New Insights into Metabolic Diseases
Fueling Growth Aspirations in Kalamazoo

Over coffee in Irving’s Market in Kalamazoo, MI, in 2006, the vision for Metabolic Solutions Development Company (MSDC), was created.

During that meeting of the minds, founding scientists Jerry Colca, Ph.D., and Rolf Kletzien, Ph.D., concluded no one was going to figure out how a blockbuster insulin sensitizer used to treat diabetes worked — a drug they had identified and led the early development of while at The Upjohn Company in the late 1980s and early 1990s. Despite the uncertainty about the agent’s mechanism of action, the drug (Actos®) went on to help hundreds of thousands of patients and generate worldwide sales for Takeda Pharmaceutical Company of nearly $5 billion in 2011.

“We could see that there was something there that no one else could see. It’s a powerful motivator.”

OUT OF THAT DRIVING MOTIVATION, MSDC was born. The researchers pooled their resources, attracted funding from the state of Michigan and local investors such as SWMF Life Science Fund and Hopen Life Science Ventures, established laboratory space in the Southwest Michigan Innovation Center, and set out to build a new pharmaceutical company in Kalamazoo.

Over the past seven years, the company has built a team of 14 researchers and business professionals, and utilizes a network of contract research organizations and service providers in Michigan and across the country to conduct its drug discovery and development activities. To date, MSDC has raised nearly $65 million from Michigan investors, the National Institutes of Health (NIH) and patient advocacy foundations. Raised funds have been used to establish a robust pipeline of new drug candidates that are being investigated for the treatment of a number of metabolic diseases, including diabetes, polycystic kidney disease, and neurodegenerative diseases such as Alzheimer’s and Parkinson’s disease, myotrophic lateral sclerosis (ALS), adrenoleukodystrophy (ALD), and possibly epilepsy.

BREAKTHROUGH DISCOVERY
Having been among the original researchers in the field of insulin sensitizers, Drs. Colca and Kletzien had long questioned the prevailing hypothesis that insulin sensitizers initiate their effects through a receptor protein primarily responsible for stimulating lipid uptake and producing fat storage cells. This conventional wisdom has been largely responsible for preventing the development of new insulin sensitizing agents, as evidenced by the fact that no new insulin sensitizers have been approved for use in treating type 2 diabetes since 1999.

About three years ago, MSDC researchers made the breakthrough discovery of a target located in the inner mitochondrial membrane through which insulin sensitizers exert their anti-diabetic pharmacology. The new drug target, mTOT™, functions as a metabolic “sensor switch” through which carbohydrate, lipid, and amino acid metabolism are coordinated with cell function. This discovery upends the dogmatic paradigm that has existed for nearly two decades as to how insulin sensitizers exert their anti-diabetic pharmacology.
NEW CLASS OF INSULIN SENSITIZERS SHOW PROMISE IN CLINICAL TRIALS

Capitalizing on its discovery of the mTOT complex, MSDC has developed two novel insulin sensitizers, the prototype drug MSDC-0160 and a second-generation drug called MSDC-0602. Insulin sensitizers are the only drugs shown over the past 14 years of clinical use to treat the core physiological defects associated with type 2 diabetes: β-cell dysfunction and insulin resistance.

In phase 2 clinical trials, these first-in-class mTOT Modulators™ have been shown to effectively lower glucose in diabetic patients to the same extent as pioglitazone (Actos®), with an improved side effect profile. A six-month Phase 2b study of MSDC-0602, the company’s lead compound for the treatment of type 2 diabetes, is targeted to begin in 2014.

ALZHEIMER’S DISEASE: TYPE 3 DIABETES?

There is a known connection of metabolic disease with Alzheimer’s disease, which has fueled MSDC’s interest in whether drugs targeted for treating diabetes also could be useful in treating Alzheimer’s disease. In addition, there is known to be an apparent metabolic decline in specific regions of the brain in Alzheimer’s patients that correlate with cognitive decline. Thus, an insulin sensitizer able to treat metabolic dysfunction in the brain could be an effective means to modify and/or delay disease progression.

With grant funding from the Alzheimer’s Drug Discovery Foundation, MSDC recently completed a study of a prototype mTOT modulator, MSDC-0160, in patients with dementia due to Alzheimer’s disease. Results from this clinical trial are expected to be published later this year.

NEW HOPE FOR PARKINSON’S PATIENTS

MSDC-0160 also is being studied in animal models of dyskinesia induced by L-dopa treatment of Parkinson’s disease. This research is being conducted in collaboration with Patrik Brundin, Ph.D., of the Van Andel Institute (Grand Rapids) with funding provided by the Michael J. Fox Foundation. If successful, MSDC-0160 could soon move forward into human clinical trials in Parkinson’s patients with L-dopa-induced dyskinesia.

A POWERFUL MOTIVATOR FOR GROWTH

MSDC’s founders Drs. Colca and Kletzien saw something no one else could see. Their vision has driven this emerging Kalamazoo-based start-up to the forefront of discovery of novel insulin sensitizers, and today fuels the company’s mission to bring to patients the world over: “New Hope for the Treatment and Prevention of Metabolic Diseases.”

Metabolic Solutions Development Company (MSDC) is a drug discovery and development company investigating new molecular targets and developing novel therapeutics to treat metabolic diseases associated with age-related mitochondrial dysfunction, especially insulin resistance and type 2 diabetes.

For more about MSDC, visit www.msdrx.com.