AVI BioPharma Presents Preclinical Results Preventing and Treating Diabetes Using Its ESPRIT Exon Skipping Technology

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Positive Data Presented at the Prestigious Federation of Clinical Immunology Societies (FOCIS 2006) Annual Meeting

AVI BioPharma, Inc. (Nasdaq:AVII), has announced preclinical data evaluating the use of antisense-based exon skipping pre-RNA interference technology (ESPRIT) on the development of diabetes in a mouse model. Results were presented at the Federation of Clinical Immunology Societies (FOCIS) annual meeting yesterday in San Francisco. The study demonstrated the effectiveness of AVI's exon skipping technology in significantly delaying the onset of diabetes and in reversing the disease after onset. This work validates the application of ESPRIT technology in regulating the immune response in autoimmune diseases.

AVI's presentation, titled "Ligand independent form of CTLA-4 induced by antisense exon skipping in NOD mouse inhibits autoimmune diabetes," was presented by Dan Mourich, Ph.D., AVI senior scientist. In the study, scientists modulated cytotoxic lymphocyte-associated antigen-4 (CTLA-4), a mediator in the development of diabetes, using ESPRIT compounds. The expected result was the prevention or alteration of the onset of diabetes in mice that are predisposed to developing diabetes (NOD mice).

Diabetes and other autoimmune diseases are modulated in part by CTLA-4, which is found primarily on the surface of white bloods cells called T lymphocytes (T cells). CTLA-4 is a down-regulating signal that turns T cells off or prevents them from causing autoimmunity. The ESPRIT compounds produced a form of CTLA-4 that would not frequently occur in the diabetic mice, which transmitted a continual "off" signal to the T cells producing diabetes.

In the first studies, mice were treated shortly after birth for 10 days with antisense to induce exon skipping. This short treatment delayed onset of diabetes by approximately 28 days compared to controls. In a second set of therapeutic experiments, adult mice with early signs of diabetes exhibiting elevated blood glucose levels were treated for 10 days with antisense exon skipping therapy. Over 50% of these animals were protected from full diabetes onset for the duration of the experiment (over 200 days). Both of these observations were statistically significant.

AVI scientists documented that a down-regulating form of CTLA-4 was readily induced and confirmed by the most sensitive techniques including DNA sequencing. To determine the relevance of this approach to delay or eliminate diabetes, mice were treated prophylactically or therapeutically with antisense targeted to induce the down-regulating form of exon skipping in CTLA-4.

"These preclinical results in this commonly used animal model demonstrate the feasibility of our exon skipping technology," said Patrick Iversen, Ph.D., senior vice president of research and development. "By altering the form of a down-regulator that is central to the immune mechanism, we have been able to delay or stop the disease process. We believe these preclinical studies may be relevant to insulin-dependent, Type 1 diabetes in man."

In addition to the primary data in these studies, AVI scientists intentionally triggered the opposite effect by inducing another altered splice form of CTLA-4 by employing a different antisense sequence. An enhanced immune activity was observed, leading to enhanced diabetic onset and severity. This may be relevant to medical situations where enhanced immune activity is desirable, such as in cancer or certain infections.

"ESPRIT technology can be used in two different disease settings," said Denis Burger, Ph.D., chief executive officer of AVI. "This study demonstrated the impact of ESPRIT in interrupting an autoimmunity cascade, and we have previously shown that exon skipping can correct a genetic mutation in a muscular dystrophy model. We believe this study identifies a credible way to regulate the immune response in settings where T cells play a central role, as is the case in most autoimmune diseases."

About ESPRIT Technology

In normal genetic function, gene transcription produces a full-length pre-RNA that is then processed to a much shorter and functional messenger RNA. The mRNA is the template for creating a protein. During pre-RNA processing, packets of useful genetic information, called exons, are snipped out of the full-length RNA and spliced together to make the functional mRNA template. AVI's proprietary third-generation NEUGENE(R) chemistry can be used to target splice-joining sites in the pre-RNA, thus forcing the cell machinery to skip over targeted exons, providing altered mRNA, which in turn produces altered proteins.

The first use of AVI's ESPRIT therapeutics was conducted in collaboration with Dr. Steve Wilton, associate professor and head of the Experimental Molecular Medicine Group at the Australian Neuromuscular Research Institute in Western Australia. Targeting the defective Duchenne muscular dystrophy (DMD) dystrophin gene with an ESPRIT compound, Dr. Wilton was able to force the cell to snip out the disease-causing mutation in that region. Using this approach, a functional dystrophin protein can be made from a DMD gene that would previously have only made a nonfunctional protein.

About Diabetes

Type 1 diabetes is an autoimmune disease that occurs when the insulin-producing beta cells within the pancreas are gradually destroyed and eventually fail to produce insulin. Insulin is a hormone that helps the body's cells use glucose for energy. Blood glucose (or blood sugar) is manufactured from the food we eat (primarily carbohydrates) and by the liver. If glucose can't be absorbed by the cells, it builds up in the bloodstream

instead, and high blood sugar is the result. Over time, the high blood glucose levels of uncontrolled diabetes can be toxic to virtually every system of the body.

Type 1 diabetes accounts for between 5% and 10% of all diagnosed diabetes in the United States. Although type 1 diabetes develops most often in children and young adults (one in every 400-500 children has type 1 diabetes), the disease can be diagnosed at any age throughout the lifespan, and is equally distributed among males and females. Unlike type 2 diabetes, type 1 diabetes is more common in Caucasians than in those of Hispanic, African-American, or other non-Caucasian backgrounds.

About AVI BioPharma

AVI BioPharma develops therapeutic products for the treatment of life-threatening diseases using third-generation NEUGENE antisense drugs. AVI's lead NEUGENE antisense compound is designed to target cell proliferation disorders, including cardiovascular restenosis, cancer and polycystic kidney disease. In addition to targeting specific genes in the body, AVI's antiviral program uses NEUGENE antisense compounds to combat disease by targeting single-stranded RNA viruses, including hepatitis C virus, influenza A virus, West Nile virus, dengue virus and Ebola virus. AVI has introduced a NEUGENE-based exon-skipping technology called ESPRIT therapy. More information about AVI is available on the company's Web site at http://www.avibio.com.

"Safe Harbor" Statement under the Private Securities Litigation Reform Act of 1995: The statements that are not historical facts contained in this release are forward-looking statements that involve risks and uncertainties, including, but not limited to, the results of research and development efforts, the results of preclinical and clinical testing, the effect of regulation by the FDA and other agencies, the impact of competitive products, product development, commercialization and technological difficulties, and other risks detailed in the company's Securities and Exchange Commission filings.

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