

For NuSirt Biopharma, Less is More

Company Looks to Enhance Pharmaceutical Effectiveness While Lowering Dosages

By CINDY SANDERS

In the last few months, Nashville-based NuSirt Biopharma has initiated its first clinical trial in humans, completed one of the year's most successful capital campaigns, and presented two papers at the American Diabetes Association's 74th Scientific Sessions. NuSirt also holds two patents and has 13 active patent applications under review for its proprietary technology platform ... not bad for a company that hasn't even celebrated its first decade in business, yet.

Incorporated in 2010 by Michael Zemel, PhD, who has authored more than 200 peer-reviewed articles primarily focused on metabolic regulation, NuSirt's technology combines the essential amino acid leucine with existing human medications that target diabetes, obesity and other metabolic diseases. Zemel served as a professor of Nutrition and Medicine and director of the Nutrition Institute at the University of Ten-



Dr. Michael Zemel, Founder

nessee for more than two decades. The company's chief scientific officer left his academic post in 2012 to focus his full efforts on growing NuSirt's technology and applications.

On the business side, Joe C. Cook, Jr., a veteran pharmaceutical industry executive, leads NuSirt in his role as president and executive chairman of the board. After retiring from Eli Lilly in 1993, Cook led a small biotech company for the next 10 years. Upon 'retiring' again, he returned to his native Tennessee where he was introduced to Zemel's research.

"All of his work was focused on the components of nutrition that affected energy and metabolism," Cook explained, adding the science was similar to other research he had seen throughout his pharma career. However, Zemel's work focused on leucine and took a different approach by honing in on fat cells.

"Of all the amino acids he had stud-

ied, leucine was the only one that really promoted efficiency in animals and humans handling energy,"

Cook said. "A gram of protein has four calories; a gram of carbohydrate has four calories; but a gram of fat has nine calories," he continued. "On a mass-to-mass basis, the body's most efficient storage mechanism is a fat cell."

Cook said the data was convincing that Zemel's methodology could positively impact cellular activity by adding a specific amount of the branched chain amino acid leucine to amplify metabolism. A principal and co-founder of Nashville-based Mountain Group Capital, Cook decided to invest in the fledgling company that had the potential to improve the treatment of obesity and type 2 diabetes.

"Diabetes is growing in the United States at a rate greater than our population," Cook said. "That kind of epidemiology clearly illustrates that we haven't solved the problem."

He added the multifactorial nature of most metabolic conditions and resulting impact on body systems has made it difficult to create a cure. However, he believed Zemel's approach offered a way to achieve much better glucose control by enhancing the effectiveness of the existing pharmaceutical metformin.

Less is More

Metformin is used by millions of Americans as the recommended first-line oral treatment for type 2 diabetes if control cannot be achieved through diet and exercise alone. "Metformin is the most widely prescribed medicine for diabetes in the world," Cook stated.

Although quite effective and with fewer issues than other glucose control medications, the popular drug still comes with a significant profile of side effects, typically manifesting as gastrointestinal distress. "It's always been my experience that almost every drug has side effects and almost always it's associated with the quantity of drug needed," Cook noted.

He continued, "The literature has shown between 30-50 percent of people who take metformin experience some GI distress from mild to major. A much smaller percentage ... estimated between 6-10 percent ... suffer more serious adverse events with metformin to the point where they take it less frequently, lower the dose, or stop taking it altogether."

NuSirt's working theory was to utilize leucine to amplify the effect of metformin thereby allowing for lower, more tolerable dosing levels. The theory was

borne out in animal models resulting in glucose control with a reduction in fatty deposits with a significantly lower dosage of metformin.

"Most drugs activate a signal in the body. They either bind to or block a receptor ... you either stimulate a cell or suppress it," Cook explained. "Leucine works on the sirtuin pathway," he continued. "It makes that receptor system more sensitive to metformin, and that gives rise to a potentially lower dose. That's the really novel observation."



Joe C. Cook, Jr., President

Human Trials Launched

Cook said the success demonstrated in animal models in 2013 led the company to file an investigational new drug (IND) application with the U.S. Food & Drug Administration earlier this year. "In July, the FDA gave us the green light to proceed with our human studies," he added.

The first randomized, double blinded study is currently active at eight sites, including Vanderbilt and Meharry in Nashville. To reduce any latent effects of the drug, Cook said all participants in the study must come off of their oral diabetes

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November is American Diabetes Month

Diabetes is a chronic condition at epidemic proportions in the United States. According to the American Diabetes Association nearly 30 million children and adults in the U.S. have diabetes and another 86 million Americans have pre-diabetes.

Whether or not medication management is required, the ADA stresses everyone with diabetes benefits from healthy lifestyle choices. For 2014, the national organization has adopted the theme, "America Gets CookingSM to Stop Diabetes." The message this year centers on engaging in improved nutrition and moderate physical activity in a social manner to make it fun to opt for the healthy choice.

