metabolic solutions development company

MEDIA ADVISORY

Metabolic Solutions Development Company Presents Update on Ongoing Clinical Evaluation of First in Class mTOT Modulator™ in Mild Alzheimer's Disease at 13th International Conference on Alzheimer's Drug Discovery

KALAMAZOO, MI September 7, 2012 – Metabolic Solutions Development Company, LLC (MSDC) will provide an update on the clinical evaluation of MSDC-0160, a first in class mTOT Modulator™ that is being investigated in an ongoing Phase 2a trial in subjects with mild to moderate dementia due to Alzheimer's disease. The update will be presented at the Alzheimer's Drug Discovery Foundation (ADDF) *13th International Conference on Alzheimer's Drug Discovery* in Jersey City, NJ September 10-11, 2012.

MSDC-0160 is a novel insulin sensitizer that modulates mitochondrial metabolism. Growing evidence suggests that loss of mitochondrial function, resulting in a corresponding decline in brain glucose metabolism, could be a contributing cause of Alzheimer's disease.

Presentation
Monday, September 10, 12:05 – 12:25 p.m.
"Clinical Evaluation of MSDC-0160 in Subjects with Mild Alzheimer's Disease"
Jerry Colca, PhD, MSDC founder, president and CSO
Hyatt Regency, Jersey City, NJ

Key Points

- MSDC-0160 is a first in class mTOT modulating insulin sensitizer with pharmacology potentially useful in Alzheimer's as well as diabetes.
- The mitochondrial target of this agent, mTOT, is a newly identified complex that regulates the metabolism of pyruvate.
- This places the site of action at the crossroads of metabolism.
- Data from a 90 day phase 2b trial of MSDC-0160 in diabetic patients supports efficacy separation from side effects.
- MSDC-0160 is being evaluated in an ongoing Phase 2a trial in subjects with mild Alzheimer's disease.
- New insights into the mTOT mechanism may have important implications for the development of future therapeutic treatments for Alzheimer's disease.

About the Clinical Study
In the clinical study ongoing at the Rush Memory Clinic at the Rush Alzheimer's Disease Center, Chicago, Dr. Raj C. Shah, Center director and the study's principal investigator, is looking to determine if MSDC-0160 improves the brain's use of glucose. A special brain imaging

technique called fluordeoxyglucose positron-emission tomography, or FDG-PET, is being used to measure brain cell glucose utilization.

Patients who are 55-85 years of age, who do not have diabetes, and who have been diagnosed with mild dementia due to Alzheimer's disease are being enrolled in the clinical trial. Patients in the study will be randomized to receive either MSDC-0160 or a placebo once daily for 90 days. Patients will also undergo two FDG-PET brain imaging scans.

An earlier preclinical study in a mouse model conducted by researchers at the University of Illinois at Chicago indicated that MSDC-0160 may reduce Alzheimer's-like pathology in mouse brains. As a result of this finding, investigators at Rush University Medical Center in Chicago are conducting a Phase IIa trial that will help determine if the drug therapy affects glucose utilization in specific regions of the brain.

This clinical study, as well as the preclinical study at the University of Illinois at Chicago, has been funded by a grant from the Alzheimer's Drug Discovery Foundation.

For more information about the clinical trial for Alzheimer's disease, contact Lindsay Franti at (312) 563-4111 or Lindsay_Franti@rush.edu.

About mTOT Modulators

MSDC researchers have identified a mitochondrial protein complex that connects mitochondrial metabolism to important cellular activities that are out of balance in patients with metabolic disorders. The newly identified mitochondrial target is being referred to as the mitochondrial Target of Thiazolidinediones, or mTOT™.

Key proteins in this complex include Mpc2 (BRP44) and Mpc1 (BRP44-Like), which have recently been shown to function as the mitochondrial pyruvate carrier[1,2].

The mTOT complex functions as a molecular "sensor switch" connecting mitochondrial metabolism to important cellular activities, such as carbohydrate and lipid metabolism, that are out of balance in patients with type 2 diabetes. Activation of mTOT increases cell differentiation and favors fat oxidation, resulting in increased insulin sensitivity, generation of brown fat and preservation of pancreatic β-cells.

mTOT Modulators represent a new way forward to treat age-related diseases associated with mitochondrial dysfunction, such as Alzheimer's disease and insulin resistance, the primary cause of type 2 diabetes.

mTOT Modulators appear to play a central role in the regulation of biochemical pathways essential to maintaining the appropriate level of blood sugar (glucose). These new drugs are intended to improve the body's sensitivity to insulin (which moves blood sugar (glucose) into cells, where it is stored and later used for energy), lower the percent of calorie-storing "white" fat, increase the production of calorie-burning "brown" fat, preserve the function of pancreatic beta cells (which produce insulin), and possibly protect neurons in the brain (which could be important in treating diseases such as Alzheimer's and Parkinson's disease).

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[1] Bricker *et al*. Science. 2012 Jul 6;337(6090):96-100. Epub 2012 May 24.

[2] Herzig *et al*. Science. 2012 Jul 6;337(6090):93-6. Epub 2012 May 24.

About the Conference
This annual Alzheimer's Drug Discovery Foundation (ADDF) conference brings together academic and industry scientists intent on accelerating the development of innovative treatments for Alzheimer's disease and related dementias.

For more information about the meeting, please visit the 13th International Conference on Alzheimer's Drug Discovery website at:
http://www.worldeventsforum.com/addf/addrugdiscovery/index.html.

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.

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