(5): e62012. doi:10.1371/journal.pone.0062012.

¹⁶ 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.