For promotional materials and more ideas to share with your patients, go online to diabetes.org and click on "In My Community."

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medication for a month prior to beginning the active phase of the trial.

Inclusion criteria include being on only one oral medication for glucose control and having an A1C between 7 and 8.5. "If during the four-week washout period their glucose goes up too much, there is an escape route to get them out of the study and back onto medication," Cook said of the careful monitoring.

During the 28-day trial, the 100 participants wear a blood sugar monitoring device and measure their blood glucose levels frequently. The control arm of the trial is receiving standard doses of metformin as clinically prescribed compared to the other three arms receiving one of three lower doses of the metformin combined with the NuSirt technology. The goal is to assess the general effectiveness of the combination therapy and find the lowest dose possible to achieve glucose control. Initial results are expected by first quarter 2015. NuSirt plans to substantially increase its clinical trial program leading to the filing of a New Drug Application with the FDA pending positive results from this first clinical trial.

If the success seen in animal models is replicated in humans, it could signal transformational change in how healthcare providers approach and manage glucose control and pave the way for new treatment options for other metabolic conditions.

Medical Groups, Area YMCA Collaborate to Prevent Type 2 Diabetes

This fall, the American Medical Association, along with the YMCA of Middle Tennessee, the Tennessee Medical Association and the Tennessee Nurses Association, held a summit for area physicians, nurses and other medical professionals to learn about new resources for preventing type 2 diabetes and introduce a new diabetes prevention program.

"More than one out of every three American adults has pre-diabetes and only about 11 percent are even aware that they are at risk of developing type 2 diabetes," AMA President Robert M. Wah, MD, said of his organization's push to raise awareness. "In addition to crippling the health and well-being of our patients and citizens, type 2 diabetes is also one of the key drivers of healthcare costs. The AMA is working with the YMCA, Tennessee Medical Association and Tennessee Nurses Association to improve health outcomes of individuals in Nashville through better prevention, thereby contributing to reduced healthcare costs for this disease."

The September summit focused on specific goals of diabetes prevention programs, including:

Increasing education and awareness

of pre-diabetes by promoting physician practice screening of those at risk; and

Increasing physician and other healthcare provider referrals of people with pre-diabetes to the evidence-based YMCA's Diabetes Prevention Program.

Recent reports rank Tennessee as having the sixth highest incidence of diabetes by population in the United States with more than one in 10 adult Tennesseans with diabetes and an estimated 50,000 more struggling with pre-diabetes.

"Changing outcomes often means changing behaviors that have led to Tennessee's high rates of diabetes, such as obesity, poor diet and lack of regular physical activity. We want to give patients, through their healthcare providers, resources to help address these lifestyle issues and avoid unnecessary medical complications," said Ted Cornelius, vice president of Health Innovation for the Middle Tennessee Y.

The YMCA initiative is part of the CDC's National Diabetes Prevention Program, which includes 16 weeks of core education on healthy eating and physical activity from a trained lifestyle coach, as well as peer and goal-setting support. Following the initial sessions, participants

meet monthly for up to a year to monitor their progress. The program is based on research funded by the National Institutes of Health, which has shown, among adults with pre-diabetes, a 58 percent reduction in the number of new cases of type 2 diabetes and a 71 percent reduction in new cases among those over age 60.

In his opening remarks, Nashville Mayor Karl Dean thanked the participating organizations and acknowledged the increasing number of Middle Tennesseans affected by diabetes and pre-diabetes. He added physical activity plays a major role in prevention.

"By investing in greenways, bike-ways and parks that encourage physical activity, Nashville has made a strong statement that we are committed to being a healthy city," Dean pointed out. The mayor, who has spearheaded more than \$130 million in public infrastructure to support active lifestyles, is hosting his next community-wide healthy living event on Sunday, Nov. 9 with the annual Mayor's Challenge 5K.

For more information about the YMCA Diabetes Prevention Program, visit ymcamidtn.org/diabetes-prevention.

Meet Some of the Faces Behind Our Healthcare Experience.



Andrew Bissonnette

Jeff McCorpin

Andrew McDonald

Lisa Nix

Sharon Powlus

Brian Tate

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Meet Greg Eli, CPA

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Healthcare Practice Leader

Greg brings over 25 years of experience in public accounting and healthcare to his role as leader of LBMC's healthcare practice. He initiated the development of the firm's healthcare practice several years ago and is responsible for the firm's strategic direction, development of solutions and service delivery to address the ever changing needs of the healthcare industry. Greg is a partner in the firm's accounting and assurance practice, serving on a number of healthcare engagements, which include for-profit and not-for-profit healthcare organizations, of all types of specialty.

Greg was recently recognized by the Nashville Post as one of Middle Tennessee's "Accounting's Finest", by the Nashville Business Journal as one of Nashville's "Power Leaders in Accounting" and by the Nashville Medical News "InCharge Healthcare" as one of the key decision-makers in the healthcare industry.



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